

TESC questions 2002/3 Authors' comments and "best answer" selection.

Here are the TESC questions for 2002/3 with the authors' comments and suggested "best answers". A contact email is provided for each author. The format of some of the questions differs from that on the website as some questions had to be adapted to fit the online format. It should not be too difficult to match your answer to each scenario and question despite this.

1. Withdrawal of antiepileptic medication	Margaret Jackson, Newcastle upon Tyne Email: margaret.jackson@ncl.ac.uk
Scenario	
<p>A 22 year old female sales representative is referred for review. At the age of 14 she had been referred to you with her first tonic clonic seizure; you had taken a careful history which revealed she had experienced myoclonic seizures shortly after waking for the previous 2 years. An EEG showed spontaneous bursts of generalised polyspike and slow wave activity and a photoparoxysmal response accompanied by a myoclonic jerk. You prescribed lamotrigine but she continued to have generalised tonic clonic seizures and myoclonus. The dose of lamotrigine was increased to 500mg daily, her seizures continued and valproate was added. She did not become seizure free until she was prescribed lamotrigine 200mg daily and valproate 2000mg daily.</p>	
<p>She has been stable on this combination for 2 years and has a driving licence. She has read about the potential risks of antiepileptic drugs in pregnancy and wishes to stop taking them before she becomes pregnant, but she is concerned that if she does she will have a further seizure, lose her driving licence and job.</p>	
For each question part you should offer only a single best answer.	
Question 1	
In advising her about antiepileptic drug withdrawal, what approximate risk of seizure recurrence will you give her?	
Less than 5%	
5-10%	
10-15%	
20-30%	
50-60%	
More than 75%	Best answer 6
Question 2	
If she remains on her current antiepileptic drugs, what is the best estimate of risk you can give her of her child having major malformation?	
Less than 5%	
5-10%	
10-15%	Best answer 3
20-30%	
50-60%	
More than 75%	
Question 3	
Which of the following factors is most likely to be the most help in predicting the risk of recurrence?	
An up to date EEG with photic stimulation.	
The number of seizures prior to starting antiepileptic drugs.	
A family history of epilepsy in a first degree relative.	
Taking more than one antiepileptic drug at the time of withdrawal	Best answer 4

A history of status epilepticus.	
Question 4	
If she chooses to withdraw her antiepileptic drugs, what advice do you give about driving?	
To inform the DVLA and stop driving until further advice from DVLA.	
To continue driving.	
To stop driving during AED withdrawal.	
To stop driving during AED withdrawal and 6 months thereafter.	Best answer 4
Question 5	
If she has a myoclonic jerk as she withdraws from the valproate, what do you advise her to do with regard to her driving licence?	
To inform the DVLA and stop driving until further advice from DVLA.	Best answer 1
To continue driving	
To stop driving during AED withdrawal.	
To stop driving during AED withdrawal and 6 months thereafter.	

Answers and comments

Q1

Answer 6: 75%+.

This woman has juvenile myoclonic epilepsy, a syndrome with a very high risk of relapse on cessation of AEDs. She had multiple seizures after starting AEDs which increases the probability of relapse after AED withdrawal.

Reference

MRC antiepileptic drug withdrawal study group, Randomised study of antiepileptic drug withdrawal in patients in remission. *Lancet* 1991;**337**:1175-80.

Q2

Answer 3: 10-15%.

Valproate monotherapy is associated with a risk of major malformation of 6-8%, polytherapy increases that risk.

References

1. Samren EB, van Duijn CM, Koch S, *et al.* Maternal use of antiepileptic drugs and the risk of major congenital malformations: a joint European prospective study of human teratogenesis associated with maternal epilepsy. *Epilepsia* 1997;**38**:981-90.
2. Craig JJ, Russell AJC, Morrison P, *et al.* Antiepileptic drugs in pregnancy: Update of the UK Epilepsy and Pregnancy Register. *J Neurol Neurosurg Psychiatr* 2002;**73**:215-6. (Abstract.)

Q3

Answer 4.

Patients taking more than one AED have a significantly higher risk of seizure recurrence on AED withdrawal. The number of seizures prior to starting an AED, family history and history of status epilepticus do not affect risk of recurrence significantly (MRC antiepileptic drug withdrawal study group *Lancet* 1991;**337**:1175-80, as above). An EEG with photic stimulation will not alter the advice you give her significantly and may provoke a seizure resulting in withdrawal of her licence.

Q4

Answer 4.

This is current DVLA advice (though it is advice rather than regulation).

Q5

Answer 1.

A myoclonic “jerk” is a seizure and the DVLA regulations for epilepsy should apply.

2. Familial risk of multiple sclerosis	Neil Robertson, Cardiff Email: RobertsonNP@cf.ac.uk
Scenario	
<p>A 35 year old woman returns to a follow-up appointment in a general neurology clinic shortly after a diagnosis of multiple sclerosis had been made on the basis of the clinical history and supportive paraclinical tests.</p> <p>During the consultation she mentions that a maternal first cousin also had had multiple sclerosis and died as a result, having developed severe irreversible disability within five years of onset. She is aware that there are genetic factors involved in multiple sclerosis and has become concerned about the implications for the rest of her family. This includes two female siblings (an identical twin and a sister aged fifty), and two children aged five and seven, all of whom are currently well.</p>	
For each question part you should offer only a single best answer.	
Question 1	
<i>She would like to know how commonly another family member is affected in this disease: what do you tell her?</i>	
1 in 24	
1 in 12	
1 in 9	
1 in 6	Best answer 4
1 in 3	
Question 2	
<i>She would like to know the risk of her twin sister developing the disease: what do you tell her?</i>	
1 in 50	
1 in 25	
1 in 10	Best answer 3
1 in 5	
1 in 2	
Question 3	
<i>She would like to know the risk of her non-twin sister developing the disease: what do you tell her?</i>	
Less than 1 in a 100	Best answer 1
1 in 75	
1 in 50	
1 in 25	
1 in 10	
Question 4	
<i>She would like to know what is the risk to her children of developing the disease: what do you tell her?</i>	
Less than 1 in a 100	
1 in 75	
1 in 50	Best answer 3
1 in 25	
1 in 10	
Question 5	
<i>She would like to know what is the likelihood of her developing a similar disease course to her severely affected maternal cousin.</i>	
Less than 1 in a 100	
1 in 75	
1 in 50	Best answer 3
1 in 25	
1 in 10	

Answers and comments

Q1

Answer 4.

Most contemporary studies suggest familial recurrence of MS in northern European families of around 1 in 5 to 1 in 7.

Q2

Answer 3.

Although the overall lifetime risk is around one in three for monozygotic twins, she has already lived through more than 50% of her time at risk.

Q3

Answer 1.

Since her sister is aged fifty she has largely lived past the at risk age of developing disease.

Q4

Answer 3.

The life time risk of developing disease in the offspring of a single affected parent is approximately 1 in 50.

Q5

Answer 3.

The family history does not have a major influence on disease course so her risks are unchanged to that of the general population with MS. However, rates for this do vary across studies between 1 in 10 and 1 in 50 who have a hyper acute form of the disease.

References

Sadovnick, AD, Baird PA, and Ward RH. Multiple sclerosis: Updated Risks for Relatives. *Am J Med Genet* 1988. **29**: 533-541.

Robertson, N, Deans J, Fraser M, Walker N, Clayton D, and Compston DAS. Recurrence risks for relatives of patients with multiple sclerosis. *Brain* 1996. **119**: 449-455.

Carton, H, Vlietinck R, Debruyne J, *et al.* Risks of multiple sclerosis in relatives of patients in Flanders, Belgium. *J Neurol Neurosurg Psychiatry* 1997. **62**: 329-333.

Age specific age adjusted recurrence risks for relatives of patients with multiple sclerosis

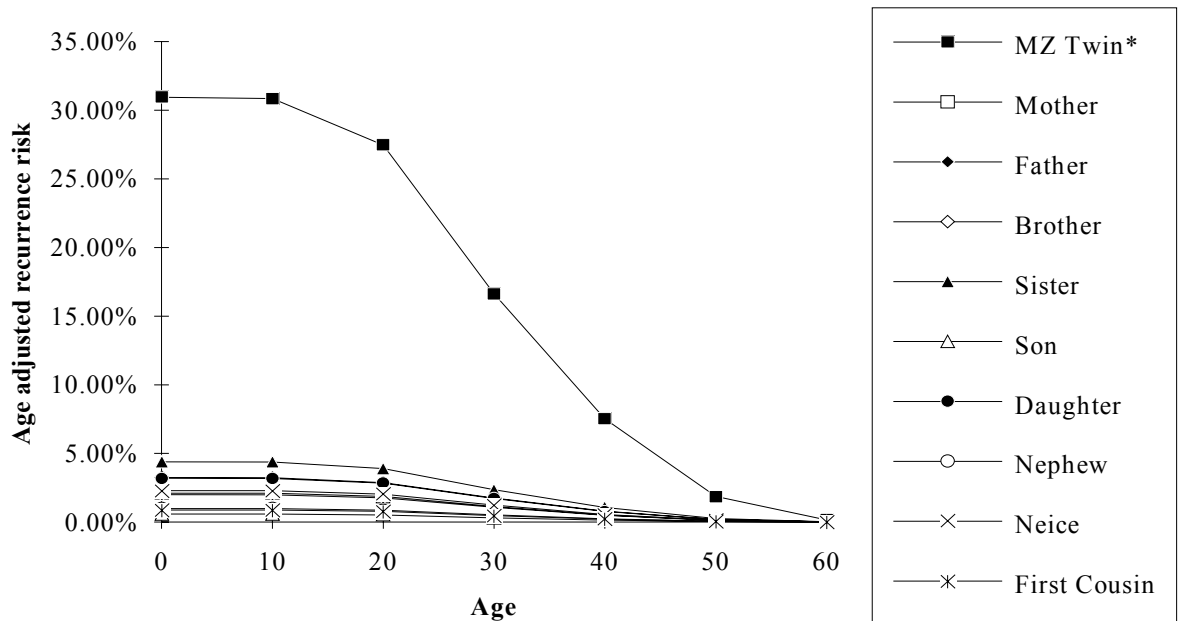


Table 4.

