

Dr Paul Holmes

Guy's and St Thomas' NHS Foundation Trust, London

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HIV and Lumbar punctures in 2018

Paul Holmes

Consultant Neurologist

Guy's and St Thomas' Hospitals

I have no competing interests

Summary of the talk

- Basics of lumbar punctures and safety aspects
- Use of lumbar puncture in PLWH in whom their presenting condition is unlikely to be linked to their HIV
- Complex and difficult infections and IRIS phenomena
- Current views on the use of lumbar puncture and CSF analysis in patients with cognitive decline possibly linked to their HIV infection

Quincke performed the first lumbar puncture (LP) in 1891 to relieve increased intracranial pressure in children with tuberculous meningitis

- LP is essential or extremely useful in the diagnosis of bacterial, fungal, mycobacterial, and viral CNS infections and, in certain settings, for help in the diagnosis of subarachnoid hemorrhage, some CNS malignancies, demyelinating diseases, and Guillain-Barré syndrome
- The findings on CSF analysis also may help distinguish bacterial meningitis from viral infections of the central nervous system
- Patients require lumbar puncture if **two or more** of the following features are present:

1. Headache
2. Fever
3. Neck stiffness
4. Altered mental status (delirium or confusional state)

OR: Persisting headache in HIV-infected patients with CD4 count <100 to rule out cryptococcal meningitis

LP is a relatively safe procedure, but minor and major complications can occur, including headache, infection, bleeding, cerebral herniation, as well as minor neurologic symptoms such as radicular pain or numbness

- Meningitis is a very rare complication of LP
- LP is contraindicated in patients with a suspected spinal epidural abscess.
- Suspected bacteraemia is NOT a contraindication to LP
- Bleeding in the epidural or subdural space following LP may occur in up to 2 % of patients, primarily in those patients with thrombocytopenia or other bleeding disorders or in those who have received anticoagulant therapy
- Antiplatelet therapy with aspirin and nonsteroidal anti-inflammatory agents is NOT clearly associated with an increased risk of bleeding after LP. The bleeding risk associated with clopidogrel) is unknown. It is reasonable to suspend therapy, when possible, prior to elective LP
- Anticoagulation therapy is generally suspended prior to elective LP
- Platelet counts 50, or an INR >1.4 should be corrected prior to LP.

Meningitis versus encephalitis

- Meningitis is an inflammation of the leptomeninges and underlying subarachnoid cerebrospinal fluid
- Classic features – bacterial
 - Pyrexial onset
 - Severe headache and photophobia
 - Rapid development of neck stiffness and backache
 - Bacteria are *N. meningitis*, *S. Pneumonia*, HI, TB
- Classic features – viral
 - Prodrome fever
 - Muscle aches
 - Headache
 - Then neck stiffness
 - Enteroviruses (respiratory tract), mumps

Encephalitis

- Encephalitis is an acute inflammatory process affecting the brain
- Classic features
 - Fever
 - Headache
 - Behavioural changes
 - Altered level of consciousness
 - Focal neurologic deficits
 - Seizures
- Viral infection is the most common and important cause, with over 100 viruses implicated worldwide
- Incidence of 3.5–7.4 per 100,000 persons per year

Meningitis associated with HIV infection

- Cryptococcal - severe headache, change in mental status, fever, nuchal rigidity, and focal signs, or with a subacute course of malaise and headache without stiff neck over several weeks
- Tuberculous
- Syphilitic
- Listeria species
- Lymphomatous
- CMV (ventriculoencephalitis)
- Aseptic

Meningitis associated with HIV infection

- HIV itself (Aseptic meningitis may be caused by HIV-1 at seroconversion)
- cryptococcosis, coccidioidomycosis, histoplasmosis, or other fungal infections occurs typically in patients with very low CD4 counts.
- Medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), trimethoprim-sulfamethoxazole, and intravenous immunoglobulin (IVIG) may cause an asymptomatic lymphocytic meningitis

