Neurological infections

Physician Associate Teaching December 2021

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Consultant Microbiologist

Learning outcomes – PA curriculum

- Diagnose and initiate management of acute bacterial meningitis
- Diagnose and manage Lyme disease
- Diagnose and manage shingles
- Broadly understand about viral encephalitis
- Broadly understand how HIV affects the brain
- Awareness of prion disease, TB meningitis, syphilis and non-typical Lyme disease

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Overview

- Introduction to CNS infections
- Case studies
  - Meningitis – bacterial and viral
  - Viral encephalitis
  - Shingles
- Overview of other CNS infections
- Cerebrospinal fluid and its interpretation
- CSF interpretation workshop

Introduction:
Clinical presentations of CNS infections

- Meningitis
- Encephalitis/meningoencephalitis
- Abscess/Space occupying lesions
- Encephalopathy
- Congenital

How does infection enter the CNS?

- From blood
- Local extension of established infection
  - Bacteria from sinuses, teeth, middle ear
- Via direct implantation
  - traumatic, iatrogenic
- Trans-placental
- Along nerve fibres (Herpes simplex, shingles/herpes zoster, rabies)

The Blood Brain Barrier

- > 100 years ago Ehrlich discovered that if blue dye was injected into the bloodstream of an animal, the tissues of the whole body EXCEPT the brain and spinal cord would turn blue.
- To explain this, scientists thought that a "Blood-Brain-Barrier" (BBB) existed which prevents materials from the blood from entering the brain.

The Blood Brain Barrier

- Capillaries are lined with endothelial cells.
  - These usually have small spaces between them so substances can move readily in and out of the vessel.
  - but in the brain, the endothelial cells have tight junctions which prevent this
- Semi-permeable - allows some materials to cross, but prevents others.
- Hydrophilic molecules do not penetrate into the brain.
- Lipophilic molecules, such as barbiturate drugs, do so rapidly.

Functions of the BBB

- Protects the brain from substances in the blood that may injure the brain.
- Maintains a constant environment for the brain.
- Important consideration in antibiotic therapy.
- In meningeal inflammation, BBB is disrupted
  - Increasing CSF protein and cell count (immune response)
  - Increased entry of water-soluble antibiotics

Cerebrospial fluid (CSF)

- Brain and spinal cord are bathed in CSF
- When CNS infections are suspected, it is often useful to obtain a sample of CSF
- This is done by lumbar puncture (LP)

When isn’t it safe to LP?

- LP is contra-indicated if there is a possibility of a space-occupying lesion (SOL) in the brain, as there is a risk of ‘coning’
- CT scan should always be done first especially if:
  - Reduced GCS
  - signs of raised intracranial pressure (eg papilloedema)
  - Focal neurological signs

Other contraindications to LP

- Seizures (unless controlled)
- Clotting abnormality (anti-platelet agents?)
- Infection at LP site

Case 1

- 19 year old female student presented to GP at University Health centre

PC

Flu-like illness began yesterday

Fever, myalgia, headache, photophobia

PMH

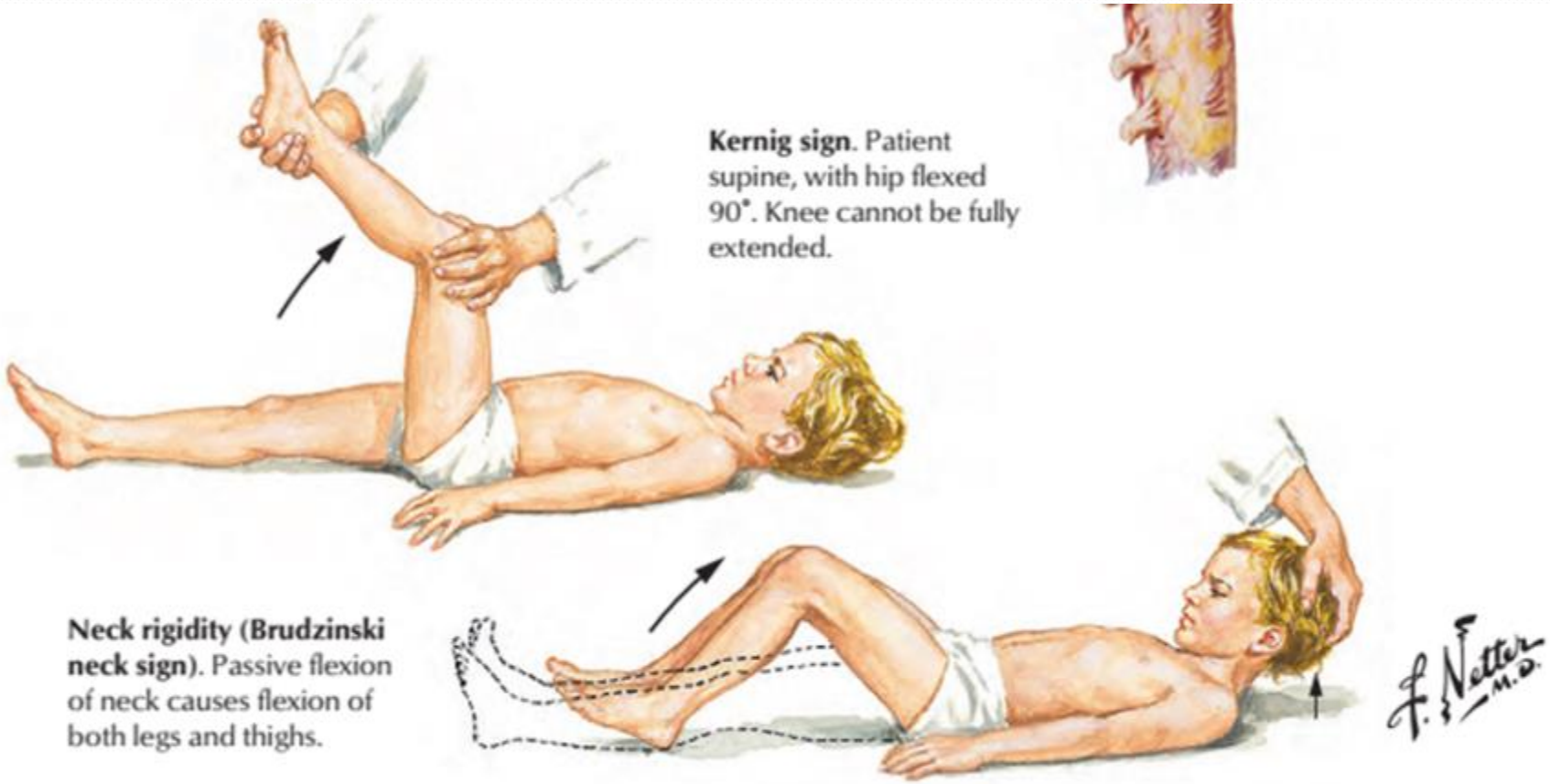
Nil.

Examination

- T = 37.5
- CVS
  - BP 95/55
  - HR 100
- Abdomen
  - Soft non-tender
  - Purpuric non-blanching rash
- RS
  - RR 18
  - Normal breath sounds
- CNS
  - Oriented though a little drowsy
  - No focal neurological signs
  - Neck stiffness
  - Kernig’s sign positive


Medrevise.co.uk


Source: Meningitis Research Foundation



Kernig sign. Patient supine, with hip flexed 90°. Knee cannot be fully extended.

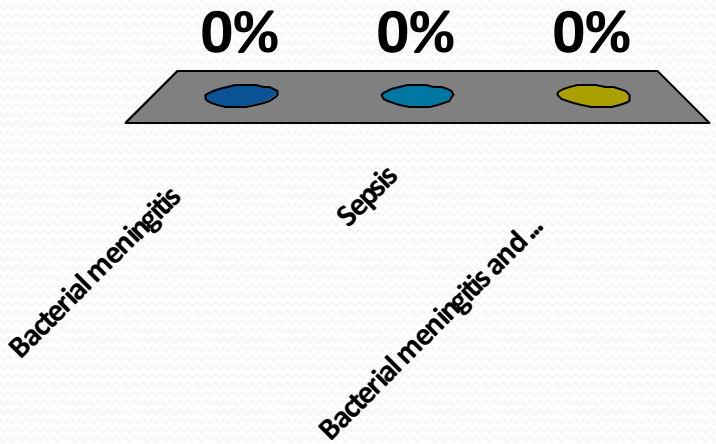
Neck rigidity (Brudzinski neck sign). Passive flexion of neck causes flexion of both legs and thighs.

F. Netter M.D.

https://www.grepmed.com/?q=brudzinski

What is the likely diagnosis?