Age specific recurrence risks for relatives of patients with multiple sclerosis

Age(yrs)	0	10	20	30	40	50	60
MZ Twin*	30.95%	30.85%	27.47%	16.64%	7.52%	1.87%	0.15%
Mother	2.11%	2.10%	1.87%	1.13%	0.51%	0.13%	0.01%
Father	1.99%	1.98%	1.77%	1.07%	0.48%	0.12%	0.01%
Brother	3.24%	3.23%	2.88%	1.74%	0.79%	0.20%	0.02%
Sister	4.39%	4.38%	3.90%	2.36%	1.07%	0.26%	0.02%
Son	0.58%	0.58%	0.51%	0.31%	0.14%	0.04%	0.00%
Daughter	3.19%	3.18%	2.83%	1.71%	0.78%	0.19%	0.02%
Nephew	0.98%	0.98%	0.87%	0.53%	0.24%	0.06%	0.00%
Neice	2.29%	2.28%	2.03%	1.23%	0.56%	0.14%	0.01%
First Cousin	0.88%	0.88%	0.78%	0.47%	0.21%	0.05%	0.00%

*Derived from Mumford et al Neurology 1994; 44: 11-15. Not based on the Cambridgeshire population.

3. Screening for familial subarachnoid haemorrhage		Jackie Palace, Oxford Email: jacqueline.palace@clinical-neurology.oxford.ac.uk
Scenario		
A 32 year old girl attends your outpatient clinic. She explains that her brother died recently of a subarachnoid haemorrhage (SAH) aged 42 years, and her mother died of a brain haemorrhage. She has heard that there can be a familial predisposition to this and asks to be screened. Which of the following would you advise?		
<i>For each question part you should offer only a single best answer.</i>		
Question 1		
No investigations are indicated.		
Arrange an MR brain scan with MR angiography or CT angiogram in the first instance.		
Go straight to the 'gold standard' cerebral angiogram.		
Obtain the brother's and grandmother's details before deciding what to do.		Best answer 4 (or 2)
Question 2		
She is screened and is found to have an aneurysm. You need to counsel her about the risks of rupture and its consequences, versus the risks of treatment.		
<i>Which one of the following statements is incorrect?</i>		
Incidental aneurysms of less than 10mm diameter rarely rupture.		
An aneurysm's growth predicts an increased rupture risk.		
The shape of an aneurysm influences its risk of rupture.		
Peripherally sited aneurysms are more likely to rupture than midline aneurysms.		Best answer 4
Question 3		
<i>Which one of the following statements is incorrect?</i>		
Young age is associated with a reduced overall risk of rupture.		Best answer 1
Stopping smoking reduces the rupture risk.		
Hypertension increases the risk of rupture.		
The risk of aneurysm surgery in the anterior cerebral circulation approximately equals that of endovascular embolisation.		

Answers and comments

Q1

Answer 4 or answer 2

This is clearly a controversial area. Although it is clearly essential to obtain further details of the family history if possible, this often is unrewarding and ends without a definite conclusion. I end up arranging an MRA (or more recently a CT angiogram) in the majority of patients. Clearly patients are concerned enough to get referred for screening or reassurance, and I do not think there is enough evidence to do the latter. The incidence of aneurysms in those with a family history is about 10%.

What to do about an asymptomatic aneurysm when identified is not clear, and the patient needs counselling about the uncertainty at the outset. The uncertainty lies mainly in the risk of rupture; most studies quote 1-2% per year, giving a young person a greater cumulative risk. The low risk previously quoted by the International Study of Unruptured Intracranial Aneurysms (ISUIA) was way below rates quoted from other studies, and is probably an underestimate. It was a large retrospective study and the recruitment methods would have biased towards preferentially including patients not having a subsequent event. Supporting the suggestion that the low rates are an underestimate is that the prevalence in the general population would have to be much higher than ever reported in order to give the known prevalence of SAH.

There are many other factors (see below) that influence the risk of rupture and the use of these can help to refine the risks and make a decision about management. MRA is without risk and will identify aneurysms large enough to be at risk of rupture. CT angiogram is a low risk procedure and is probably as good as conventional angiogram. Angiogram need only be performed in those with an identified aneurysm (the minority) who wish to take things forward. The risk of an ischaemic event during angiography in an otherwise healthy person is said to be 0.07%, although it is more than 10 times this if the person has cerebrovascular disease.

Although the risks of surgery for aneurysms are higher than previously thought, endovascular embolisation by an experienced neuroradiologist carries a lower risk. So the risk benefit ratio can be improved by using data to intervene in those with high risks of rupture using a lower risk procedure. Because endovascular embolisation is the treatment of choice now, the conventional angiogram is performed within the same procedure.

Q2

Answer 4.

Size is correlated with increasing risk of rupture overall but there are many other factors that influence the risk also. In this case where there has been no past history of SAH in the patient, size is likely to be important. The size of aneurysms found in 'ruptured cohorts' is much smaller than in those which rupture in 'prospectively followed cohorts with unruptured aneurysms'. This may reflect an early predisposition to rupture when the aneurysm is developing (over a short period of time) and a later tendency in longer-standing aneurysms which have escaped the early bleed and have 'reinforced collagen walls' being stretched to their limit. It is this latter group that are likely to be preferentially picked up in screening for asymptomatic aneurysms. Most studies support the suggestion that aneurysms <3-5mm are safe and it is these that MRA will tend to miss.

Growth. Most aneurysms that rupture increase in size beforehand.

Shape. Aneurysms with larger depth to neck width ratio (aspect ratio), with loculation or lobulation are associated with increased rupture risks and their absence are good predictors. Midline sites. The risk of rupture increases for aneurysms in proximal sites, and particularly in the anterior communicating artery.

Q3

Answer 1.

Age. Life expectancy influences the cumulative risk i.e. younger age greater overall risk.

Smoking strongly predicts rupture, and patients are presently advised to stop. However no study has examined the effects of giving up smoking so the answer here is probably.

Hypertension is associated with an increase risk in the majority of studies, but the influence is weaker than smoking.

Surgical risk. Recent ISAT data in patients with anterior sited aneurysms showed about 7% better outcome with embolisation than surgery. Embolisation is starting to replace surgery as the standard treatment for aneurysms, except where the aneurysm is not amenable to endovascular management.

References

1. Ronkainen A, et al. Risk of harboring an unruptured intracranial aneurysm. Stroke 1998;29:359-62.
2. Juvela S. Recommendations for the management of patients with unruptured intracranial aneurysms. Stroke 2001;32:815-6.

The Journal of Neurosurgery 2002,96(1) is devoted to this subject. A good overview can be obtained in the articles/reviews by:

1. Weir B, et al. Sizes of ruptured and unruptured aneurysms in relation to their sites and the ages of patients. J Neurosurg 2002;96:64-70.
2. Winn HR, et al. Prevalence of asymptomatic incidental aneurysms: review of 4568 arteriograms. J Neurosurg 2002;96:43-9.
3. Dumont AS, et al. Unruptured aneurysms. J Neurosurg 2002;96:52-6.

4. Difficulty standing still	Paul Morrish, Brighton Email: Paul.Morrish@bsuh.nhs.uk
Scenario	
History: A 64 year old man presents with difficulty standing still. He can walk without difficulty. Past medical history includes diabetes mellitus for four years. His medication is Gliclazide, atenolol, aspirin, simvastatin. Examination: The tone, power, and coordination are normal. The knee and ankle reflexes are absent and plantars are flexor. He has normal sensation in the arms and legs. There is a postural tremor in his right arm. Investigations: MRI of lumbo-sacral spine (requested by orthopaedic surgeons) suggests spinal stenosis at L4/5.	
<i>For each question part you should offer only a single best answer.</i>	
Question 1	
What is the likely diagnosis of his difficulty standing still?	
Diabetic neuropathy.	
Spinal stenosis.	
Primary orthostatic tremor.	Best answer 3
Restless legs.	
Painful legs and moving toe syndrome.	
Question 2	
Assuming a diagnosis of primary orthostatic tremor, what physical sign might confirm diagnosis?	
"Helicopter hum" (audible over the legs)	Best answer 1
Striatal toe sign.	
Sciatic stretch test.	
Return of reflexes after walking.	
Moving toes.	
Question 3	
What investigation would be the most helpful in confirming orthostatic tremor?	
Nerve conduction studies.	
Electromyography.	Best answer 2
Myelography.	
Thyroid function tests.	
Syphilis serology.	
Dopamine Transporter (DAT) scan.	
HbA1c	
Question 4	
Which one of the following medications would be unlikely to help orthostatic tremor?	
levodopa	
clonazepam	
gabapentin	
phenobarbitone / primidone	
pramipexole	
propranolol	Best answer 6
Question 5	
Should he undergo spinal decompressive surgery?	
Probably yes	
Probably no	Best answer 2

Answers and comments

Q1

Answer 3.
The most likely diagnosis is primary orthostatic tremor.

Although relatively recently recognised and generally considered rare, orthostatic tremor may be an under-recognised cause of disability in the elderly. (see review: Britton TC, Thompson PD. Primary orthostatic tremor. BMJ 1995;310:143-4.)

Q2

Answer 1.

A "helicopter hum" is heard with stethoscope (diaphragm) over the legs. It was described by Brown P, Lancet 1995;346:306-7.

Q3

Answer 2

EMG of quadriceps shows rhythmic grouped discharge at about 15Hz.

Nerve conduction studies may confirm/refute presence of diabetic neuropathy but would not give direct evidence of orthostatic tremor.

It might also be interesting to time his upper limb tremor since this might also be orthostatic.

Orthostatic tremor has been reported in syphilis (Brotman DJ, Fotuhi M. Syphilis and orthostatic shaking limbs. Lancet 2000;356:1734) and so syphilis serology should be checked.

Q4

Answer 6.

All of these medications have been shown to be effective for orthostatic tremor with the exception of propranolol.

Q5

Answer 2.

Surgery would probably not be helpful for his tremor. The mechanism of orthostatic tremor is thought to be due to central tremor generation. The importance of afferent pathways not known. A peripheral contribution can not completely be eliminated, though if there is a 15Hz tremor in arms it would seem unlikely that surgery to the back will help.

