Infections of the nervous system

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Organisms

- Bacteria
- Viruses
- Fungi
- Parasites
- Prions

Bacterial meningitis and HSV encephalitis are life-threatening emergencies and not uncommon

- dealt with in dedicated lectures

Clinical presentations of CNS infections

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

Meningitis

- Bacterial
- Viral
- Tuberculous
- Fungal

- Non-infectious eg malignancy
- Amoebic

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 - y**oung children commonly shed in stool
  - E.g. Coxsackie virus A and B
  - poliovirus
- Mumpsvirus
- Many others, less commonly
- Diagnosis:
  - CSF is to exclude bacterial infection
  - If CSF taken, send for enterovirus PCR
  - Stool and throat swabs for enterovirus PCR

Poliovirus

- Enterovirus
- Can cause infection and death of anterior horn cells

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%

Polio eradication?

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

be eradicated

- Afghanistan, Pakistan and Nigeria have never stopped transmission of endemic wild poliovirus
  - 21 cases in 2017
  - 29 cases in 2018
  - 168 cases in 2019 (138 Pakistan)

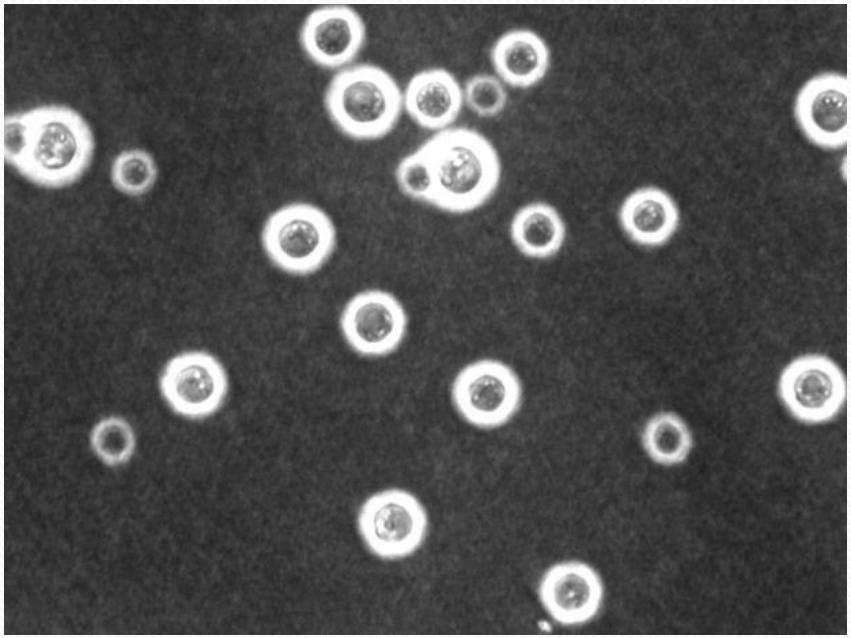
Tuberculous meningitis

- 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
- Treatment – anti-TB therapy with involvement of chest team

Fungal meningitis

Cryptococcus neoformans

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



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

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/other cranial neuritis
  - Encephalopathy/cognitive problems
  - Neuropsychiatric – mood changes/depression

Long-term Lyme disease 'actually chronic fatigue syndrome'

10 October 2019

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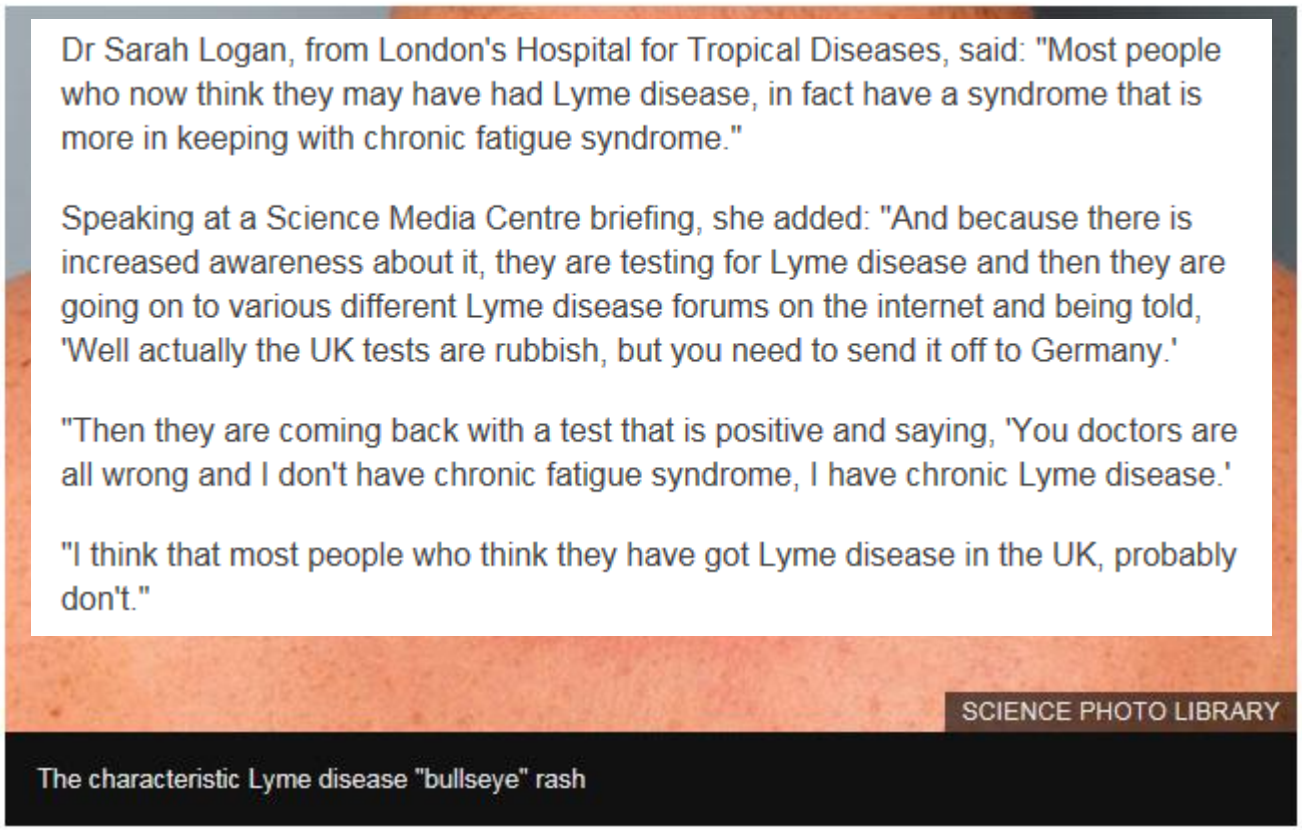
Dr Sarah Logan, from London's Hospital for Tropical Diseases, said: "Most people who now think they may have had Lyme disease, in fact have a syndrome that is more in keeping with chronic fatigue syndrome."