A. Bacterial meningitis
B. Sepsis
C. Bacterial meningitis and sepsis



Meningism

- Symptoms/signs of meningeal irritation
  - Photophobia
  - Neck stiffness
  - Kernig's sign

Sepsis

- Purpuric rash
- Low BP

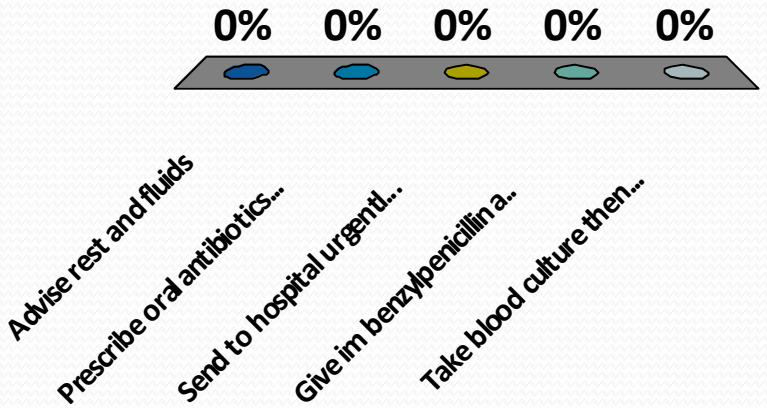
Bacterial meningitis: clinical presentation

- Acute onset
- Fever, headache, meningism
- Nausea, vomiting
- Drowsiness
- Seizures *not* common

- May or may not be accompanied by generalised sepsis as well as meningitis.
  - Purpuric rash may be evident

What should the GP do?

A. Advise rest and fluids
B. Prescribe oral antibiotics and review next day
C. Send to hospital urgently without delay
D. Give im benzylpenicillin and send to hospital urgently
E. Take blood culture then send to hospital urgently



Bacterial meningitis

- Medical emergency, important to recognise
- 100% mortality if untreated
- Neurologic sequelae ,e.g. deafness, are common

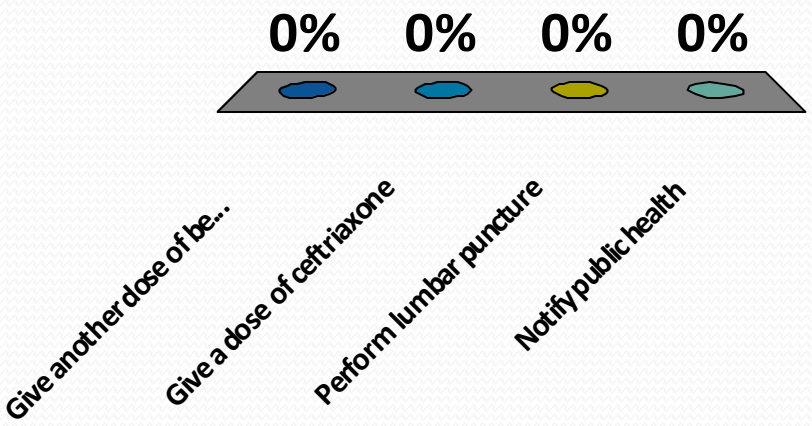
Treatment of suspected bacterial meningitis in primary care

- In primary care, give im benzylpenicillin and transfer urgently to hospital

- Upon arrival in hospital, the patient is assessed and a clinical diagnosis of bacterial meningitis and sepsis is made.
- She is stabilised in A&E

What is next step in management?

A. Give another dose of benzylpenicillin
B. Give a dose of ceftriaxone
C. Perform lumbar puncture
D. Notify public health



Management of bacterial meningitis

- Assessment and stabilisation
- Airway, Breathing, Circulation
- Seizure control
- Do not delay antibiotics
- LP when safe/no contra-indications
- Ventilatory/inotropic support
- Fluid management

Bacterial meningitis

- Common pathogens – adults
  - *Streptococcus pneumoniae* (pneumococcus)
    - Gram positive diplococci
  - *Neisseria meningitidis* (meningococcus)
    - Gram negative diplococci
  - *Listeria sp* (elderly, immunocompromised)
    - Gram positive bacilli

Empirical Treatment of bacterial meningitis in secondary care

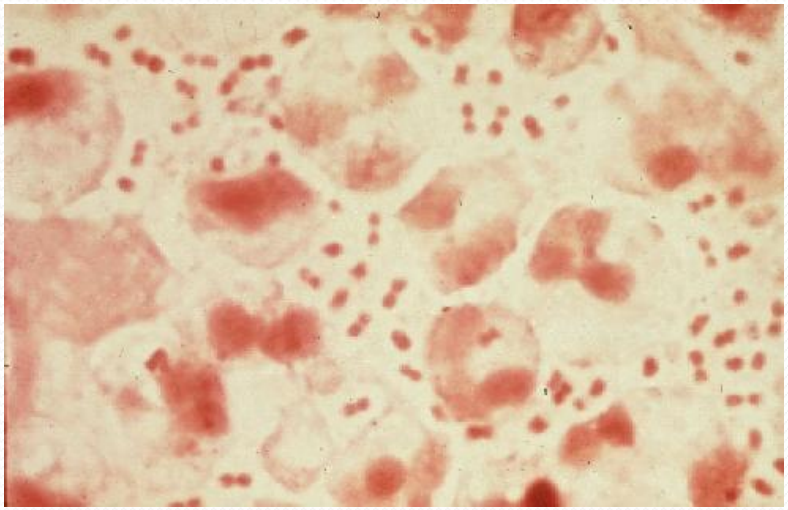
- Adults:
  - iv Ceftriaxone 2g
  - In following groups, also add iv ampicillin
    - ‘elderly ‘ – age >60
    - Immunocompromised
    - This is because of risk of *Listeria* infection

In hospital: investigations

- Blood culture
- CSF
  - microscopy, culture & sensitivities
  - Protein
  - Glucose
  - PCR for *N. meningitidis & S. pneumoniae*
- Throat swab for culture for *N. meningitidis*
- EDTA blood for PCR for *N. meningitidis & S. pneumoniae*

CSF results

- Cloudy CSF
- Gram stain: Gram negative diplococci seen
- WCC: 750, predominantly polymorphs (neutrophils)
- RCC: 15
- Protein: 1.2 g/l (H)
- Glucose: 2 mmol/l (L)



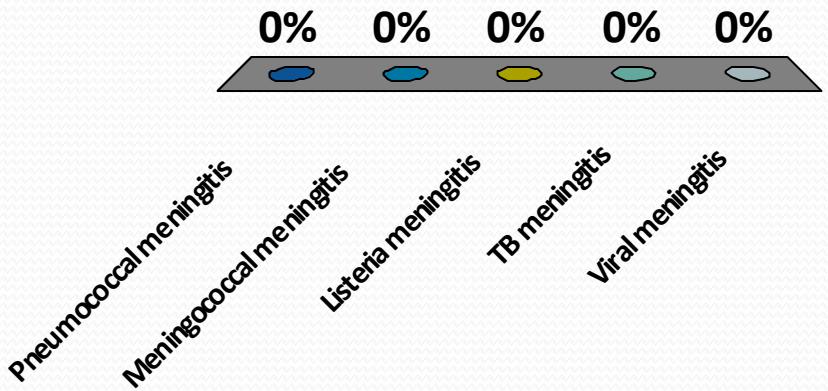
CSF changes in bacterial and viral infections

	Normal	Bacterial	Viral
Opening pressure	15-22 cm CSF	High	Normal / high
Cell count	<3 WBC	100-50000	5-1000
Differential	None / lymphocytes	Neutrophils	Lymphocytes
Glucose CSF:serum ratio	>50%	<40% (ie CSF glucose low)	Normal
Protein	<=0.45g/l	High, >1 g/l	Normal to high, 0.5-1 g/l

From: T. Solomon et al., Journal of Infection. 2012. 64:347

What is the likely diagnosis?

A. Pneumococcal meningitis
B. Meningococcal meningitis
C. *Listeria* meningitis
D. TB meningitis
E. Viral meningitis



Bacterial meningitis - neonates

- Off feeds
- Floppy
- Irritable
- Crying – high-pitched
- drowsy

Common pathogens – neonates

- Group B streptococcus
- *Escherichia coli*
- *Listeria sp*

Empirical treatment of suspected meningitis – neonates/infants

- First 3 months: ampicillin plus cefotaxime
- >3 months – iv ceftriaxone

Role of corticosteroids

- Much discussed, benefits are uncertain
- In adults, given prior to or along with first dose of antibiotics, may be beneficial in terms of hearing loss, neuro sequelae and deaths
- Dexamethasone 10mg stat is recommended (BIA/PHE)

- Do not use <3 months old
- In older children dexamethasone if:
  - CSF WCC >1000
  - very high protein
  - positive Gram stain (NICE)

Public health aspects

- Notifiable to public health
- Close contacts are given antibiotic prophylaxis to eradicate throat carriage, unless contra-indicated
- Contacts must be made aware of signs and symptoms to watch out for

- Isolate hospital patients with meningococcal meningitis until had ceftriaxone for 24 hours

Prevention

- Immunisations:
  - *Haemophilus influenzae*
  - Meningococcus C and B
  - *Streptococcus pneumoniae*

- Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management: NICE guidelines [CG102] Published date: June 2010

  http://www.nice.org.uk/guidance/cg102/chapter/1-recommendations#pre-hospital-management-of-suspected-bacterial-meningitis-and-meningococcal-septicaemia

- British Infection Association/Meningitis Research Foundation guidance for suspected bacterial meningitis in adults:

  http://www.meningitis.org/assets/x/51738

https://www.antibioticaware.com

AWARE Home | AWARE project | Medical Students | News | Cymraeg | Contact

Follow

Infection & Antibiotics for Medical Students

This webpage has been set up to provide a virtual learning resource about infection and antibiotics for medical and physician associate students. Scroll down or click here to find a variety of useful resources, guidelines, games and lecture slides.