- **CONTRAINDICATIONS** — Although there are no absolute contraindications to performing the procedure, caution should be used in patients with:
 - Possible raised intracranial pressure
 - Thrombocytopenia or other bleeding diathesis (including ongoing anticoagulant therapy)
 - Suspected spinal epidural abscess
 - In a patient with HIV infection LP should not be performed if
 1. The patient is comatose and does not respond to voice or deep painful stimuli
 2. Focal weakness is present (limbs or cranial nerves)
 3. Papilloedema is identified by an experienced clinician

In a patient with HIV infection that is well controlled and they have features as previously described which indicate that a lumbar puncture should be done, the CSF should be sent for

M, C & S

Protein and glucose (WITH A SERUM GLUCOSE)

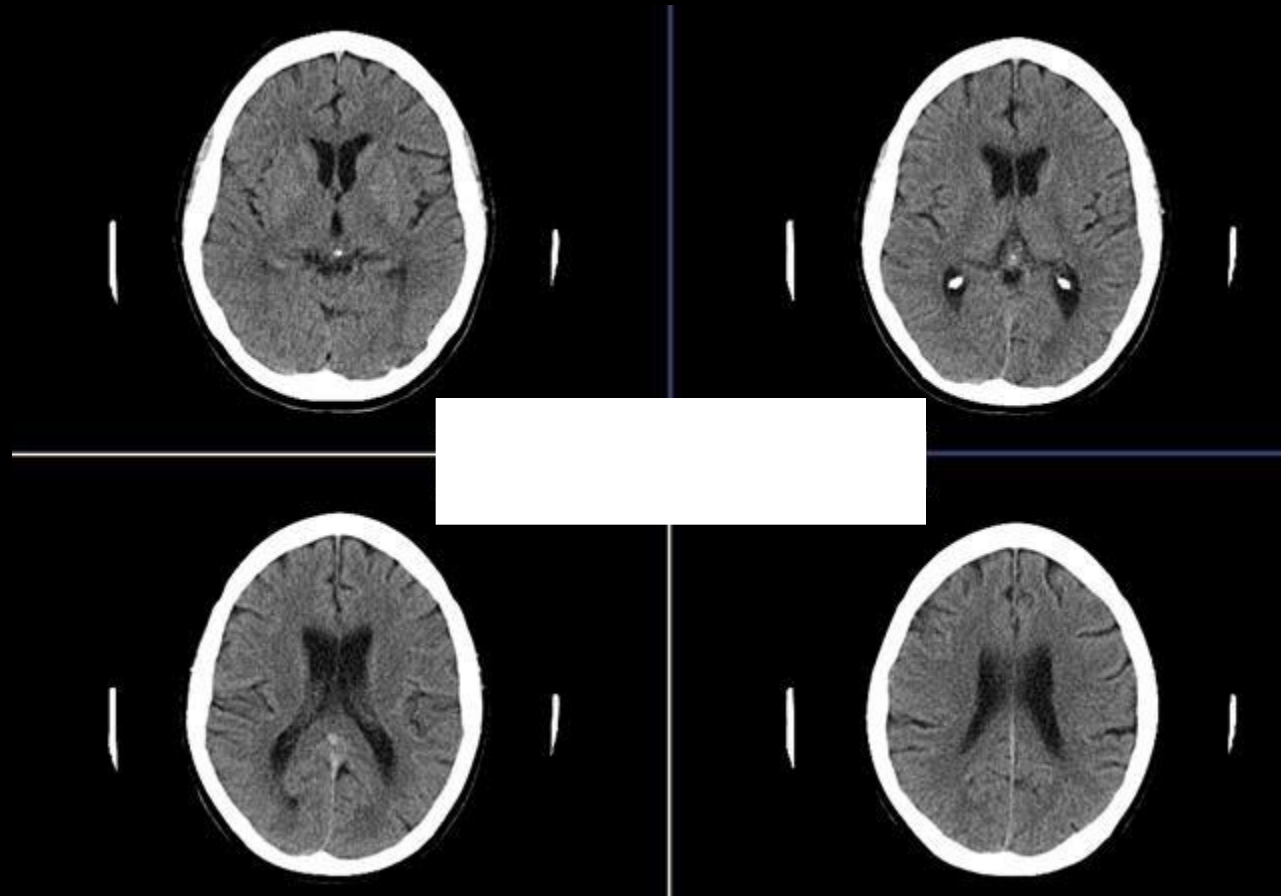
OCB (WITH MATCHED SERUM)