5. The confused immunosuppressed patient	Ian Bone, Glasgow email: i.bone@clinmed.gla.ac.uk
Scenario	
<p>You are asked by the haematologists to review a patient at the weekend on their ward. The patient is a 36 yr. old male with a history of Chronic Myeloid Leukaemia (CML). This underwent blast transformation into Acute Myeloid Leukaemia. He was given chemotherapy with some response but in view of the overall poor prognosis allogeneic bone marrow transplantation was carried out. Prior to this he underwent standard "conditioning" with total body irradiation, cyclophosphamide and Alemtuzumab (Campath-1H) anti-lymphocytic globulin. On reading his notes you see that he was pyrexial and confused immediately after the transplant and was treated with antibiotics, antiviral and antifungals. He recovered well and was discharged, continuing on treatment with cyclosporin, steroids and antihypertensives.</p> <p>It is two months since his marrow transplant and he now presents with a short history of agitation, confusion, pyrexia and a single tonic clonic seizure.</p> <p>His CT scan (fig 1 a & b) was carried out on admission and is as yet unreported. On examination (two hrs-post ictal) he is pyrexial and in an agitated, confused state. He has mild meningism but no focal signs.</p> <p>You have been asked to advise on differential diagnosis, further investigations and immediate management</p> <p><i>For each question part you should offer only a single best answer.</i></p>	

Question 1	
What is the most likely nature of this patient's immunosuppression?	
Impaired granulocyte function	
Impaired B-lymphocyte function (humoral immunity)	
Impaired T-lymphocyte function (cellular immunity)	
A mixture of all	Best answer 4
The patient will not be immunosuppressed	
Question 2	
Which statement regarding the side effects of cyclosporin is not correct?	
Cyclosporin may cause tremor	
Cyclosporin may cause convulsions	
Cyclosporin may be associated with meningism	
Cyclosporin may be associated with an encephalopathy	
Neurological side effects do not occur with therapeutic plasma levels	Best answer 5
Question 3	
What is your interpretation of the CT appearances?	
The appearances are suggestive of progressive multifocal leukoencephalopathy	
The appearances are suspicious of lymphoma	
The scan shows areas compatible with infarction	
The scan shows areas compatible with infection	
Neither infarction nor infection can be ruled out	Best answer 5
Question 4	
Which further investigation would you suggest next?	
Immediate lumbar puncture for CSF examination and MRI next day	Best answer 1
Defer CSF examination until MRI brain scan has been performed	
Basic lab tests (ESR, C-RP WBC), blood cultures and serology	
Brain biopsy should be carried out after MRI	
Repeat CT brain scan with contrast	
Question 5	
What immediate therapeutic advice would you give?	
Cyclosporin should be stopped	
Steroids should be stopped	
Start anticonvulsant therapy	
Start antibiotic/antifungal/antiviral treatment after the infective process has been defined	
Start anticonvulsant and antibiotic/antifungal/antiviral treatment immediately	Best answer 5

Answers and comments

Q1

Answer 4

After allogenic marrow transplantation 3 phases are recognised

Phase 1 < 30 days: Neutropenia (impaired granulocyte function)

Phase 2 30 days to 3 months: Impaired cellular immunity

Phase 3 > 3 months: Impaired cellular and humoral immunity

These phases relate to the intensity of immunosuppression and graft versus host rejection.

There is considerable overlap and it is not possible to predict a likely pathogen. Treatment related lymphoproliferative complications (i.e. lymphoma) are rare within 6 months of transplant.

Q2

Answer 5

Side effects (especially reversible posterior leukoencephalopathy with blindness) should be recognised by all who consult in renal and other transplant units. The encephalopathy is related to blood levels of cyclosporin (therapeutic range 250-500 ng/ml). Other side effects do not appear to be "dose related", especially tremor.

Q3

Answer 5

The patient is immunocompromised. Endocarditis from bacterial or fungal infection could result in cardiembolic stroke. Certain fungal infections are angioinvasive (aspergillus/mucormycosis) while lymphoma may also be intravascular and present with territorial infarction. It would be wrong here to make the diagnosis of "stroke in an ill person", on the basis of wedge shaped infarct with haemorrhagic transformation, and not investigate further. The final (autopsy) diagnosis here was ASPERGILLUS.

Q4

Answer 1

CSF examination should be carried out straight away. There are no clinical or radiological features to suggest raised intracranial pressure that might contra-indicate this procedure. Early CSF analysis will inform on the possibility of leukaemia involvement (unlikely given the CT appearances) as well as allow identification of bacterial pathogens etc. The case should be discussed prior to CSF sampling with haematologists/bacteriologists/pathologists to ensure all the appropriate PCR and antigen tests are done to cover the considerable range of potential pathogens. "Routine" laboratory tests (ESR, WBC etc) are often unhelpful when the systemic immune response is impaired. Chest X-ray may be helpful where fungal infection is possible, as might sinus radiology (mucormycosis). MRI brain scanning provides more information although the appearances are rarely diagnostic of a specific pathogen. A brain biopsy may be eventually necessary (e.g. for progressive multifocal leukoencephalopathy or lymphoma), but only when there is failure to respond to initial treatment.

Q5

Answer 5

The potential damage from further seizures in the critically ill should not be minimised and anticonvulsant therapy given. There is no indication to withdraw immunosuppression in this case, and the patient could reject their transplant. Once CSF examination is complete, broad-spectrum treatment should start aimed at covering bacteria, viruses and fungi. This should involve discussion with microbiological specialists.

References

Leather HL Wingard JR Infectious Diseases Clinics of North America 2001;15(2):483-520

Cohen J A Rapps E C. Critical neurological illness in the immunocompromised. Neurologic Clinics 1995; 13(3):659-77

Davenport C Dillon WP Sze G. Neuroradiology of the immunocompromised state. Radiol Clin North America 1992;30(3):611-37

Fishman JA Rubin RH. Infections in organ transplant recipients N Engl J Med 338(24):1741-51.

6. Headaches with neurological deficit	Peter Humphrey, Liverpool. Email: moores-s@wcn-tr.nwest.nhs.uk
Consider the following five clinical cases and then decide on a differential diagnosis and plan of investigation.	
First, choose the best diagnosis for each description.	
Question 1	
A 48-year-old man presents with headache over the right eye spreading across the forehead. It started suddenly and built up over a few hours. He smokes. He has no other symptoms. On examination he looks well; he has a mild right ptosis and a small reactive right pupil. There are no other abnormal signs.	
Carcinoma of the lung	
Thoracic aortic dissection	
Internal carotid dissection	Best answer 3
Subarachnoid haemorrhage	
Vertebral artery dissection	
Intracavernous aneurysm	
Basilar artery aneurysm	

Cerebral venous thrombosis	
Migraine	
Extrinsic brain stem mass	
Ectatic basilar artery	
Intrinsic brain stem mass	
Spinal cord infarction	
Myelitis	
Spinal cord compression	
Pituitary apoplexy	
Occipital transient ischaemic attack	
Brain stem arteriovenous malformation	
Question 2	
<i>A 34-year old woman presents with two episodes of vertical double vision. One lasted two hours; the other lasted two weeks and was followed by sudden headache for 4 weeks. Then, three months later, she developed a severe right hemiplegia for 3 minutes. Further episodes of sudden right hand weakness and difficulty with speech, lasting up to 2 hours occurred over the next 4 weeks. On one occasion she developed a transient altitudinal visual field defect in the left eye. She was aware of left pulsatile tinnitus. She smokes 20 cigarettes per day. On examination, she was mildly dysphasic. Otherwise there were no signs. CT head showed a left parietal low attenuation area. (I am grateful to Drs Doran & Enevoldson for permission to use this case)</i>	
Carcinoma of the lung	
Thoracic aortic dissection	
Internal carotid dissection	Best answer 3
Subarachnoid haemorrhage	
Vertebral artery dissection	
Intracavernous aneurysm	
Basilar artery aneurysm	
Cerebral venous thrombosis	
Migraine	
Extrinsic brain stem mass	
Ectatic basilar artery	
Intrinsic brain stem mass	
Spinal cord infarction	
Myelitis	
Spinal cord compression	
Pituitary apoplexy	
Occipital transient ischaemic attack	
Brain stem arteriovenous malformation	
Question 3	
<i>A 39-year-old lady presented to Casualty with a two-week history of occipital headaches. She had a CT scan, which was reported as normal and she was discharged. The headaches continued at home and she developed neck stiffness and photophobia. On the morning of her admission she transiently collapsed and went vacant. On recovery she was aware of double vision. There was a past history of asthma, anxiety, and hypothyroidism. On examination she was alert, had a GCS of 15/15. She was photophobic, had mild neck stiffness and a subhyaloid haemorrhage on fundoscopy. She could not abduct the left eye. There were no other abnormal signs.</i>	
Carcinoma of the lung	
Thoracic aortic dissection	
Internal carotid dissection	
Subarachnoid haemorrhage	
Vertebral artery dissection	Best answer 5
Intracavernous aneurysm	
Basilar artery aneurysm	
Cerebral venous thrombosis	

Migraine	
Extrinsic brain stem mass	
Ectatic basilar artery	
Intrinsic brain stem mass	
Spinal cord infarction	
Myelitis	
Spinal cord compression	
Pituitary apoplexy	
Occipital transient ischaemic attack	
Brain stem arteriovenous malformation	
Question 4	
<i>A 35 year old woman presents with acute onset of complete bilateral visual loss for one hour followed by a left homonymous hemianopia which lasted half an hour. This was followed by a headache, which was occipital and lasted 2 weeks. There was mild photophobia. There was no past history of migraine and she was otherwise well.</i>	
Carcinoma of the lung	
Thoracic aortic dissection	
Internal carotid dissection	
Subarachnoid haemorrhage	
Vertebral artery dissection	Best answer 5
Intracavernous aneurysm	
Basilar artery aneurysm	
Cerebral venous thrombosis	
Migraine	
Extrinsic brain stem mass	
Ectatic basilar artery	
Intrinsic brain stem mass	
Spinal cord infarction	
Myelitis	
Spinal cord compression	
Pituitary apoplexy	
Occipital transient ischaemic attack	
Brain stem arteriovenous malformation	
Question 5	
<i>A 42-year-old man presented as an emergency with neck pain, headache and difficulty with walking. Over the previous four days he had developed mild neck stiffness. Over the 36 hours prior to admission, he noticed tingling in the left arm, trunk, and leg. On examination the cranial nerves were normal; he had increased tone in the left arm and leg with a mild left hemiparesis. Both plantars were extensor and the reflexes on the left were brisk. Light touch was impaired on the left. Pain and temperature sensations were impaired in the right arm and leg.</i>	
Carcinoma of the lung	
Thoracic aortic dissection	
Internal carotid dissection	
Subarachnoid haemorrhage	
Vertebral artery dissection	Best answer 5
Intracavernous aneurysm	
Basilar artery aneurysm	
Cerebral venous thrombosis	
Migraine	
Extrinsic brain stem mass	
Ectatic basilar artery	
Intrinsic brain stem mass	
Spinal cord infarction	
Myelitis	
Spinal cord compression	
Pituitary apoplexy	
Occipital transient ischaemic attack	