New! 'One Minute Micro'

1-2 minute revision video animations on clinical microbiology.
Use with the 'Bugs' and 'Drugs' cribsheets

BIAMM British Infection Association

Public Health England

The Royal College of Emergency Medicine

intensive care society

ASSOCIATION OF BRITISH NEUROLOGISTS

sam

Meningitis Research Foundation

Early Management of Suspected Meningitis and Meningococcal Sepsis in Immunocompetent Adults

3rd Edition
Jan 2016

Early recognition is crucial

Consider meningitis or meningococcal sepsis if ANY of the following are present:

- Headache
- Fever
- Altered Consciousness
- Neck Stiffness
- Rash
- Seizures
- Shock

Warning Signs

The following signs require urgent senior review +/- Critical Care input:

- Rapidly progressive rash
- Poor peripheral perfusion
  - Capillary refill time > 4 secs, oliguria or systolic BP < 90mmHg
- Respiratory rate < 8 or >30 / min

- One Minute Micro 6. Meningitis (adobe.com)

Viral meningitis

- Commonest cause of meningitis in all ages
- usually self-limiting
- May be preceded by sore throat
- Headache, nausea, vomiting, meningism
- No alteration in consciousness, no neuro signs
- CSF
  - Lymphocytes
  - Normal protein
  - Normal glucose

Viral meningitis - management

- Symptomatic – analgesia, fluids
- Self-limiting

Causes of viral meningitis

- **Enteroviruses -** young children commonly shed in stool

- Mumpsvirus
- Many others, less commonly

- Diagnosis:
  - Role of CSF is to exclude bacterial infection
  - If CSF taken, send for enterovirus PCR
  - Stool and throat swabs for enterovirus PCR

Poliovirus

- Was common in young children
- Neuro complications much commoner in teens/young adults (10%) – problem as hygiene improved in 20th Century so infections occurred later in life
- paralysis and limb-wasting, with death from respiratory failure in 5-10%

John Prestwich, BBC photo

Evan Kirstel #RemoteWork @EvanKirstel · Nov 25

Children in an iron lung before the advent of the **polio vaccination** in 1937 😞 Many children lived for months in these machines, though not all survived #VaccinesWork #vaccines #wednesdaythought @IrmaRaste @eViRaHealth

6 29 34

Poliovirus

- Enterovirus
- Can cause infection and death of anterior horn cells of the spinal cord

Polio eradication?

- Global polio eradication initiative
- ?will it be second human disease to be eradicated

- Afghanistan, Pakistan and Nigeria hav transmission of endemic wild poliovir
  - 21 cases in 2017
  - 29 cases in 2018
  - 168 cases in 2019
  - 169 cases in 2020 (Pakistan and Afghanistan)

POLIO GLOBAL ERADICATION INITIATIVE

every last child

25/08/2020

Africa Kicks Out Wild Polio

Visit the "Africa Kicks Out Wild Polio" website for content on the WHO African Region's efforts to eradicate wild polio.

WHO Pakistan @WHOPakistan · Oct 2

In the fight against polio, more than 260,000 frontline workers travel miles and defy all odds to reach each & every child that needs **polio vaccination**! #WHOPakistan recognises their contributions and salutes their selfless efforts in achieving #poliofreePakistan.

5 35 82

Dr Nirmal Kandel #VaccineSocialism @kandelnirmal · Sep 2, 2020

A vaccinator from #Nepal ensuring continuity of essential service of #immunization despite #pandemic and #disaster.
Video source: Pratima Koirala and thank you for your hard work and commitment.🙏 @vismitag @gabbystern @supriyabez

14 272 692

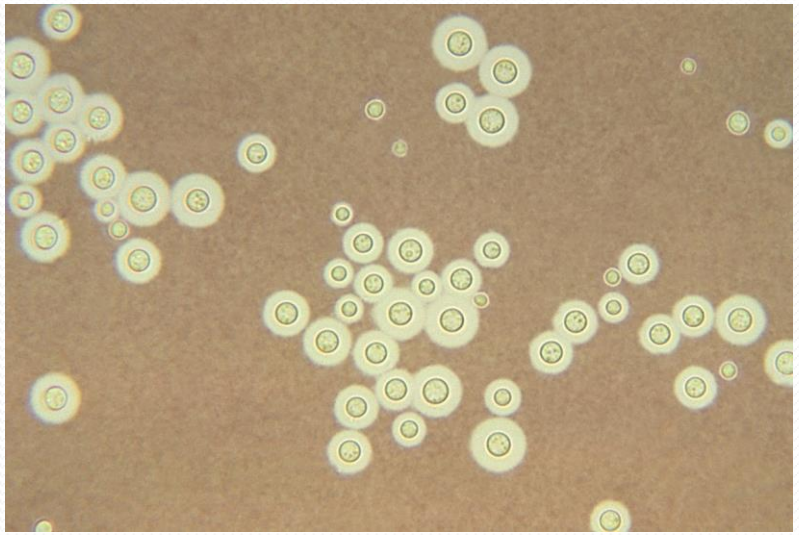
Tuberculous meningitis

- Gradual insidious onset
- Fevers, sweats, headache, meningitic symptoms over several weeks
- Typical CSF findings
  - Lymphocytic picture
  - Greatly elevated protein, may be up to 5g/l
  - Reduced glucose
  - Culture for mycobacteria is the most sensitive test
  - PCR also available

Fungal meningitis

Cryptococcus neoformans

- In HIV AIDS/transplant recipients
- Diagnosis is by
  - India Ink stain
  - CSF cryptococcal antigen test
  - blood serology
- Treatment: amphotericin + flucytosine



Wikipedia

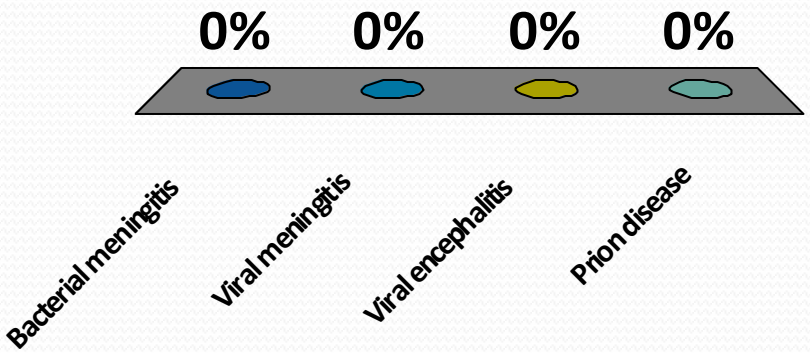
Case 2

- A previously well 32 year old man presents with headache lasting 24 hours, fever and confusion

- On examination he has a fever of 37.9°c, and is disorientated in time and place
- There is no meningism
- During the examination, he suffers a generalised seizure

What is your working diagnosis?

A. Bacterial meningitis
B. Viral meningitis
C. Viral encephalitis
D. Prion disease



Viral encephalitis

- Confusion
- headache
- Fever
- Seizures

Viral encephalitis

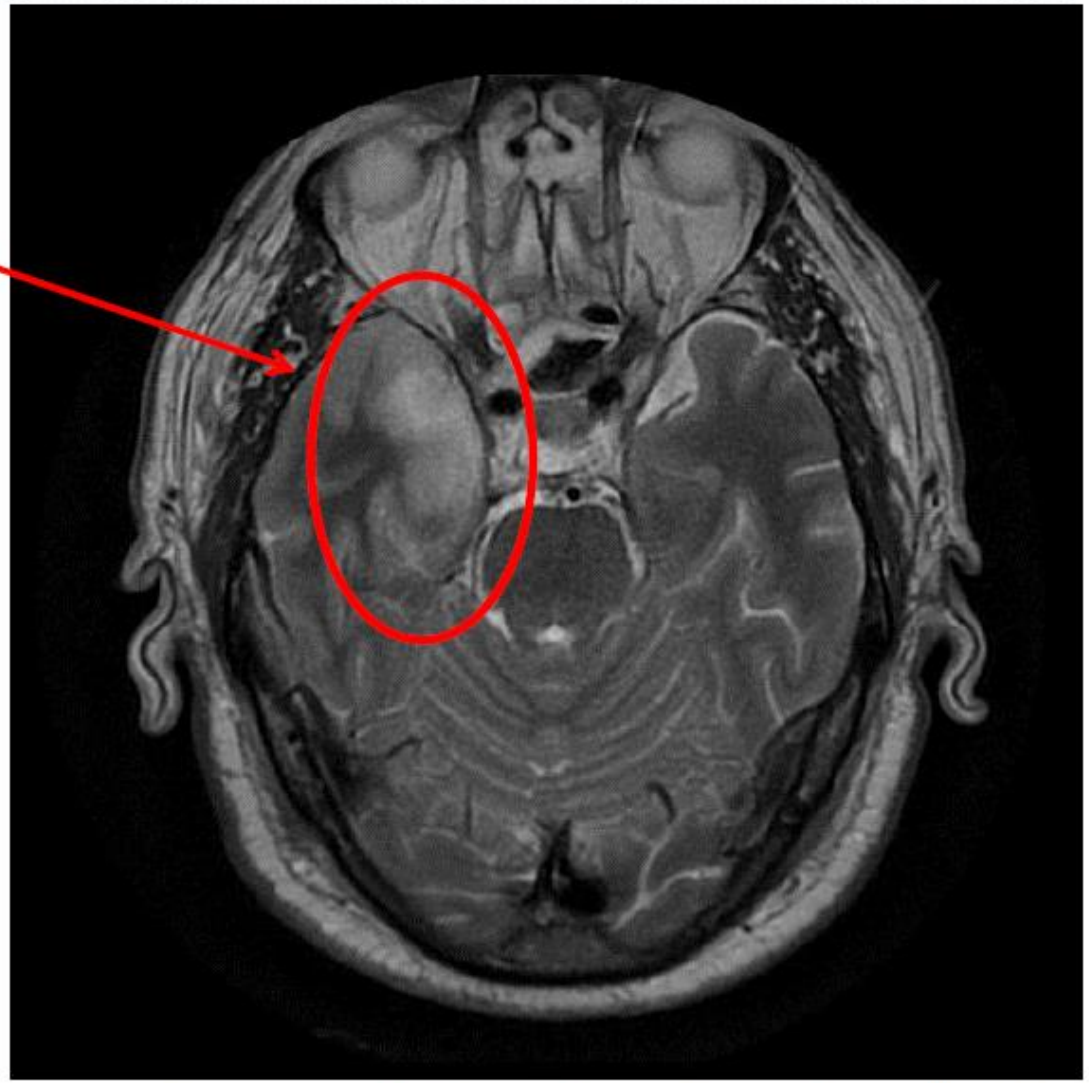
- **Herpes simplex virus type 1 is commonest cause in UK**