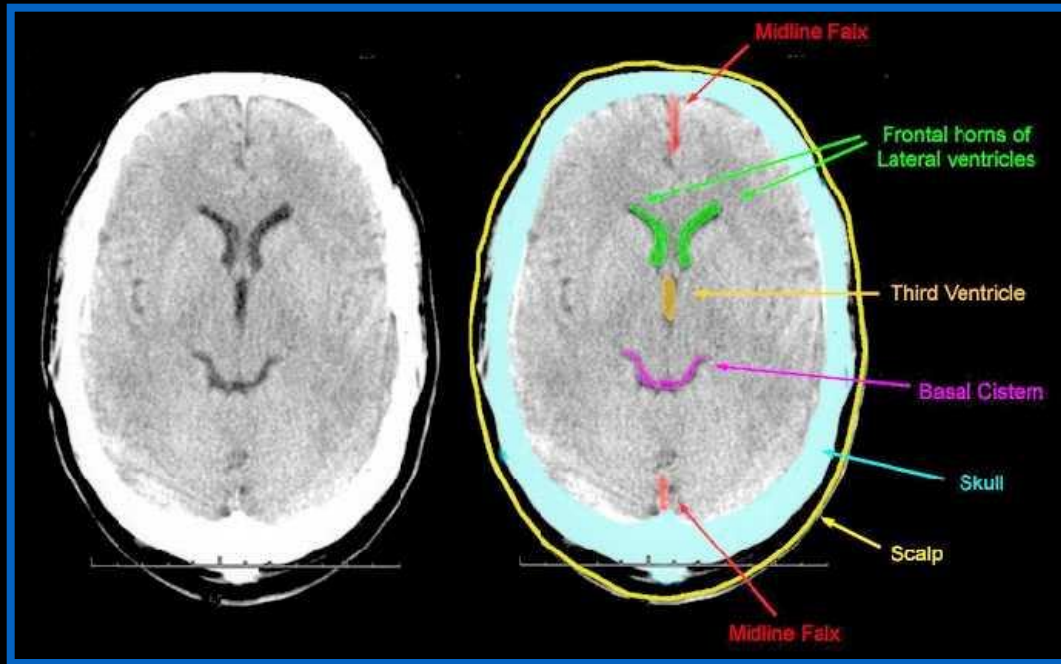
Viral PCR for common viruses – enterovirus, HSV, VZV