Brain stem arteriovenous malformation	
7: Headaches with neurological deficit continued...	
Now, choose the best investigation in each case.	
Question 1	
<i>A 48-year-old man presents with headache over the right eye spreading across the forehead. It started suddenly and built up over a few hours. He smokes. He has no other symptoms. On examination he looks well; he has a mild right ptosis and a small reactive right pupil. There are no other abnormal signs.</i>	
None	
Routine haematological vascular screen	
Young stroke vascular screen	
CT head scan	
MRI head	
MRA head	
MRI neck	Best answer 7
MRA neck	
Echocardiogram	
Doppler/Duplex ultrasound	
Chest X-ray	
ECG	
Conventional angiography	
Lumbar puncture	
Question 2	
<i>A 34-year old woman presents with two episodes of vertical double vision. One lasted two hours; the other lasted two weeks and was followed by sudden headache for 4 weeks. Then, three months later, she developed a severe right hemiplegia for 3 minutes. Further episodes of sudden right hand weakness and difficulty with speech, lasting up to 2 hours occurred over the next 4 weeks. On one occasion she developed a transient altitudinal visual field defect in the left eye. She was aware of left pulsatile tinnitus. She smokes 20 cigarettes per day. On examination, she was mildly dysphasic. Otherwise there were no signs. CT head showed a left parietal low attenuation area. (I am grateful to Drs Doran & Enevoldson for permission to use this case)</i>	
None	
Routine haematological vascular screen	
Young stroke vascular screen	
CT head scan	
MRI head	
MRA head	
MRI neck	
MRA neck	
Echocardiogram	
Doppler/Duplex ultrasound	
Chest X-ray	
ECG	
Conventional angiography	Best answer 13
Lumbar puncture	
Question 3	
<i>A 39-year-old lady presented to Casualty with a two-week history of occipital headaches. She had a CT scan, which was reported as normal and she was discharged. The headaches continued at home and she developed neck stiffness and photophobia. On the morning of her admission she transiently collapsed and went vacant. On recovery she was aware of double vision. There was a past history of asthma, anxiety, and hypothyroidism. On examination she was alert, had a GCS of 15/15. She was photophobic, had mild neck stiffness and a subhyaloid haemorrhage on fundoscopy. She could not abduct the left eye. There were no other abnormal signs.</i>	
None	

Routine haematological vascular screen	
Young stroke vascular screen	
CT head scan	
MRI head	
MRA head	
MRI neck	
MRA neck	
Echocardiogram	
Doppler/Duplex ultrasound	
Chest X-ray	
ECG	
Conventional angiography	Best answer 13
Lumbar puncture	
Question 4	
<i>A 35 year old woman presents with acute onset of complete bilateral visual loss for one hour followed by a left homonymous hemianopia which lasted half an hour. This was followed by a headache, which was occipital and lasted 2 weeks. There was mild photophobia. There was no past history of migraine and she was otherwise well.</i>	
None	
Routine haematological vascular screen	
Young stroke vascular screen	
CT head scan	
MRI head	
MRA head	
MRI neck	Best answer 7
MRA neck	
Echocardiogram	
Doppler/Duplex ultrasound	
Chest X-ray	
ECG	
Conventional angiography	
Lumbar puncture	
Question 5	
<i>A 42-year-old man presented as an emergency with neck pain, headache and difficulty with walking. Over the previous four days he had developed mild neck stiffness. Over the 36 hours prior to admission, he noticed tingling in the left arm, trunk, and leg. On examination the cranial nerves were normal; he had increased tone in the left arm and leg with a mild left hemiparesis. Both plantars were extensor and the reflexes on the left were brisk. Light touch was impaired on the left. Pain and temperature sensations were impaired in the right arm and leg.</i>	
None	
Routine haematological vascular screen	
Young stroke vascular screen	
CT head scan	
MRI head	
MRA head	
MRI neck	Best answer 7
MRA neck	
Echocardiogram	
Doppler/Duplex ultrasound	
Chest X-ray	
ECG	
Conventional angiography	
Lumbar puncture	

Answers and comments

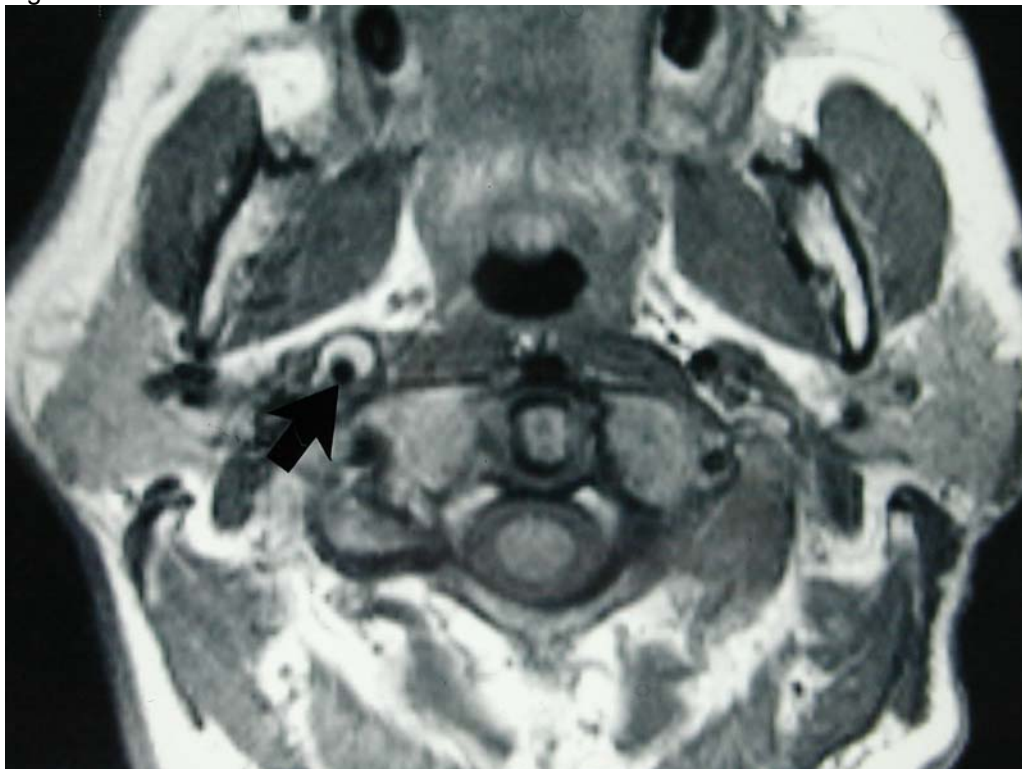
Question 1

Diagnosis: Internal (extracranial) carotid dissection

Investigation: MRI neck. T1 weighted sequence showing the typical appearance of a carotid dissection (Figure 1): it is important to use fat suppression sequences. Note the MRI head will miss the dissected artery. MRA may show a string sign but while this is suggestive of dissection, it is NOT PATHOGNOMONIC.

MRA is a physiological image and a string sign will occur on MRA when there is only a trickle of flow in the internal carotid artery from whatever cause – e.g. a pseudo-occlusion of the carotid artery due to atherosclerosis.

Figure 1

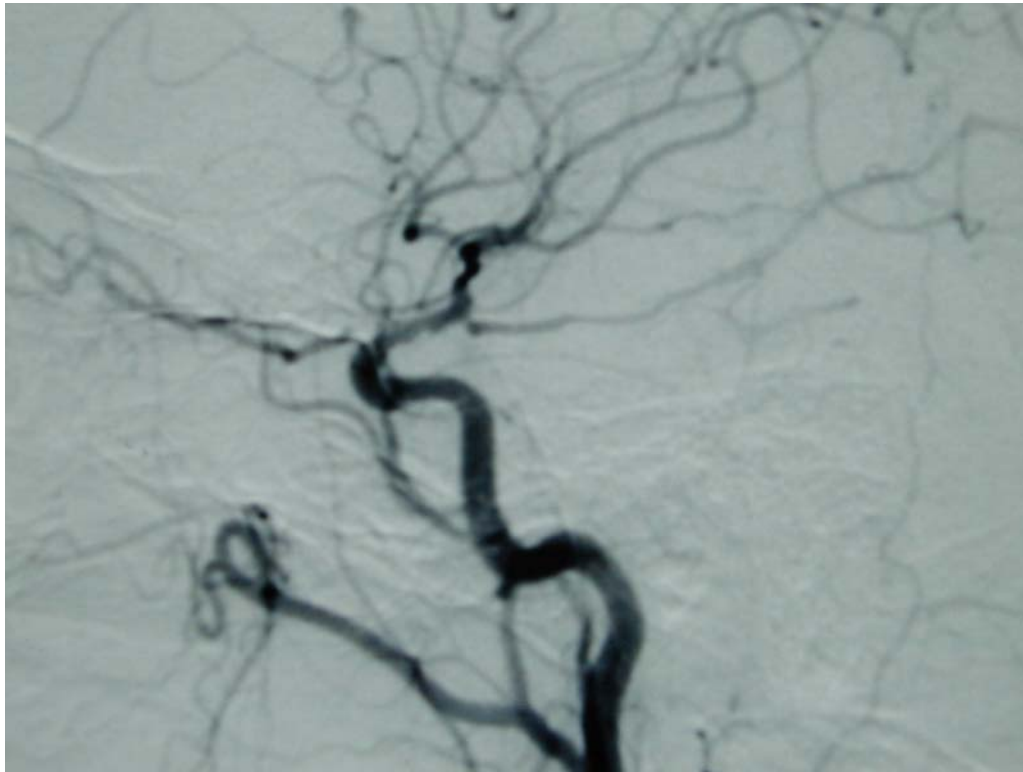


Question 2

Diagnosis: Internal (intracranial) carotid dissection

Investigation: Carotid angiogram shows intracranial carotid dissection in the siphon (Figure 2).

Figure 2



Question 3

Diagnosis: Vertebral artery dissection

Investigation: Angiogram (Figure 3) showing vertebral dissection with spasm of the basilar artery. Most vertebral dissections are low in the neck and may be missed if the angiogram fails to include low neck views. The radiologist then just sees the basilar artery spasm: in this situation a repeat angiogram some weeks later is often normal as many dissections heal, and a diagnosis of aneurysmal negative SAH is made – the true diagnosis of vertebral dissection is then missed. The CT scan had shown blood in the subarachnoid space.