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.

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

Clinical presentations

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

Bacterial brain abscess

- Most follow a bacteraemia which may be occult
  - 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

Chronic infective SOLs

- Tuberculoma
- *Toxoplasma*
- Cysticercosis (pork tapeworm, *Taenia solium*)
- *Echinococcus* (hydatid cyst)

Toxoplasma gondii

- Intracellular protozoan parasite
- Common worldwide: up to 34% UK population may have been infected
- Usually asymptomatic/mild flu-like symptoms
- Contracted from:
  - Handling/eating raw, cured or undercooked infected meat
  - Cat is the definitive host – so exposure to cat litter a risk factor, but probably less important

Toxoplasmosis – immunocompromise

- Infection is not cleared and can reactivate in CNS and in eye if immunosuppressed

- In severe immunocompromise/HIV AIDS
  - The leading cause of focal CNS disease in AIDS
  - Prophylaxis should be given if CD4 count is low

Toxoplasmosis – congenital infection

- If mother is infected in pregnancy, congenital toxoplasmosis can result – classic triad of hydrocephalus, intracranial calcification, chorioretinitis

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Saturday, 10 August, 2002, 23:03 GMT 00:03 UK

Dirt infection link to car crashes

Drivers could be at increased risk

Scientists warn that the parasitical disease toxoplasmosis could increase the risk of having a road accident.

Is your cat making you crazy? Feline parasite 'can cause schizophrenia in humans'

- Toxoplasma microbe 'takes over' the human brain
- A person will become less risk-averse
- Part of 'circle of life' for parasite

By CHARLES WALFORD FOR THE DAILY MAIL
UPDATED: 16:41, 10 February 2012

Mail Online

Cat parasite that worms into humans' brains can drive victims to suicide

By FIONA MACRAE SCIENCE CORRESPONDENT

PUBLISHED: 00:03, 18 August 2012 | **UPDATED:** 00:03, 18 August 2012

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A parasite found in cats is tampering with people's brains and driving them to suicide, research suggests.

Scientists have shown that men and women infected with a bug that breeds in cats' stomachs and worms into people's brains are seven times more likely to attempt suicide than others.

They say that Toxoplasma gondii may tinker with the delicate chemistry of the brain and screening people for it could help identify those at risk of taking their own lives.

A parasite found in cats is tampering with people's brains and driving them to suicide, research suggests

??association with schizophrenia/personality change/risk taking – but small scale studies only

Clinical presentations

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

TSEs – Transmissible Spongiform Encephalopathies

- Bovine Spongiform Encephalopathy
- Scrapie
- Creutzfeldt-Jakob Disease
- 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

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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

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

Transmission of TSEs – UK precautions

- All blood used for transfusion is leucodepleted
- Synthetic (recombinant) clotting factor for treatment of haemophilia
- Plasma, for the manufacture of plasma products, is obtained from non-UK sources
- Individuals who received a transfusion of blood components since 1980, or are unsure if they have had a blood transfusion, are excluded from donating blood or platelets.

Clinical presentations

- Meningitis
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- Encephalopathy
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Congenital infections of CNS

- 'TORCH'
  - Toxoplasma
  - Other (syphilis + others – an expanding list...)
  - Rubella
  - Cytomegalovirus (CMV)
  - Herpesviruses

- Clinical features are not confined to CNS
- CNS features can include: microcephaly, seizures, intracranial calcifications, hydrocephalus, intellectual disability

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

Shingles

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

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

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

Summary

- Neurological 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

CSF interpretation

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
- Fungal meningitis
- Lymphocytic leukaemias