HIV viral load with matched serum for viral load

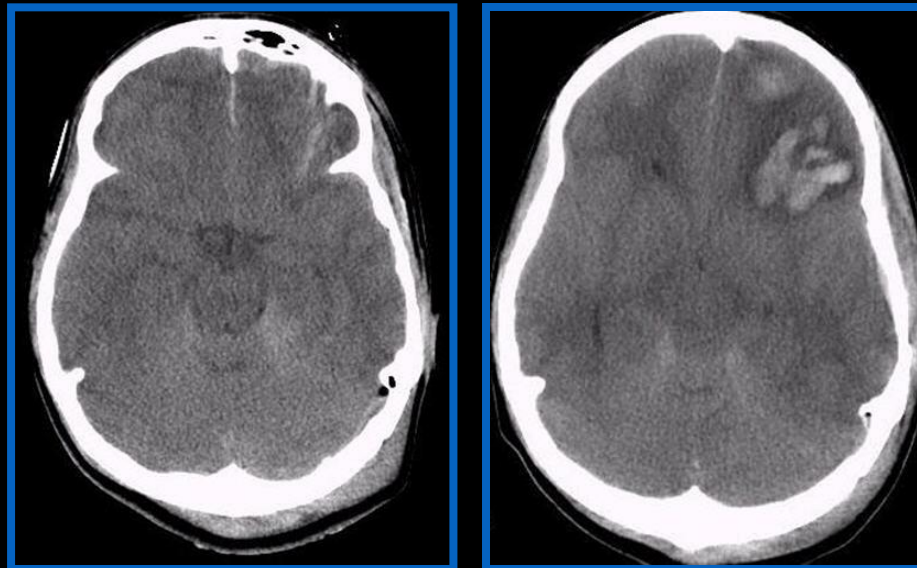
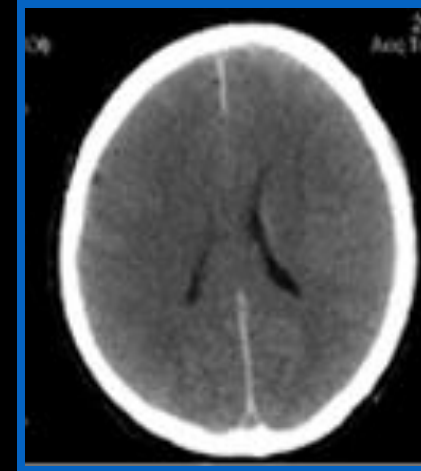
If you were the only person available to review the scan what are the features of a CT that would reassure you that the scan was normal and which are those that would make you defer LP?

CT Brain





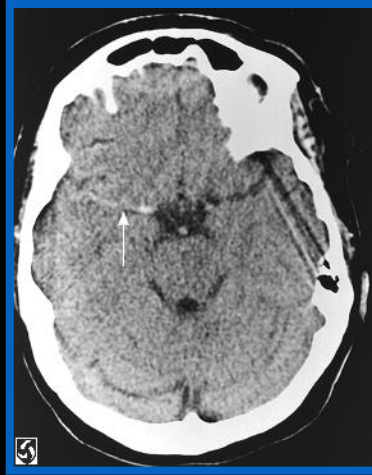
Cerebral oedema



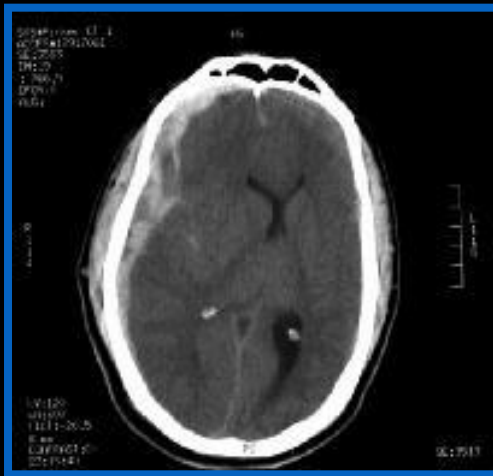
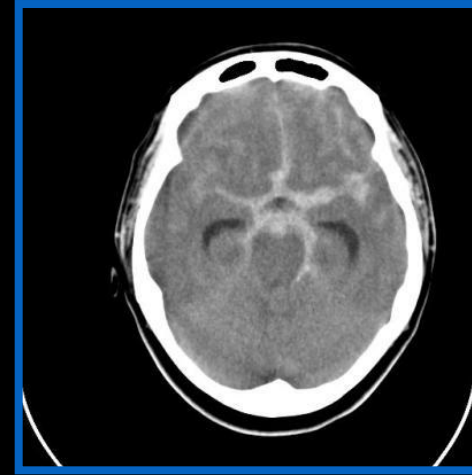
Loss of basal cisterns