Figure 3

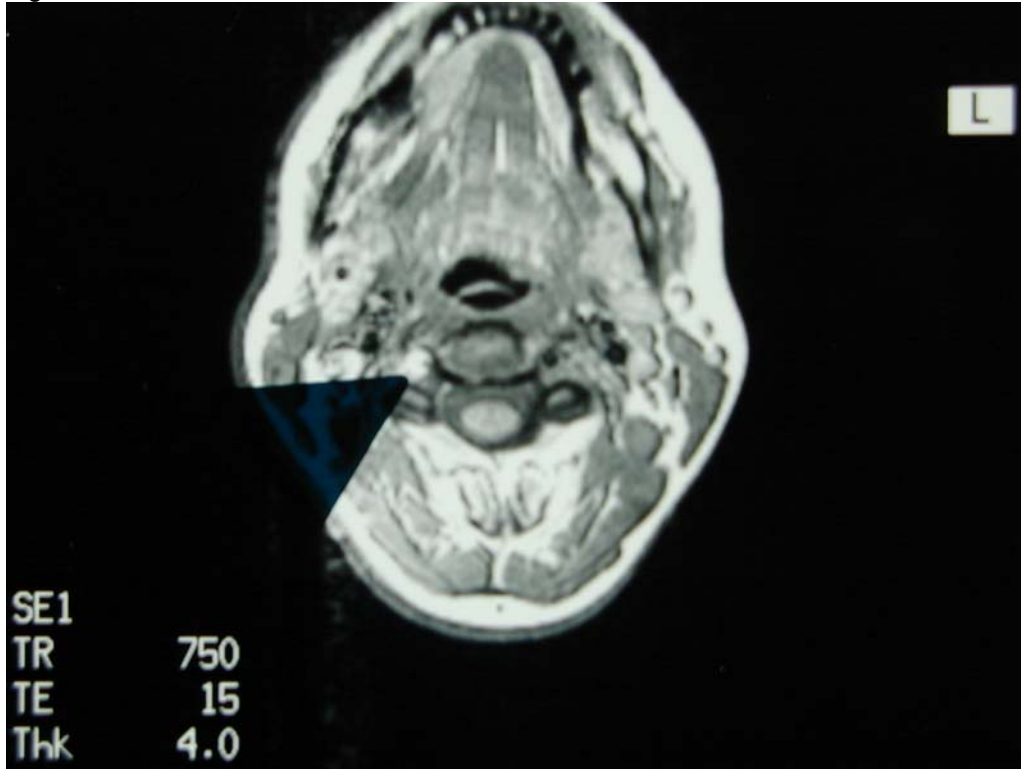


Question 4

Diagnosis: Vertebral artery dissection

Investigation: MRI neck (Figure 4) T₁-weighted sequences showing the typical appearance of a vertebral dissection. Please note the dissected vertebral artery with pinpoint “black” lumen and “white” blood filling most of the artery.

Figure 4



Question 5

Diagnosis: Vertebral artery dissection

Investigation: MRI neck

Explanation

In all these patients, the final diagnosis was either carotid or vertebral dissection. Although arterial dissection is now recognised as one of the commoner causes of non-arteriosclerotic stroke, especially in the young, it can present in a wide variety of ways. Patients with carotid dissection typically present with TIAs, stroke, Horner's syndrome, and pain. The pain may precede the focal symptoms by some days - unusual in arteriosclerotic stroke. Acute Horner's syndrome is one of the commoner presentations due to rapid expansion of the carotid artery, damaging the sympathetic fibres which are wrapped round the internal carotid artery in the neck (Case 1 – see fig. 1).

This rapid expansion of the carotid arteries can also damage the neighbouring cranial nerves. In extracranial carotid dissection, the lower cranial nerves (especially IX, X and XII) can be affected.¹ With intracranial dissection (these are rare), the oculomotor nerve is one of the nerves that can be damaged (Case2 – Fig. 2).² The combination of a 3rd nerve palsy and contralateral hemiplegia usually suggests a brain stem stroke. Case 2 emphasises the need to consider intracranial carotid dissections.³

Carotid dissections are usually extracranial and virtually never present with haemorrhage. Intracranial carotid dissections are rare: they also usually present with ischaemic symptoms although there are the occasional case reports of haemorrhage.

Vertebral dissections (Cases 3, 4 and 5) can be both extracranial and intracranial. In fact, it is not uncommon for extracranial vertebral dissections to spread above the base of skull (unlike extracranial internal carotid dissections). Subarachnoid haemorrhage is a more frequent presentation once the vertebral dissection has spread intracranially (Case 3 – see Fig. 3).⁴

Case 4 could easily have been diagnosed as migraine.⁵ The MRI scan through the neck was diagnostic of vertebral dissection (Fig. 4). There was no past history of migraine and the pattern and timing of the visual loss would be unusual in migraine. The symptoms presumably arise in the occipital lobes and were due to embolism from the dissection. It is important to remember that the anterior spinal artery arises from the terminal part of the vertebral arteries and therefore cases of cervical infarction are well recorded after vertebro-basilar dissection (Case 5).⁶ There have even been reports of vertebral dissections compressing the cervical nerve roots and presenting with a cervical root syndrome. Two good reviews of dissections are given in references 7 & 8.

References

1. Mokri B, Schievink WI., Olsen KO, Piepgras DG. Spontaneous dissection of the cervical internal carotid artery: presentation with lower cranial nerve palsies. *Arch Otolaryngol Head Neck Surgery* 1992;118:431-5
2. Schievink W.I., Mokri B, Garritty J. A., Nichols D.A., Piepgras D. G. Ocular Motor Nerve Palsies in Spontaneous Dissections of the Cervical Internal Carotid Artery. *Neurology* 1993;43:1938-41
3. Bassetti C, Bogouslavsky J, Eskenasy-Cottier AC, Janzer RC, Regli F. Spontaneous Intracranial Dissection in the Anterior Circulation. Case report and review of the literature. *Cerebrovascular Disease* 1994;4:170-4
4. Biousse V, Bousser MG, Mas JL. Extracranial Vertebral Artery Dissection Presenting as Subarachnoid Haemorrhage. *Stroke* 1994;25:714-5
5. Young G, Humphrey PRD. Vertebral Artery Dissection Mimicking Migraine *J Neurol Neurosurg Psych* 1996;59:340-1
6. Goldsmith P, Rowe D, Jager R, Kapoor R. Focal Vertebral Artery Dissection causing Brown-Sequard's Syndrome *J. Neurol Neurosurg Psychiatry* 1998;64: 415-6
7. Schievink WI. Spontaneous Dissection of the Carotid and Vertebral Arteries (A Review) *NEJM* 2001;344:898-906
8. Mokri B. Cervicocephalic Arterial Dissections. In *Uncommon Causes of Stroke* Ed. J Bogouslavsky and L Caplan. Cambridge University Press 2001 p. 211-29

8. Acute onset hemiparesis in a young patient

Richard Davenport, Edinburgh
Email: rjd@skull.dcn.ed.ac.uk

Scenario

A 32 yr old man is admitted as an emergency at 04.30 hr with a left hemiparesis. He is virtually anarthric and cannot give a history. His partner went to bed at 23.00 hr, when he appeared well apart from a mild headache. At about 0330 she was awoken by him falling out of bed and she immediately noted the left weakness.

He is usually well. He is a smoker. On examination, he is haemodynamically stable (BP 160/100, pulse 70 regular), and E3, M6, V5 (score 14). He has a dense left hemiparesis, probably a left hemianopia and sensory neglect.

His admission CT brain is shown in figure 1. Routine emergency blood tests and ECG are normal.



Figure 1

For each question part you should offer only a single best answer.

Question 1

Having seen the CT brain, which one of the following further investigations is required urgently (within next 6 hours)?

MR brain and MR Angiography	
CT or MR venogram	
Conventional catheter angiography	
CSF examination	
Electroencephalogram	
Transthoracic echocardiogram	
Repeat CT brain with CT angiogram	
None of the above	Best answer 8

Question 2

Which is the single most appropriate immediate management?

Transfer to a stroke unit	Best answer 1
Transfer to an intensive care unit	
Transfer to standard medical/neurological bed	
Intravenous thrombolysis	
Intra-arterial thrombolysis	
Immediate lowering of his blood pressure pharmacologically	
Full anticoagulation with either standard intravenous or low molecular weight heparin	
Intravenous steroids and mannitol	

Question 3

24 hours later his Glasgow Coma Score suddenly deteriorates to E1, M3, V1. The repeat CT brain is shown in figure 2.



Figure 2

Which is the single most appropriate option you would suggest to the family?

Keep him comfortable, as he will probably die within next 48 hours and there is no effective treatment	
Transfer to ICU, ventilate, and use appropriate pharmacological methods to lower his intracranial pressure, plus cooling	
Thrombolysis (either intra-arterial or intravenous)	
Heparinise	
Decompressive hemicraniectomy	Best answer 5

Answers and comments

Q1

None of the above.

Clinically the diagnosis is a stroke. The CT reveals early infarction of the right middle cerebral artery territory (i.e. not venous). A lower slice reveals the hyperdense middle cerebral artery sign (figure 3), indicative of a proximal thrombus (although it may be a most unreliable sign, particularly in older patients). There are no clues in the history or on examination to suggest that there is a potentially treatable cause such as dissection of the thoracic aorta or bacterial endocarditis. Further investigations such as MR scanning and transthoracic echocardiography may be helpful later to help elucidate the cause of the stroke, but none of the investigations would be helpful immediately. Some would suggest that an attempt to identify a dissection of the carotid system (i.e. angiography or MRI) is essential – but what would you do even if you knew this acutely?



Figure 3

Q2

Transfer to the stroke unit

At present, this is the only intervention for which there is robust evidence (1), although in some hospitals stroke units are geared for a more elderly population and therefore a neurological unit with staff interested and experienced in stroke management may be more appropriate. There is no evidence to support heparin (2), steroids (3), mannitol (4) or acute lowering of blood pressure (5) (unless one suspected either a dissection of the thoracic aorta or hypertensive encephalopathy).

The evidence regarding thrombolysis is still being accumulated. Current data suggest that there is a net benefit, particularly for patients treated within the first 3 hours of symptom onset (most of the data pertain to intravenous rather than intra-arterial thrombolysis) (6 & 7). None of the thrombolytic agents are currently licensed for use in stroke in the UK, although this will

probably change in the near future. The difficulty in this case was timing the stroke onset; this might have been as early as 2301 (*i.e.* immediately after his partner retired to bed), indicating that his symptoms began between 5 and 6 hours previously. The fact that the CT brain scan showed early extensive infarction would also dissuade some from employing “off label” thrombolysis. An ongoing trial of thrombolysis versus placebo within 6 hours of onset (IST 3) may help to resolve this issue.

Q3

Decompressive hemicraniectomy.

As in so much of neurology, there is no “right” answer, and this is reflected in the wording of the question. Clearly it is too late for thrombolysis, and heparinisation is only likely to hasten his demise. Many would transfer to the ICU, although there is little evidence to suggest that mannitol or other intracranial pressure-lowering therapies work in stroke (8). Doing nothing is clearly an option, but given his previous biological fitness many would opt for surgery, despite the lack of evidence (9 &10). Decompressive hemicraniectomy surgery was performed in this case (see figure 4). He was beginning to recover (albeit with a persisting dense hemiparesis) when he died suddenly of septic shock four weeks later (chest source). A post mortem did not reveal the cause of the stroke.