- Investigations:
  - Routine bloods – usually normal
  - **MRI brain** – usually abnormal (CT may be normal)
  - EEG (electroencephalogram) – often abnormal
  - **LP – lymphocytosis, PCR for HSV**

  Consider: HIV test all cases

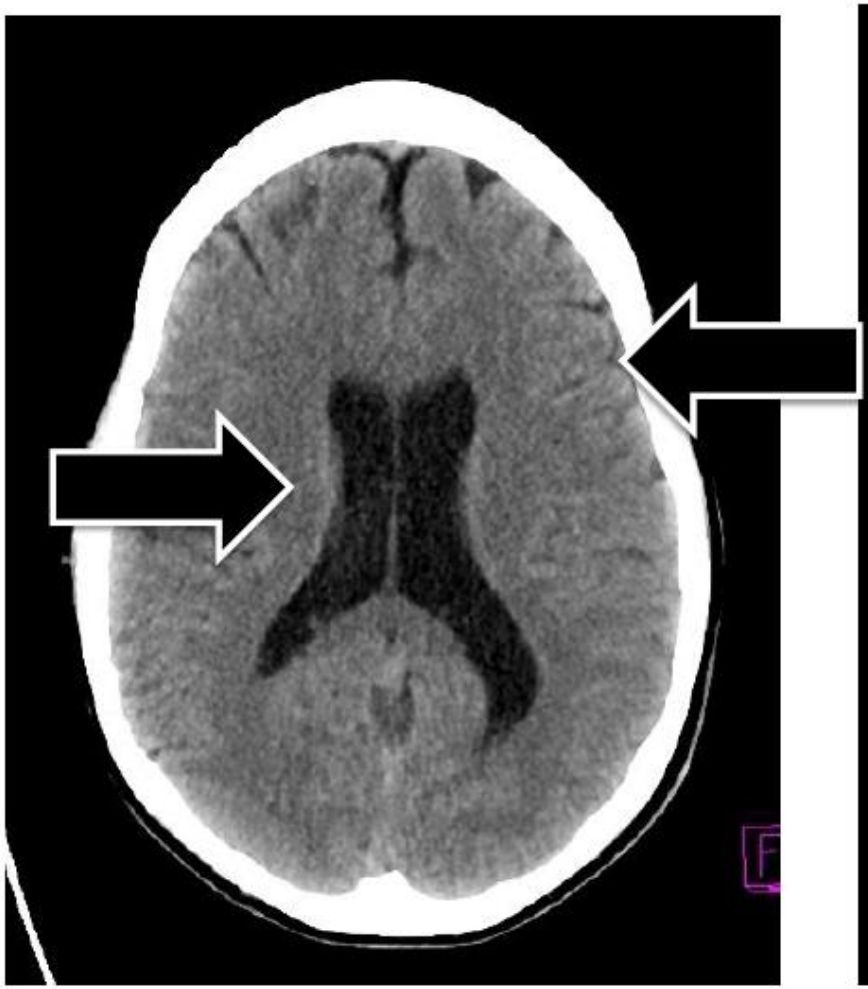
Imaging

- Signal change in medial temporal lobe
- CT useful to confirm safe to LP but too insensitive to demonstrate temporal lobe changes

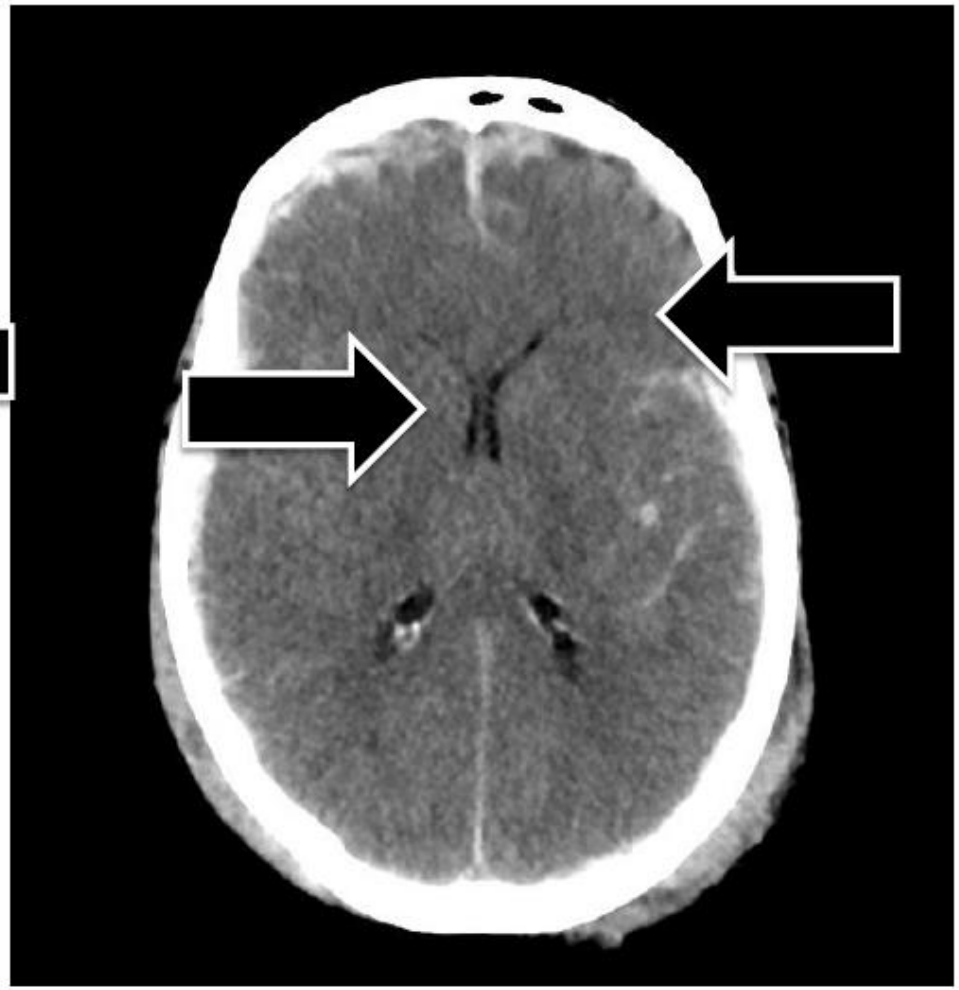


Case courtesy of Dr Andrew Dixon, Radiopaedia.org, rID: 35410

Cerebral swelling



Case courtesy of UoE Radiology, Radiopaedia.org, rID: 34158



Case courtesy of Dr Craig Hacking, Radiopaedia.org, rID: 41473

Viral encephalitis: CSF findings

- Lymphocytosis
- Normal glucose
- Protein may be elevated, 0.5 – 1 g/l
- PCR for HSV - positive

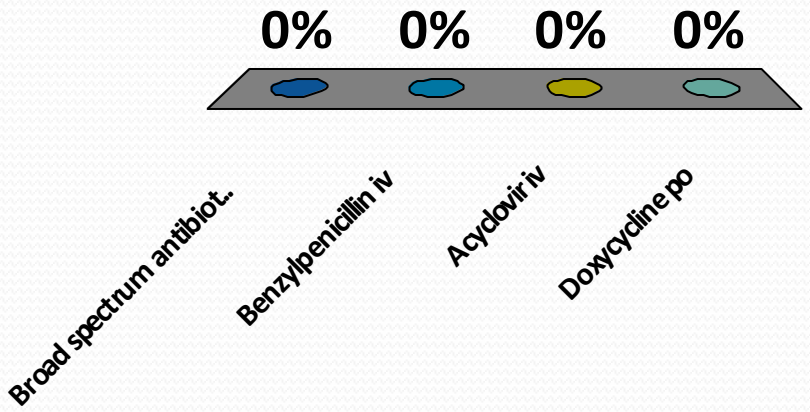
Meningitis versus encephalitis*

	Meningitis	Encephalitis
Headache	Yes	Yes
Fever	Yes	Yes
Meningism	Yes	No
Clouding of mentation	No	Yes
Focal neurological signs	No	Yes
Seizures	Rare	Common

*Some patients have a mixture - meningoencephalitis

How would you treat this patient?

A. Broad spectrum antibiotic iv
B. Benzylpenicillin iv
C. Acyclovir iv
D. Doxycycline po



Treating HSV encephalitis

- Manage seizures

- Acyclovir for 14 days (longer if immunosuppressed)
- After 14 days repeat LP for viral PCR
- If still positive, treat for further 7 days

- 14% mortality even when treated
- Neuropsychatric sequelae in 24%

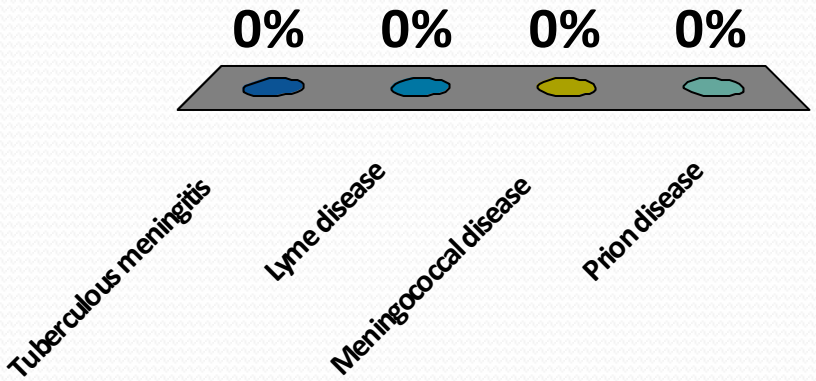
Case 3

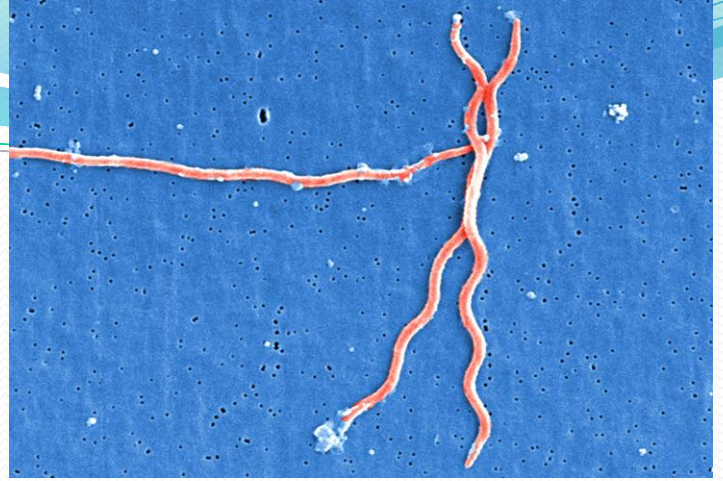
- A 47 year old woman presents with a facial nerve palsy lasting several months
- She has also consulted the GP for depression in the last couple of months
- A few months ago she had been camping in the countryside and suffered an insect bite followed by a rash

- She is referred to a neurologist who carries out some investigations:
- CSF:
  - No organisms seen
  - WCC 250/L – predominantly lymphocytes
  - RCC 5
  - Protein 0.8 g/l
  - Glucose – normal range

Which of these is most consistent with the history and CSF findings?

A. Tuberculous meningitis
B. Lyme disease
C. Meningococcal disease
D. Prion disease





Lyme Disease

- Spirochaete: *Borrelia burgdorferi*
- Transmitted by tick bites
- Characteristic erythema migrans rash often appears at site of bite
- Grows in size, expanding and

centre may clear leading to ‘target’ appearance

Journal of Family Medicine
10.14302/issn.2640-690X.jfm-18-2067

Concern about rise in UK Lyme disease cases

Monday October 12 2015

"Surging numbers of people are being diagnosed with Lyme disease as cases spread from rural areas to the suburbs," the Daily Mail reports.

The tick bite leaves a distinctive bull's eye rash

The ongoing rise in Lyme disease cases in the UK – thought to be driven by climate change, leading to warmer winters – has been known by public health officials for some time. Reported cases in England and Wales rose from 268 in 2001 to 959 in 2011, but the true figure is thought be much higher. Current estimates put the actual figure at around 3,000 cases a year in England and Wales.

It may also be the case that the disease is, as the Mail puts it, "moving into the suburbs," or least into the parks. A recent study from September 2015 found ticks that could potentially carry infection in two South London parks: Richmond Park and Bushy Park.

Lyme disease – further course

- Flu-like illness: fever, joint and muscle pains, fatigue
- After weeks/months/years can include arthritis, arrhythmias/pericarditis or conjunctivitis
- Neuroborreliosis: Nervous system involvement may occur after weeks, months or years and may include:
  - Meningitis/meningoencephalitis
  - Bell's palsy - facial nerve palsy
  - Encephalopathy/cognitive problems
  - Neuropsychiatric – mood changes/depression

Lyme disease

- Diagnosis:
  - Usually by blood serology (ELISA with Western blot to confirm)
  - CSF PCR is sometimes carried out but not v. sensitive

- Treatment:
  - Early stage: Doxycycline orally for 2 weeks
  - Neurological disease: Ceftriaxone iv for 2 weeks

Long-term Lyme disease 'actually chronic fatigue syndrome'

10 October 2019

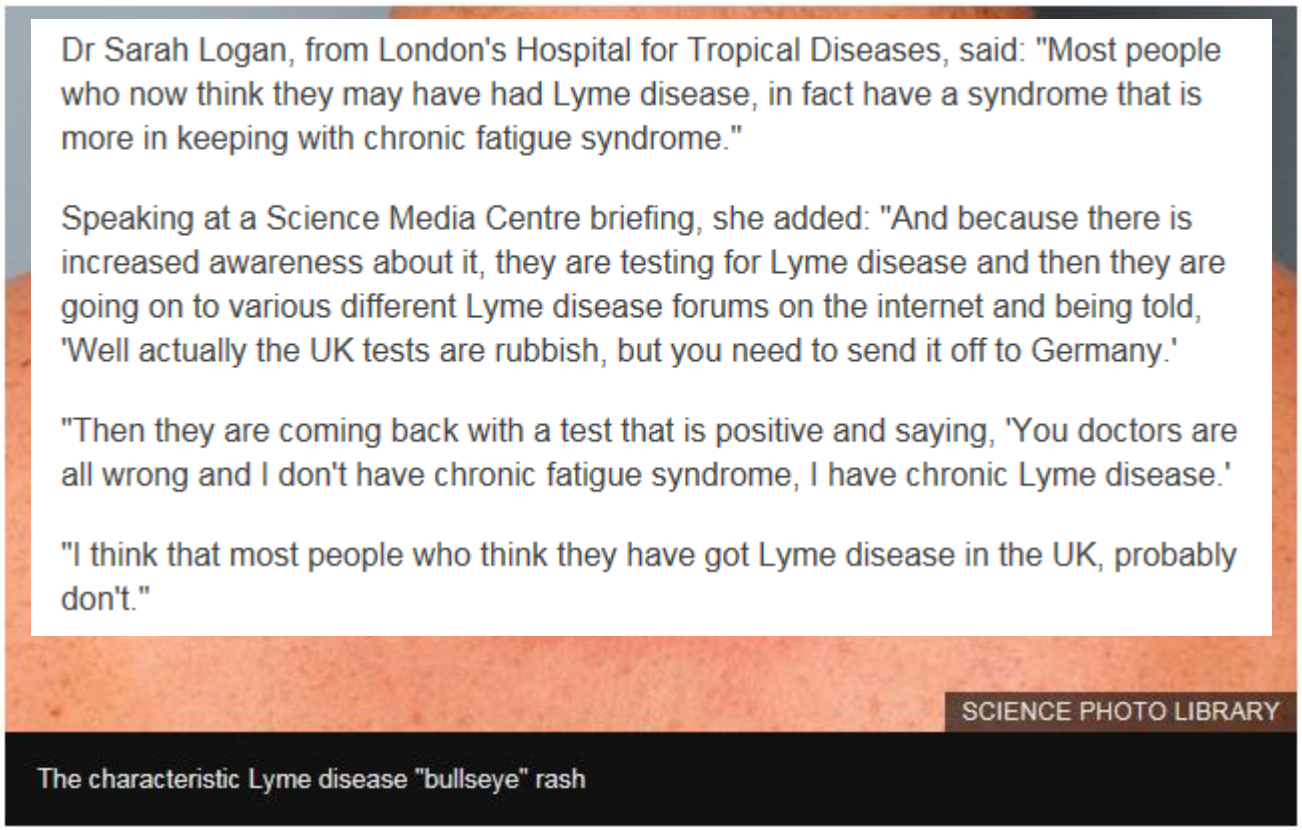
Share

Dr Sarah Logan, from London's Hospital for Tropical Diseases, said: "Most people who now think they may have had Lyme disease, in fact have a syndrome that is more in keeping with chronic fatigue syndrome."