Figure 4

References

1. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
2. Gubitz G, Counsell C, Sandercock P, Signorini D. Anticoagulants for acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
3. Qizilbash N, Lewington SL, Lopez-Arrieta JM. Corticosteroids for acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
4. Bereczki D, Liu M, do Prado GF, Fekete I. Mannitol for acute stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
5. Blood pressure in Acute Stroke Collaboration (BASC). Interventions for deliberately altering blood pressure in acute stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
6. Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolysis for acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
7. Liu M, Wardlaw J. Thrombolysis (different doses, routes of administration and agents) for acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
8. Correia M, Silva M, Veloso M. Cooling therapy for acute stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
9. Morley NCD, Berge E, Cruz-Flores S, Whittle IR. Surgical decompression for cerebral oedema in acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software.
10. Hacke W, Berge E, Dennis M, Morley N (2002). Decompressive surgery for malignant middle cerebral artery territory infarction. *Practical Neurology*, **2**, 144-153.

9. Neuromuscular disorders	David Hilton-Jones, Oxford Email: david.hilton-jones@clinical-neurology.oxford.ac.uk
-----------------------------------	---

For each of the five clinical scenarios described below, choose one option for the diagnosis and later one option with respect to the best first action or investigation.

Best diagnosis?

Question 1

A 23-year-old man complains of weakness and cramping in his hands. Examination shows marked grip myotonia and weakness of finger flexion, with mild weakness of the facial muscles, neck flexion and ankle dorsiflexion. There is no relevant family history.

Myotonia congenita	Best answer 1
Dermatomyositis	
Oculopharyngeal muscular dystrophy	
Myotonic dystrophy type 1	
HMSN type 1	
Lambert-Eaton myasthenic syndrome	
Mitochondrial chronic progressive external ophthalmoplegia	
Myasthenia gravis	
Polymyalgia rheumatica	
Proximal spinal muscular atrophy	
Myotonic dystrophy type 2	
Polymyositis	
Inclusion body myositis	
Distal spinal muscular atrophy	
Dysthyroid myopathy	

Question 2

A 15-year-old female complains of ugly, clumsy feet, and believes that she has inherited the “family feet” which also affect her mother, several maternal aunts and uncles, and her maternal grandfather.

On examination she has pes cavus, wasting of extensor digitorum brevis and tibialis anterior, and mild weakness of ankle dorsiflexion and eversion. The tendon reflexes are preserved and there is no sensory loss.

Myotonia congenita	
Dermatomyositis	
Oculopharyngeal muscular dystrophy	
Myotonic dystrophy type 1	
HMSN type 1	Best answer 5
Lambert-Eaton myasthenic syndrome	
Mitochondrial chronic progressive external ophthalmoplegia	
Myasthenia gravis	
Polymyalgia rheumatica	
Proximal spinal muscular atrophy	
Myotonic dystrophy type 2	
Polymyositis	
Inclusion body myositis	
Distal spinal muscular atrophy	
Dysthyroid myopathy	

Question 3

A 25-year-old woman presents with a 6-month history of highly variable drooping of both upper eyelids, transient double vision, especially in the evening, and “fatigue”. On examination she has striking bilateral fatiguable ptosis, double vision on sustained lateral gaze with easily visible fatiguable weakness of the medial recti, mild weakness of neck flexion and mild fatiguable weakness of shoulder abduction and hip flexion. Her forced vital capacity is normal.

Myotonia congenita	
Dermatomyositis	
Oculopharyngeal muscular dystrophy	
Myotonic dystrophy type 1	
HMSN type 1	
Lambert-Eaton myasthenic syndrome	
Mitochondrial chronic progressive external ophthalmoplegia	
Myasthenia gravis	Best answer 8
Polymyalgia rheumatica	
Proximal spinal muscular atrophy	
Myotonic dystrophy type 2	
Polymyositis	
Inclusion body myositis	
Distal spinal muscular atrophy	
Dysthyroid myopathy	

Question 4

A 65-year-old woman presents with a 5-year history of progressive but asymmetric bilateral ptosis. She has had no diplopia, but on specific enquiry says that she has noticed slight difficulty swallowing some foods. She thinks that her mother and maternal uncle had droopy eyelids in later life, and her maternal grandfather ended up in a wheelchair, but she was not aware of any other details of his illness.

On examination she had severe asymmetric bilateral non-fatiguable ptosis. Eye movements were slightly restricted in all directions of gaze, but there was no diplopia. She had mild weakness of the facial muscles, neck flexion and shoulder abduction

Myotonia congenita	
Dermatomyositis	
Oculopharyngeal muscular dystrophy	Best answer 3
Myotonic dystrophy type 1	
HMSN type 1	
Lambert-Eaton myasthenic syndrome	
Mitochondrial chronic progressive external ophthalmoplegia	
Myasthenia gravis	
Polymyalgia rheumatica	
Proximal spinal muscular atrophy	
Myotonic dystrophy type 2	
Polymyositis	
Inclusion body myositis	
Distal spinal muscular atrophy	
Dysthyroid myopathy	

Question 5

A 60-year-old woman presents with a 6-week history of progressive proximal muscle weakness, accompanied by mild aching when using those muscles. She can no longer climb stairs, get out of a chair without assistance, or lift her arms above shoulder height. Her voice has become croaky and she has had some difficulty swallowing. On examination she has proximal weakness with slight wasting of quadriceps. There is no muscle tenderness. Her cheeks are flushed and she has erythema over her knuckles and over the upper part of her anterior chest. Her serum creatine kinase the day before assessment was 250 iu/l.

Myotonia congenita	
--------------------	--

Dermatomyositis	Best answer 2
Oculopharyngeal muscular dystrophy	
Myotonic dystrophy type 1	
HMSN type 1	
Lambert-Eaton myasthenic syndrome	
Mitochondrial chronic progressive external ophthalmoplegia	
Myasthenia gravis	
Polymyalgia rheumatica	
Proximal spinal muscular atrophy	
Myotonic dystrophy type 2	
Polymyositis	
Inclusion body myositis	
Distal spinal muscular atrophy	
Dysthyroid myopathy	
10 Neuromuscular disorders continued...	
For each of the five clinical scenarios described below, choose one option with respect to the best first action or investigation	
Question 1	
<i>A 23-year-old man complains of weakness and cramping in his hands. Examination shows marked grip myotonia and weakness of finger flexion, with mild weakness of the facial muscles, neck flexion and ankle dorsiflexion. There is no relevant family history.</i>	
Blood DNA analysis (for myotonic dystrophy type 1)	Best answer 1
Blood DNA analysis (for myotonic dystrophy type 2)	
Blood DNA analysis (for HMSN type 1A)	
Blood DNA analysis (for oculopharyngeal muscular dystrophy)	
Blood DNA analysis (for mitochondrial DNA point mutations)	
Blood DNA analysis (for mitochondrial DNA rearrangements)	
Neurophysiological studies	
Slit-lamp examination of the lens	
Muscle biopsy (histology and histochemistry)	
Muscle biopsy (histology, histochemistry and immunocytochemistry)	
Muscle biopsy (histology, histochemistry and electron microscopy)	
Muscle biopsy (histology, histochemistry and mitochondrial DNA studies)	
Tensilon® test	
Anti-acetylcholine receptor antibody assay	
Initiate steroid therapy	
Question 2	
<i>A 15-year-old female complains of ugly, clumsy feet, and believes that she has inherited the “family feet” which also affect her mother, several maternal aunts and uncles, and her maternal grandfather. On examination she has pes cavus, wasting of extensor digitorum brevis and tibialis anterior, and mild weakness of ankle dorsiflexion and eversion. The tendon reflexes are preserved and there is no sensory loss.</i>	
Blood DNA analysis (for myotonic dystrophy type 1)	
Blood DNA analysis (for myotonic dystrophy type 2)	
Blood DNA analysis (for HMSN type 1A)	Best answer 3
Blood DNA analysis (for oculopharyngeal muscular dystrophy)	
Blood DNA analysis (for mitochondrial DNA point mutations)	
Blood DNA analysis (for mitochondrial DNA rearrangements)	
Neurophysiological studies	
Slit-lamp examination of the lens	
Muscle biopsy (histology and histochemistry)	
Muscle biopsy (histology, histochemistry and immunocytochemistry)	
Muscle biopsy (histology, histochemistry and electron microscopy)	
Muscle biopsy (histology, histochemistry and mitochondrial DNA studies)	

Tensilon® test	
Anti-acetylcholine receptor antibody assay	
Initiate steroid therapy	
Question 3	
A 25-year-old woman presents with a 6-month history of highly variable drooping of both upper eyelids, transient double vision, especially in the evening, and “fatigue”. On examination she has striking bilateral fatigable ptosis, double vision on sustained lateral gaze with easily visible fatigable weakness of the medial recti, mild weakness of neck flexion and mild fatigable weakness of shoulder abduction and hip flexion. Her forced vital capacity is normal	
Blood DNA analysis (for myotonic dystrophy type 1)	
Blood DNA analysis (for myotonic dystrophy type 2)	
Blood DNA analysis (for HMSN type 1A)	
Blood DNA analysis (for oculopharyngeal muscular dystrophy)	
Blood DNA analysis (for mitochondrial DNA point mutations)	
Blood DNA analysis (for mitochondrial DNA rearrangements)	
Neurophysiological studies	
Slit-lamp examination of the lens	
Muscle biopsy (histology and histochemistry)	
Muscle biopsy (histology, histochemistry and immunocytochemistry)	
Muscle biopsy (histology, histochemistry and electron microscopy)	
Muscle biopsy (histology, histochemistry and mitochondrial DNA studies)	
Tensilon® test	
Anti-acetylcholine receptor antibody assay	Best answer 14
Initiate steroid therapy	
Question 4	
A 65-year-old woman presents with a 5-year history of progressive but asymmetric bilateral ptosis. She has had no diplopia, but on specific enquiry says that she has noticed slight difficulty swallowing some foods. She thinks that her mother and maternal uncle had droopy eyelids in later life, and her maternal grandfather ended up in a wheelchair, but she was not aware of any other details of his illness.	
On examination she had severe asymmetric bilateral non-fatigable ptosis. Eye movements were slightly restricted in all directions of gaze, but there was no diplopia. She had mild weakness of the facial muscles, neck flexion and shoulder abduction	
Blood DNA analysis (for myotonic dystrophy type 1)	
Blood DNA analysis (for myotonic dystrophy type 2)	
Blood DNA analysis (for HMSN type 1A)	
Blood DNA analysis (for oculopharyngeal muscular dystrophy)	Best answer 4
Blood DNA analysis (for mitochondrial DNA point mutations)	
Blood DNA analysis (for mitochondrial DNA rearrangements)	
Neurophysiological studies	
Slit-lamp examination of the lens	
Muscle biopsy (histology and histochemistry)	
Muscle biopsy (histology, histochemistry and immunocytochemistry)	
Muscle biopsy (histology, histochemistry and electron microscopy)	
Muscle biopsy (histology, histochemistry and mitochondrial DNA studies)	
Tensilon® test	
Anti-acetylcholine receptor antibody assay	
Initiate steroid therapy	
Question 5	
A 60-year-old woman presents with a 6-week history of progressive proximal muscle weakness, accompanied by mild aching when using those muscles. She can no longer climb stairs, get out of a chair without assistance, or lift her arms above shoulder height. Her voice has become croaky and she has had some difficulty swallowing. On examination she has proximal weakness with slight wasting of quadriceps. There	