Speaking at a Science Media Centre briefing, she added: "And because there is increased awareness about it, they are testing for Lyme disease and then they are going on to various different Lyme disease forums on the internet and being told, 'Well actually the UK tests are rubbish, but you need to send it off to Germany.'

"Then they are coming back with a test that is positive and saying, 'You doctors are all wrong and I don't have chronic fatigue syndrome, I have chronic Lyme disease.'

"I think that most people who think they have got Lyme disease in the UK, probably don't."



The characteristic Lyme disease "bullseye" rash

The majority of people who believe they have a chronic form of Lyme disease are more likely to have chronic fatigue syndrome, experts suggest.

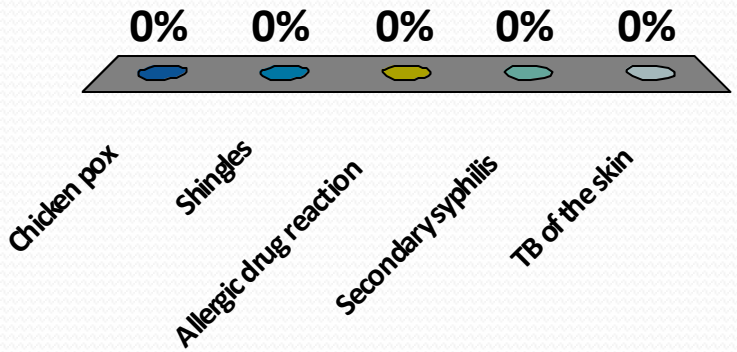
Case 4

- A 73 year old man is seen in rheumatology clinic
- He has recently taken steroid treatment for his condition
- He complains of rash which started 5 days ago
- It is painful and blistering

Viruses and Human Disease. (2021, March 6). https://bio.libretexts.org/@go/page/6612

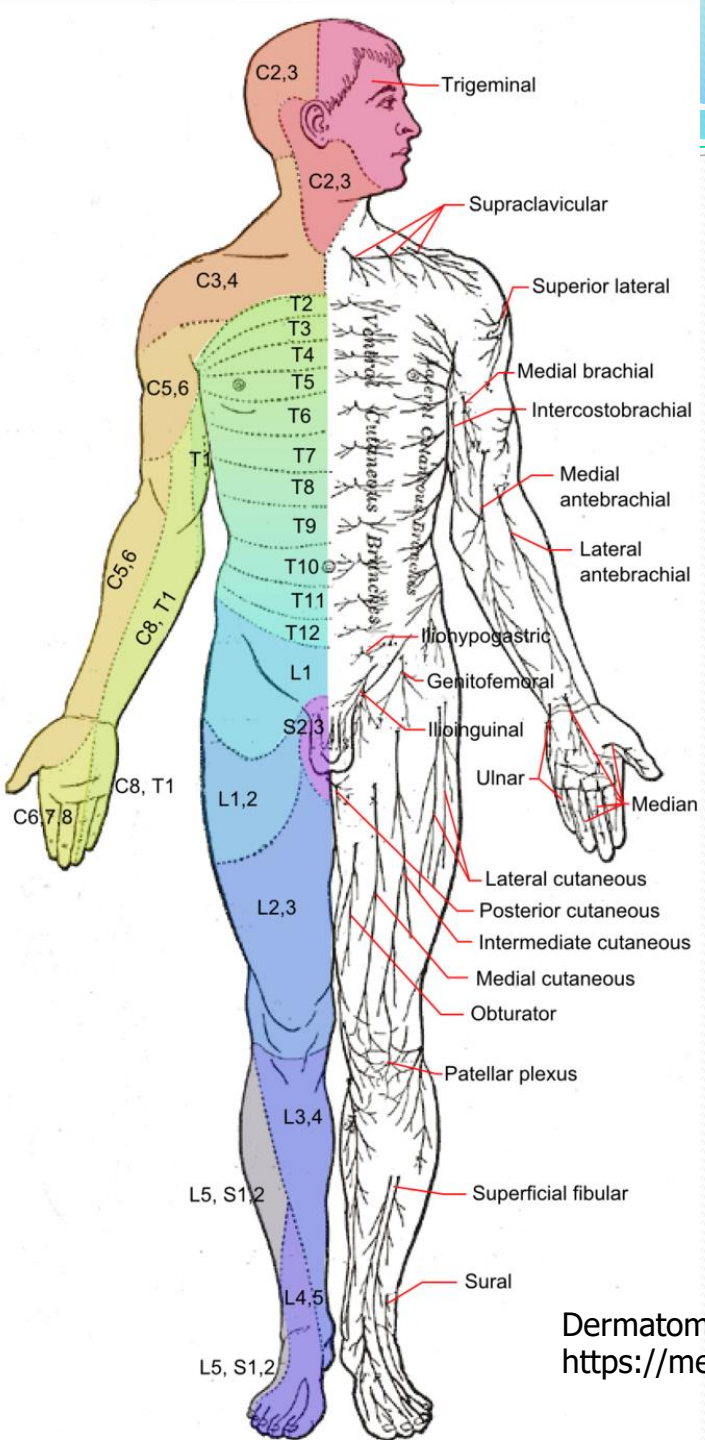
What is the diagnosis?

A. Chicken pox
B. Shingles
C. Allergic drug reaction
D. Secondary syphilis
E. TB of the skin



Shingles

- Caused by Varicella Zoster Virus (VZV), which causes chickenpox when first acquired
- Virus remains latent in spinal nerves lifelong
  - (all herpes group viruses remain latent lifelong)
- Immunosuppression /ageing causes it to reactivate and travel down peripheral nerves
- Causes a blistering rash in a *dermatomal distribution*



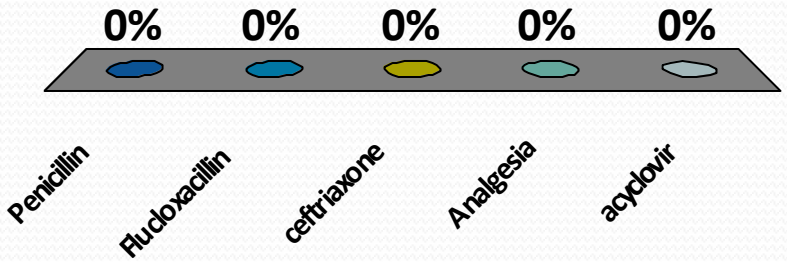
Dermatomes. (2020, August 14). https://med.libretexts.org/@go/page/7685

Shingles - diagnosis

- Usually a clinical diagnosis
- Serology unhelpful as 95% UK adults are seropositive for VZV as a past infection
- If need to confirm, blister fluid should be placed on a slide and sent for electron microscopy

How should he be treated?

A. Penicillin
B. Flucloxacillin
C. ceftriaxone
D. Analgesia
E. acyclovir



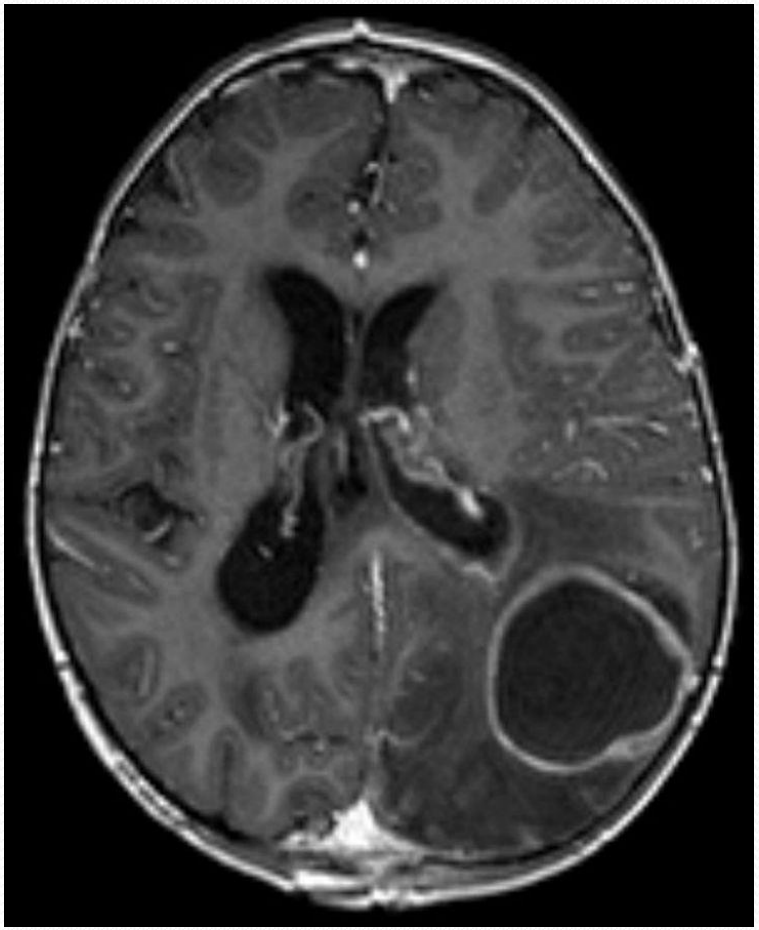
Shingles - treatment

- Painkillers – eg paracetamol
- Calamine lotion may bring some relief
- Oral acyclovir helps the infection to resolve more quickly and relieves symptoms
  - Start within 72 hours of rash
  - >50 years old/immunosuppressed/severe