<i>is no muscle tenderness. Her cheeks are flushed and she has erythema over her knuckles and over the upper part of her anterior chest. Her serum creatine kinase the day before assessment was 250 iu/l.</i>	
Blood DNA analysis (for myotonic dystrophy type 1)	
Blood DNA analysis (for myotonic dystrophy type 2)	
Blood DNA analysis (for HMSN type 1A)	
Blood DNA analysis (for oculopharyngeal muscular dystrophy)	
Blood DNA analysis (for mitochondrial DNA point mutations)	
Blood DNA analysis (for mitochondrial DNA rearrangements)	
Neurophysiological studies	
Slit-lamp examination of the lens	
Muscle biopsy (histology and histochemistry)	
Muscle biopsy (histology, histochemistry and immunocytochemistry)	Best answer 10
Muscle biopsy (histology, histochemistry and electron microscopy)	
Muscle biopsy (histology, histochemistry and mitochondrial DNA studies)	
Tensilon® test	
Anti-acetylcholine receptor antibody assay	
Initiate steroid therapy	

Answers and comments

Q1

Answer 1 then answer 1

The findings are absolutely typical of myotonic dystrophy type 1 (DM 1) and the correct answer is DNA studies seeking expansion of the (CTG)_n repeat in the myotonic dystrophy protein kinase DMPK gene (Option 1). If the test is negative, repeat it – with this clinical picture it is more likely that there is a lab error than you have got the diagnosis wrong. Slit-lamp examination of the limbs and EMG were once widely used particularly for identifying asymptomatic carriers of the gene, but for diagnostic purposes have been completely superseded by DNA testing.

Myotonic Dystrophy type 2 (proximal myotonic myopathy, PROMM) appears to be rare in the United Kingdom with only a hand-full of families having been identified (compared with a population prevalence of 1:8,000 for DM 1). Myotonia is rarely striking and is often absent, even electrophysiologically. The weakness is proximal, in marked contrast to the inevitable distal weakness in DM 1.

Myotonia congenita in all of its forms is rare. The myotonia is generalised and typically causes stiffness on first walking after sitting. Symptomatic myotonia restricted to the hands, so common in DM 1 is rare in myotonia congenita. Persistent weakness is not a typical feature of myotonia congenita.

Q2

Answer 5 then answer 3

The family history clearly indicates an autosomal dominant disorder and despite the preservation of reflexes and normal sensation, it is most likely that she has HMSN type 1. Statistically, in the UK population, it is about 75% likely that she has HMSN type 1A due to duplication involving the PMP22 gene on chromosome 17. An assessment of that should be the first investigation (Option 3), and one that is readily available. If the test is negative the next investigation is nerve conduction studies. These are likely to show slowed nerve conduction and the genetic basis may be a point mutation in the PMP22 gene (HMSN 1A) or Po gene (HMSN 1B). Tests for these are not readily available and in any case the result in this type of family, with a clear autosomal dominant inheritance, is unlikely to alter management. X-linked disease (HMSN 1X) is an important catch and must be considered when there is no male-to-male transmission in the family. Additional clues include less

severe clinical features, and faster conduction velocities, in affected female members. HMSN 1X explains about 10% of all cases of HMSN Type I. Its recognition is important because of the genetic counseling issues.

Q3

Answer 8 then answer 14

If this isn't myasthenia gravis, then there is no justice in this life. The first action is to take blood for anti-acetylcholine receptor antibody assay (Option 14), followed by writing a prescription for pyridostigmine. The antibody assay is positive in about 85% of patients with generalised myasthenia, as she obviously has. It is highly specific and in this situation, if positive, no other confirmatory diagnostic test is required. If it is negative, the best next investigation is neurophysiological studies including decremental testing and single fibre EMG.

The Tensilon® test is most useful in patients with suspected ocular myasthenia, negative antibody assay and negative or equivocal neurophysiological studies.

Q4

Answer 3 then answer 4

The differential diagnosis is essentially between oculopharyngeal muscular dystrophy (OPMD) and mitochondrial chronic progressive external ophthalmoplegia (CPEO). Mitochondrial CPEO is usually sporadic. Limitation of eye movements is mild in OPMD but often severe and sometimes complete in mitochondrial CPEO. In both, in distinction to myasthenia, diplopia is uncommon.

Most cases of mitochondrial CPEO are associated with mitochondrial DNA re-arrangements which can only be detected in muscle biopsy material, not in blood, and of course ragged-red fibres are a typical finding. In OPMD, muscle contains characteristic 8 nm filaments visible on electron microscopy.

The correct approach in this case is OPMD DNA studies on blood (Option 4) followed by muscle biopsy if this test is negative.

Her maternal grandfather may well have become wheelchair-bound because of OPMD, which can cause a severe limb-girdle syndrome, but invariably with associated oculopharyngeal signs.

Q5

Answer 2 then answer 10

The clinical picture is that of dermatomyositis. The serum CK is usually substantially elevated (typically several thousand iu/l) but is occasionally normal, even in the presence of marked weakness. Despite the use of international units, there is no agreed upper limit of normal. In the normal population, men tend to have higher levels than women, as do blacks. A young male engaging in reasonably strenuous physical activity may normally run levels around 600 iu/l. A level of 250 iu/l is somewhat borderline, but will certainly fall with steroid treatment. It may not necessarily rise even to 250iu/l if there is a subsequent relapse.

The appropriate first investigation in this case is a muscle biopsy (Option 10) immediately followed by initiation of immunosuppressant therapy. In all forms of myositis, the pathological changes may be very patchy and a normal biopsy does not exclude the diagnosis.

Immunocytochemical studies on the muscle biopsy specimen can be very useful. In particular, myositis is associated with up-regulation of MHC class I expression, and on occasion this is the only pathological marker of disease.

Dermatomyositis may be a paraneoplastic disorder and in this age range there is associated malignancy in perhaps 25% of cases. The malignancy may not become evident for up to 2 years after the onset of the myositis.

References

General texts

Karpati G, Hilton-Jones D, Griggs R, eds. Disorders of Voluntary Muscle, 7th ed. Cambridge University Press, 2001.

Hilton-Jones D. Muscle Diseases. In: Donaghy M, ed. Brain's Diseases of the Nervous System, 11th ed. Oxford University Press, 2001.

Myotonic Dystrophy

Harper P. Myotonic Dystrophy, 3rd ed. W.B.Saunders, London.

Myasthenia

Hilton-Jones D. How to diagnose myasthenia gravis. *Practical Neurology* 2002;**2**:173-7.

Vincent A, Palace J, Hilton-Jones D. Myasthenia Gravis. *Lancet* 2001;**357**:2122-8.

Oculopharyngeal Muscular Dystrophy

Hill M.E, Creed G.A, McMullan T.F.W, Tyers A.G, Hilton-Jones D, Robinson D.O, Hammans S.R. Oculopharyngeal muscular dystrophy – phenotypic and genotypic studies in a UK population. *Brain* 2001;**124**:522-526.

Myositis

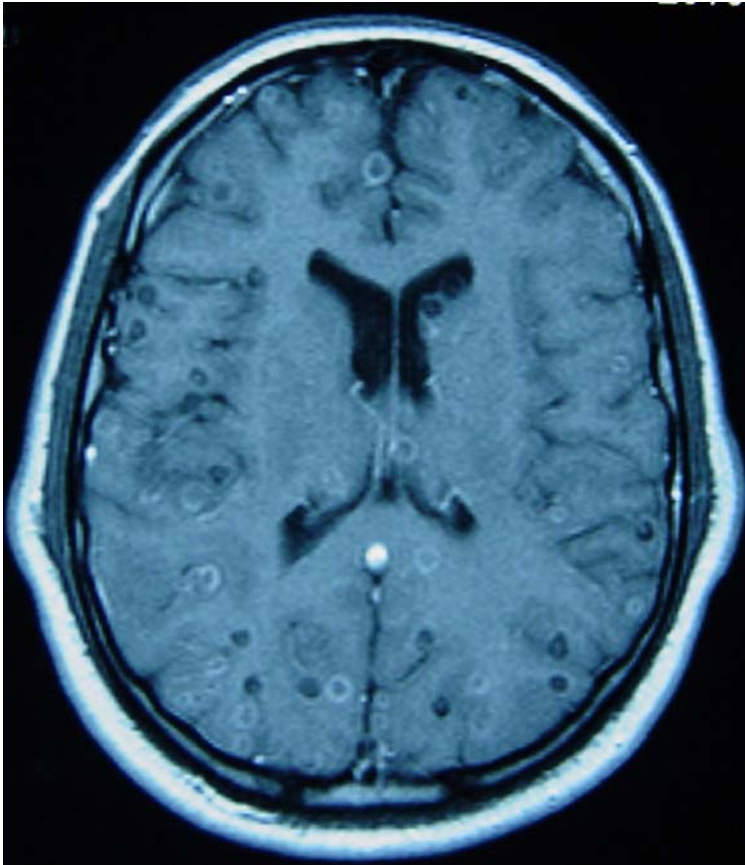
Hilton-Jones D. Inflammatory Muscle Diseases. *Curr Opin Neurol* 2001;**14**:591-6

CMT

Reilly M. Classification of the hereditary motor and sensory neuropathies. *Curr Opin Neurol* 2000;**13**:561-4.

11. Multiple Cerebral Lesions in a Young Man	Dr Peter K Newman, Middlesbrough General Hospital Email: Peter.Newman@stees.nhs.uk
<p>This MR brain image (Figure 1) is from a 22 year old health care worker who presented with seizures. There were no other symptoms or relevant family history. Three years earlier he had spent a month trekking in Nepal.</p> <p>There were no abnormal clinical signs.</p> <p>For each question part you should offer only a single best answer.</p>	
Question 1	
What is the most likely diagnosis?	
Tuberculosis	
Multiple metastases	
Cerebral abscesses	
Aspergillosis	
Neurocystercercosis	Best answer 5
Chronic cerebral schistosomiasis	
Question 2	
What first line management is indicated?	
Anticonvulsant therapy	Best answer 1
EEG	
Serological tests and appropriate antimicrobial therapy	
Antimicrobial therapy and anticonvulsant drugs	
Conservative approach	
Stereotactic biopsy of cerebral lesion	
Antimicrobial therapy with steroids and anticonvulsant drugs	

Figure 1



Answers and comments

Q1

Answer 5: Neurocysticercosis.

The scan shows multiple small round lesions in the cerebral hemispheres with protrusions into the lateral ventricles. These appearances are characteristic of cysticercosis. Typically, live cysts are not associated with oedema, but dying cysts create a localised inflammatory reaction which may produce surrounding oedema. On CT scan the inactive (dead) cysts appear as multiple foci of calcifications.

The differential diagnosis includes multiple secondary deposits, abscesses or tuberculoma but the appearances are atypical for these alternatives and it is noted that apart from seizures the patient was clinically well.

Q2

Answer 1: Anticonvulsant therapy

In most cases antiepileptic treatment is all that is required since the infestation is inactive by the time the patient presents with seizures. Neurocysticercosis is a major cause of epilepsy, accounting for more than 50% of cases in some endemic areas.

Where viable larvae persist, detected by CT or MR characteristics and sequential scanning, eradication treatment with albendazole and/or praziquantel is used. Since this may cause a potentially dangerous acute inflammatory reaction around the dying intracerebral larva, high dose steroid cover is usually given.

Discussion

Plain X-ray or CT of thighs may show multiple calcified cysticerci in muscle (Figure 2). CT brain scanning will show intracranial calcified cysts and there may be single or multiple

lesions (Figure 3). Cysticercal immunoblot gave positive bands in the serum in this patient while a stool culture for *Taenia solium* ova was negative, as would be expected some years following this form of exposure.

Man is the definitive host harbouring the tapeworm but the more serious problem of cysticercosis arises when man becomes the intermediate host by ingesting ova, often by cross infection from unhygienic food handlers. This explains why cysticercosis is seen in Muslims, Jews and vegetarians, as well as in pork-eating communities. The ova convert to immature larvae and penetrate the gut to spread via the bloodstream to other tissues, especially brain and muscle.

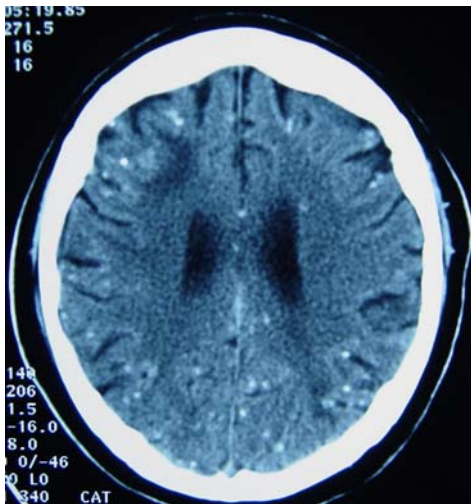


Figure 2

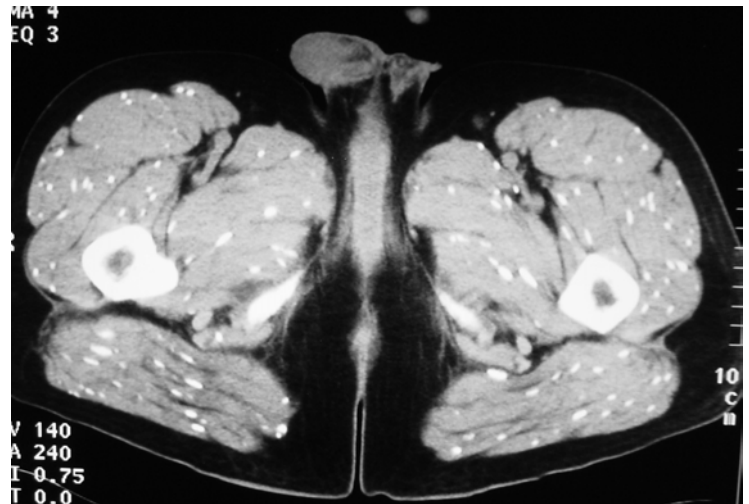


Figure 3

References

Wadia NH (1996) Neurocysticercosis. In: Tropical Neurology (eds R.Shakir, P.K. Newman, C.M. Poser) pp 247 – 273 WB Saunders & Co, London.

Acknowledgement

The patient is under the care of Raad Shakir who kindly provided clinical details and scans.

12. Painful Horner's syndrome	Giles Elrington, London Email: elrington@aol.com
A 58 year old accountant was referred by an ophthalmologist because of a right Horner's syndrome. This had been present for at least 25 years and was associated with excess sweating on the left forehead, and right loin. On direct questioning he admitted to at least 14 years of daily, severe, right frontal pain lasting half to one hour. He did not want this investigated because he was sure he had a brain tumour and was simply waiting for its natural progression. About eight years earlier he had been admitted to a private psychiatric hospital following marital breakdown, and was treated with lithium. He was now on no medication, and living a normal life. Examination revealed a right Horner's syndrome (ptosis, miosis, hypohydrosis) and no other abnormality.	
<i>For each question part you should offer only a single best answer.</i>	
Question 1	
<i>What is the most likely diagnosis?</i>	
Carotid dissection	
Idiopathic Horner's syndrome	
Tension-type headache	
Migraine	

Depression	
Cluster headache	
Trigeminal autonomic cephalgia	Best answer 7
Hemicrania continua	
Chronic paroxysmal hemicrania	
Question 2	
Which single investigation is most advised?	
ESR	
Chest radiograph	
CT brain scan	
MR brain scan	Best answer 4
MRI cervical spine	
MRI dorsal spine	
MRI brachial plexus	
No investigations are mandatory	
Question 3	
What treatment is likely to be most effective for the headache?	
A codeine/paracetamol combination	
An oral triptan	
A subcutaneous triptan	
Amitriptyline	
Propranolol	
Indomethacin	Best answer 6
A NSAID other than indomethacin	
A COX-II antagonist	
Lithium	
Verapamil	
Question 4	
Why is sweating increased in the right loin?	
The lateralisation is erroneous	
Denervation hypersensitivity	
A central sympathetic lesion	
A peripheral sympathetic lesion	
None of the above	Best answer 5

Figure 1



Figure 2



Answers and comments

Q1

Answer 7, alternatively 9.

The history is a little long for carotid dissection. The attacks are too short for migraine, which last a minimum of 4 hours. Depression is commonly present in people with headache but is rarely a useful diagnosis for the headache. Trigeminal autonomic cephalgias (TACs) are a group of primary headache disorders characterised by unilateral trigeminal distribution with ipsilateral autonomic features. The least uncommon TAC is cluster headache (CH): this could be chronic CH, though the absence of paroxysmal autonomic dysfunction accompanying the pain is atypical. Other TACs include hemicrania continua (2) (not the diagnosis here because his pain is paroxysmal, not continuous) and, chronic paroxysmal hemicrania (CPH), which usually lasts 10-30 minutes, though can range from 2-45 minutes. CPH typically causes more than five attacks a day though the range is 1-40. A dramatic and absolute response to indomethacin distinguishes CPH from cluster headache (1).

Best answer – Trigeminal autonomic cephalgia; alternatively – CPH.

Q2

Answer 4.

Brain imaging, preferably MRI, is advised in all people with CPH because underlying structural causes are reported (1). CXR and ESR might be wise if the history were shorter; a 10+ year history at age 58 rules out giant cell arteritis, and thoracic malignancy. The cervical spine and brachial plexus could be imaged to exclude an independent cause for the Horner's,

and the dorsal spine to interrogate the asymmetrical loin sweating. In fact, the patient had MRI of brain, cervical spine, and brachial plexus before neurological referral: no abnormality was found.

Best answer – MR brain scan.

Q3

Answer 6

Codeine/paracetamol combinations are never the right treatment of chronic headache. An oral triptan would be unlikely to work within the one hour duration of his pain and would be unlicensed as this is not migraine. Those favouring a diagnosis of CH might try subcutaneous sumatriptan, though this should be in addition to prophylactic treatment, of which verapamil is the first choice for CH. Amitriptyline is most neurologists' preferred drug for the prevention of tension-type headache, though efficacy is not high. Propranolol is unlikely to help because this is not migraine. An NSAID is worth considering; among the NSAIDs, indomethacin should be considered in all cases of daily, unilateral headache (2). The patient reported that indomethacin 50mg TDS "evaporated" his headache; he tolerates it without side effects, if he did not, then a cyclo-oxygenase-II (COX-II) antagonist could be tried. Lithium may be the prophylactic agent of first choice for chronic CH, and for hypnic headache (3); it did not abolish this patient's pain when used previously.

Best answer – Indomethacin

Q4

Answer: none of the above

The author does not know the answer to this question. This appears to be a physical sign that the patient has noticed, it is not a cause of disability. Relying on the maxim "Investigate symptoms, don't investigate signs, never investigate investigations", this has not been investigated. One of the last two suggestions must be correct. It is presumably not caused by the same lesion as the Horner's syndrome, which is caused by carotid dilatation, the consequence of severe chronic pain in the ophthalmic division of the trigeminal nerve (4), though the hypohidrosis suggests that the lesion is central.

Best answer – none of those suggested: one should not expect to understand or explain everything.

Learning point: "All cases of chronic unilateral daily headaches should receive an indomethacin trial early if not first in treatment" (2).

References

1. Matharu M, Goadsby P. Trigeminal Autonomic Cephalgias. *J Neurol Neurosurg Psychiatry* 2002;**72**(Suppl II):ii 19-26.
2. Peres M F P, Silberstein S D, Nahmias A L *et al.* Hemicrania Continua is not that rare. *Neurology* 2001;**57**:948-951.
3. Gould JD, Silberstein SD. Unilateral hypnic headache: a case study. *Neurology* 1997;**49**:1749-51.
4. Goadsby P J. Pathophysiology of cluster headache: a trigeminal autonomic cephalgia. *Lancet Neurology* 2002;**1**:251-257.

© 2003 Association of British Neurologists