Shingles – infectivity

- infectious if rash is weeping/oozing and not covered up by clothing

Brain abscess & Space Occupying Lesions



Bacterial brain abscess

- Most follow a bacteraemia e.g. from
  - Infective endocarditis
  - Congenital heart disease
  - Bronchiectasis
- Contiguous spread from adjacent bone/sinuses
  - Mastoid cavity
  - Middle ear

Clinical features

- Fever in ~50%
- Headache:
  - Worse on lying down
- Localising neuro signs
- Seizures
- Reduced consciousness/vomiting in ~50%
- Papilloedema in ~50%

Diagnosis

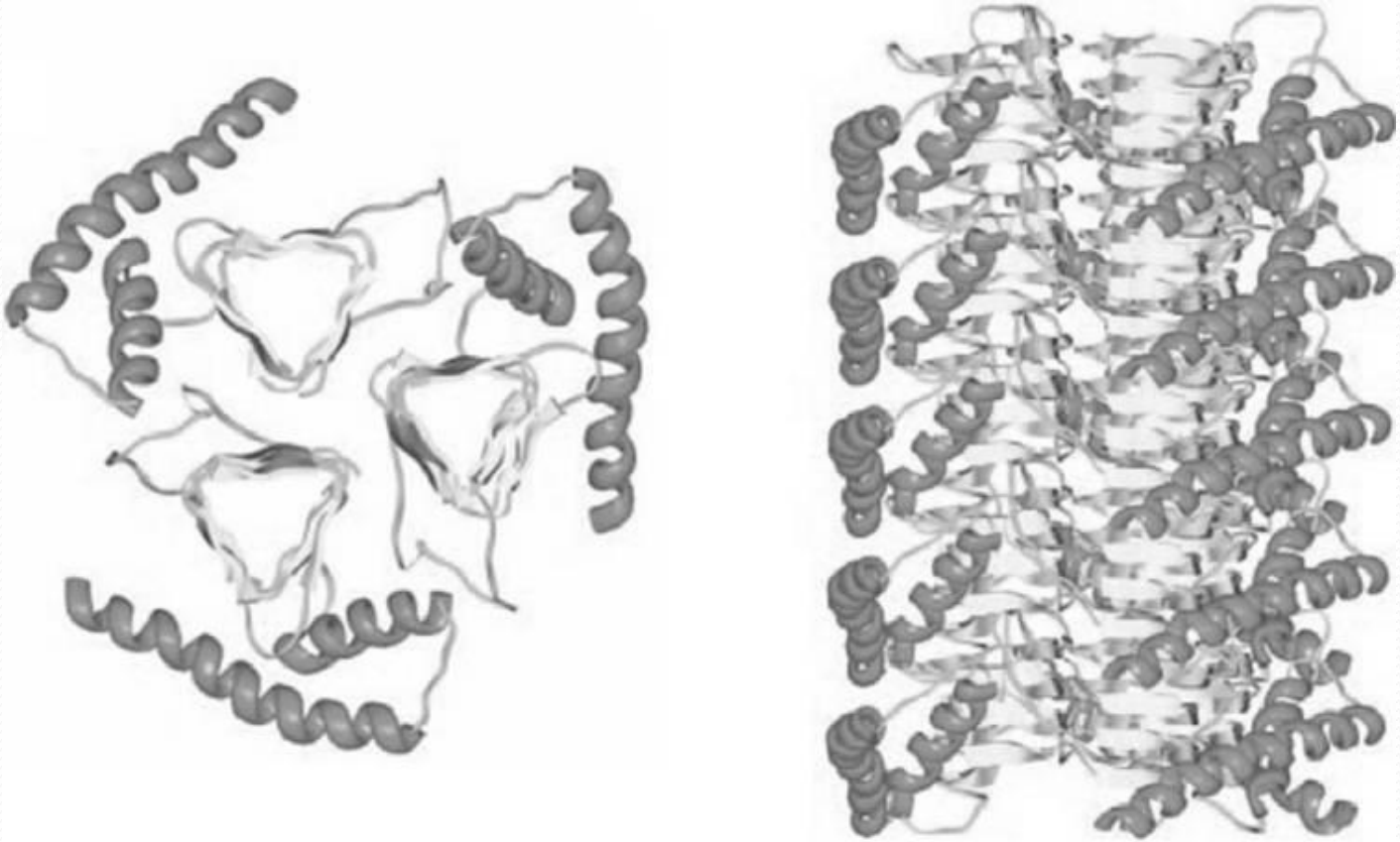
- Radiology
- Blood cultures
- ?needle aspiration/surgical drainage

- *Do not perform LP*

Treatment

- Surgical/radiological drainage, if possible, unless v small
- Broad spectrum antibiotics which penetrate the BBB and include cover for anaerobes
- Suitable empiric regimens include:
  - Cefotaxime + metronidazole
  - meropenem

Prion diseases



TSEs – Transmissible Spongiform Encephalopathies

- Bovine Spongiform Encephalopathy
- Scrapie
- Creutzfeldt-Jakob Disease
- Variant CJD (vCJD)
- Kuru
- Fatal Familial Insomnia

Kuru

- Papua New Guinea 1950's -60's
- Epidemic of 'kuru' ('shivers')
- Women and children most affected
- Ritualistic funerary consumption of human remains, especially brain
- Thought to have originated c 1900 when a single individual with sporadic CJD was consumed
- Declined after government efforts to discourage the practice
- Last case died 2005

Creutzfeld-Jakob Disease (CJD) – clinical features

- Early: psychiatric or sensory symptoms, commonly depression/apathy/anxiety
- Later: Neurological signs, including unsteadiness, difficulty walking and involuntary movements; eventually becoming completely immobile and mute.
- Universally fatal

BBC Home

ON THIS DAY 1950 - 2005

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1990: Gummer enlists daughter in BSE fight

The government has again attempted to reassure the public that British beef is safe, despite growing fears over the cattle disease, Bovine Spongiform Encephalopathy (BSE).

The Minister of Agriculture, John Gummer, even invited newspapers and camera crews to photograph him trying to feed a beefburger to his four-year-old daughter, Cordelia, at an event in his Suffolk constituency.

Although his daughter refused the burger, he took a large bite himself, saying it was "absolutely delicious".

> "Beef can be eaten safely by everyone, both adults and children, including patients in hospital"
> Chief Medical Officer Sir Donald Acheson

His reassurances were echoed by the government's Chief Medical

Watch/Listen

John Gummer tried to feed his daughter a beefburger to try to convince the public

PLAY VIDEO

BBC news report on the crisis

In Context

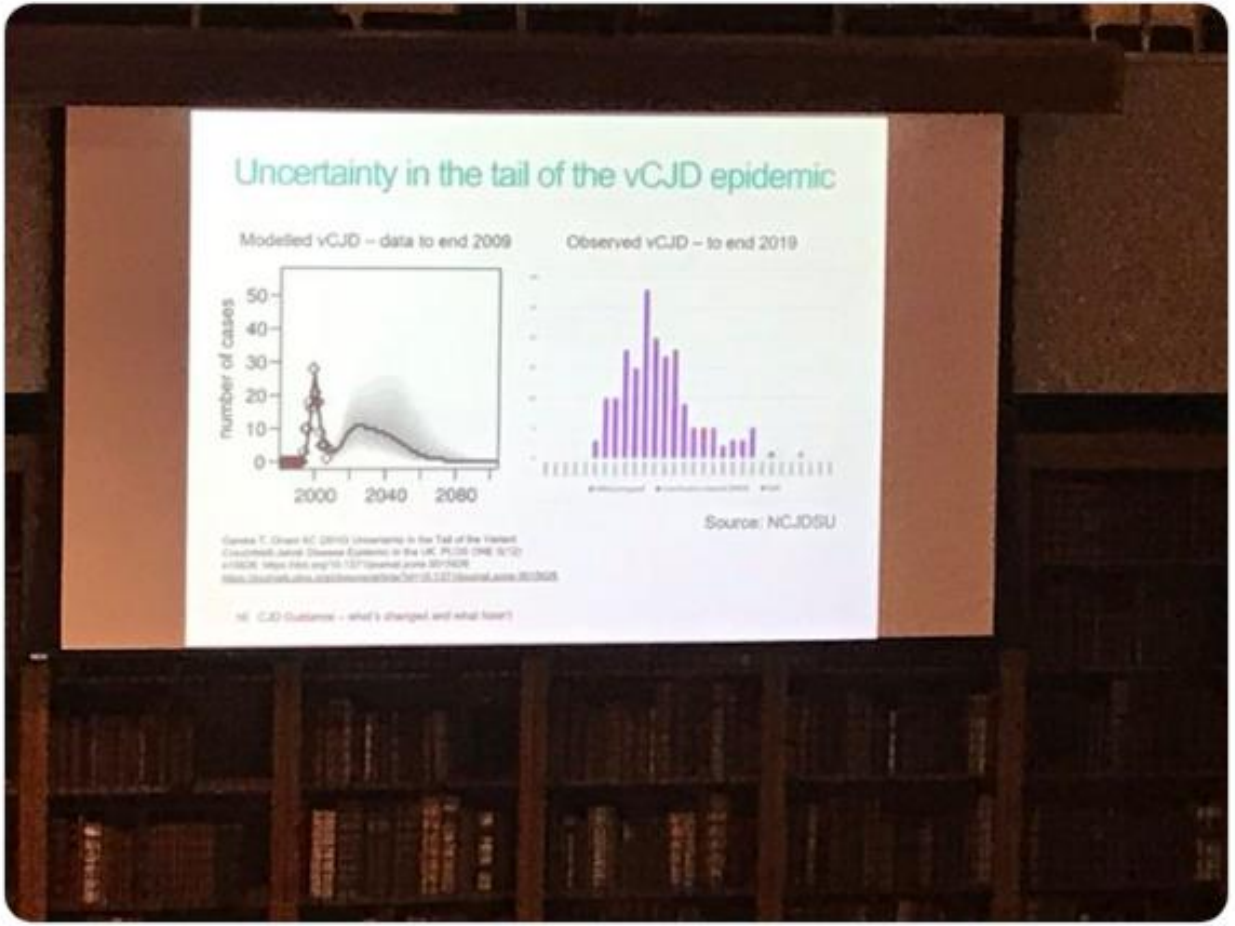
By 1992, three cows in every 1,000 in Britain had BSE.

John Gummer's attention-grabbing photocall rebounded dramatically when, in 1996, the government was finally forced to admit there was a link between BSE and the human form of the disease, new variant CJD.

175 cases of vCJD were reported in the United Kingdom of Great Britain and Northern Ireland (United Kingdom), and 49 cases in other countries from October 1996 to March 2011

Healthcare Infection Society
@HIS_infection

"No evidence of a vCJD second wave yet" reports Dr Katy Sinka @PHE_uk during the #HISevents #DIPCday



Prions in healthcare settings

- They resist disinfection & standard sterilisation –very difficult to destroy
- They can be transmitted on surgical instruments even after standard sterilisation
- They can be transmitted by WBC in blood transfusions
- Instruments used on patients with possible prion disease or otherwise high risk should be single use wherever possible or else destroyed - specialist advice needed

https://www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group

Neurosyphilis

- Syphilis is a sexually transmitted infection (STI) caused by spirochaete *Treponema pallidum*
- Had become rare in UK, now on the rise again
- Primary
- Secondary
- Tertiary
- Congenital

- ‘the great imitator’

Acta Derm Venereol 2013; 93: XX–ZZ

Stages of syphilis

- Primary – chancre
- Secondary – generalised rash

Streight, K.L., Paranal, R.M. & Musher, D.M. The oral manifestations of syphilitic disease: a case report. *J Med Case Reports* **13,** 227

- Tertiary – years later
  - Gummatous
  - cardiovascular
  - Neurosyphilis
- Congenital –Women tested in 1st trimester of pregnancy, if positive can be treated

Neurovascular syphilis

- 10-20 years after acute infection
- General paresis (‘GPI’ – ‘general paresis of the insane’)
  - Dementia
  - tabes dorsalis – balancing difficulties, pain
  - Argyll Robertson pupils

Diagnosis

- Serological testing blood and CSF

Treatment

- penicillin

Zika-linked condition: WHO declares global emergency

By Michelle Roberts
Health editor, BBC News online

1 February 2016 | Health

Getty Images

The virus is linked to thousands of cases of microcephaly in Brazil

A disease linked to the Zika virus in Latin America poses a global public health emergency requiring a united response, says the World Health Organization.

Zika virus

Zika outbreak: What you

Neurological complications of HIV

- Usually when disease has progressed to AIDS
- About half of adults with AIDS have neurological complications
- Antiretroviral treatment helps prevent progress to AIDS and neurological disease

Neurological disease in HIV

- HIV-associated dementia/AIDS dementia complex
- Viral infections
  - Cytomegalovirus, shingles, PML
- Fungal infections – Cryptococcal meningitis
- Peripheral neuropathy
- Lymphomas – often in brain
- Anxiety/depression
- Vacuolar myelopathy – tiny holes in spinal cord fibres
  - Difficulty walking

Post-infectious NS syndromes

- Acute polyneuritis: Guillain-Barré syndrome
- Progressive ascending symmetrical paralysis
- Inflammatory demyelination – an immune response
- weakness of legs can culminate in almost total paralysis over 2-3 weeks, requiring ventilation
- Usually make good recovery
- Treatment – supportive, immunoglobulin & plasmapheresis
- Causes: *Campylobacter*, HIV, Cytomegalomvirus, Epstein-Barr virus, 'flu-like illness'; rarely, others, and vaccinations

Summary

- CNS infections manifest in many different ways
- Viral meningitis is common but self-limiting
- Bacterial meningitis and viral encephalitis are serious and not uncommon in UK – important to recognise
- Prion diseases raise a number of very complex issues around hospital decontamination/sterilisation/blood products
- A number of infections cause devastating neurological effects if transmitted to foetus in pregnancy

Interpreting CSF results

- Gram stain – should be negative – sterile site
- WBC
  - Lymphocytes seen in early bacterial infection or in viral or TB infection
  - Neutrophils seen later in bacterial infection
- RBC
  - indicators of haemorrhage...
  - ...or a 'bloody tap'
- Protein
  - elevated in bacterial meningitis; greatly so in TB meningitis
  - Normal in viral meningitis
- Glucose CSF: serum ratio
  - Should be >60%: low CSF glucose in bacterial infection, normal in viral

CSF interpretation – normal:

- opening pressure 10-20cm H_2O
- Appearance: Clear & colourless
- White Cells

  $0 – 5 \times 10^6$ per litre (all lymphocytes, with no neutrophils)
- Red Cells

  $0 – 10 \times 10^6$ per litre
- Protein

  <0.45 g/l
- Glucose CSF: serum ratio

  >60%

Interpreting CSF results

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

Some causes of CSF lymphocytosis

- Tuberculous meningitis (high protein, low gluc)
- Partially treated/early bacterial meningitis
- Lyme disease
- Viral encephalitis
- Lymphocytic leukaemias

CSF from a 39 year old man who recently suffered skull fracture

- Gram stain: Gram positive diplococci ++
- WBC: 760 x 10^6 per litre (neutrophils)
- RBC: 3 x 10^6 per litre
- Protein: 1 g/l
- Glucose: 1.6 mmol/l
-
- What is the likely diagnosis?
-
- What treatment would you commence?
-
-

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

CSF from a 72 year old with headache and fever

- Gram stain: Gram positive bacilli +
- WBC: 139 x 10^6 per litre (neutrophils)
- RBC: 6 x 10^6 per litre
- Protein: 0.8g/l
- Glucose: 2 mmol/l
-
- What is the likely diagnosis?
-
- What is the correct treatment?
-
-

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

CSF from a 12 year old with headache

- Gram stain: no organisms seen
- WBC: 2 x 10^6 per litre (Lymphocytes)
- RBC: 1000 x 10^6 per litre
- Protein: 0.27 g/l
- Glucose: 3.5 mmol/l
- What is the likely explanation for this result?

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

CSF from an 18 year old with headache, neck stiffness and photophobia

- Gram stain: no organisms seen
- WBC: 287 x 10^6 per litre (Lymphocytes)
- RBC: 4 x 10^6 per litre
- Protein: 0.3 g/l
- Glucose: 4.2 mmol/l
-
- What is the likely diagnosis?
-
- What treatment is indicated?

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

CSF from a 33 year old Lithuanian with six weeks history of worsening headache

5.

- Gram stain: no organisms seen
- WBC: 1300 x 10^6 per litre (Lymphocytes)
- RBC: 2 x 10^6 per litre
- Protein: 3 g/l
- Glucose: 2 mmol/l
- What needs to be excluded, and how?

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45

A 43 year old man presents with fever and headache, which started acutely earlier in the day.

- Talking to him, he appears disorientated in time and place.
- Examination reveals fever and papilloedema but no other focal signs.
-
- What investigation do you need to do next?

- Later on, the consultant neurologist decides it is safe to do an LP.
- The LP results are:
-
- Gram stain: no organisms
- WCC 670 (95% lymphocytes)
- RCC 15
- Protein 0.5 g/l
- Glucose: normal
-
- What is the most likely diagnosis?
-
-
- How would you treat this?
-
-

	Viral meningo encephalitis	Bacterial	Tuberculous	Fungal	Normal
Opening pressure	Normal or high	High	High	High/ very high	10 – 20 cm
Colour	Clear	Cloudy	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	5 - 1000	100 - 50000	25 - 500	0 -1000	<5
Differential	Lymphocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
CSF/plasma glucose ratio	Normal	Low	Low/very low <30%	Normal /low	66%
Protein (g/l)	0.5 – 1.0	> 1.0	1.0 – 5.0	0.2 – 5.0	< 0.45