Use of CT scanning

**Hyperdense
R MCA**



**Acute
SAH**



**Acute
subdural
haematoma**



**Tumour of the
glioma series**

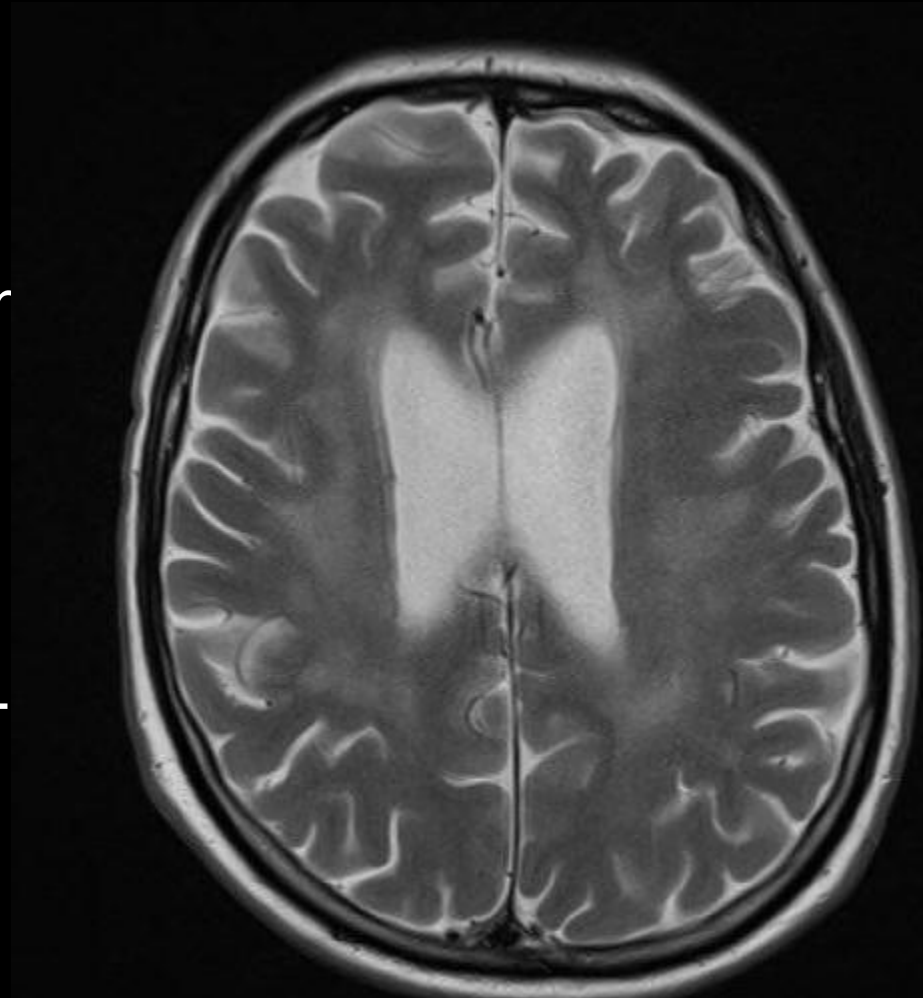
Cases in patients with HIV where CSF is helpful for specific HIV related complications.

This is the MRI of a patient presenting with a low CD4 count of 49 with PCP pneumonia.

Once recovered from the opportunistic infection his neurocognitive testing showed features of slow processing speeds and working memory impairment with forgetfulness.

His serum VL was 2840 copies/ml and CSF VL of 425490 copied/ml.

His MRI showed high signal within the white matter and this is an HIV encephalopathy presenting with cognitive issues.



This is the case of a MSM variably complaint on ART presents with headache and focal neurology including cognitive slowing. His CSF investigations showed.

Normal opening pressure of 16 cm/CSF
WCC 168 (95% lymphocytes, 5% polymorphs)

Glucose 3.6 mmol/l (serum glucose 5.1)

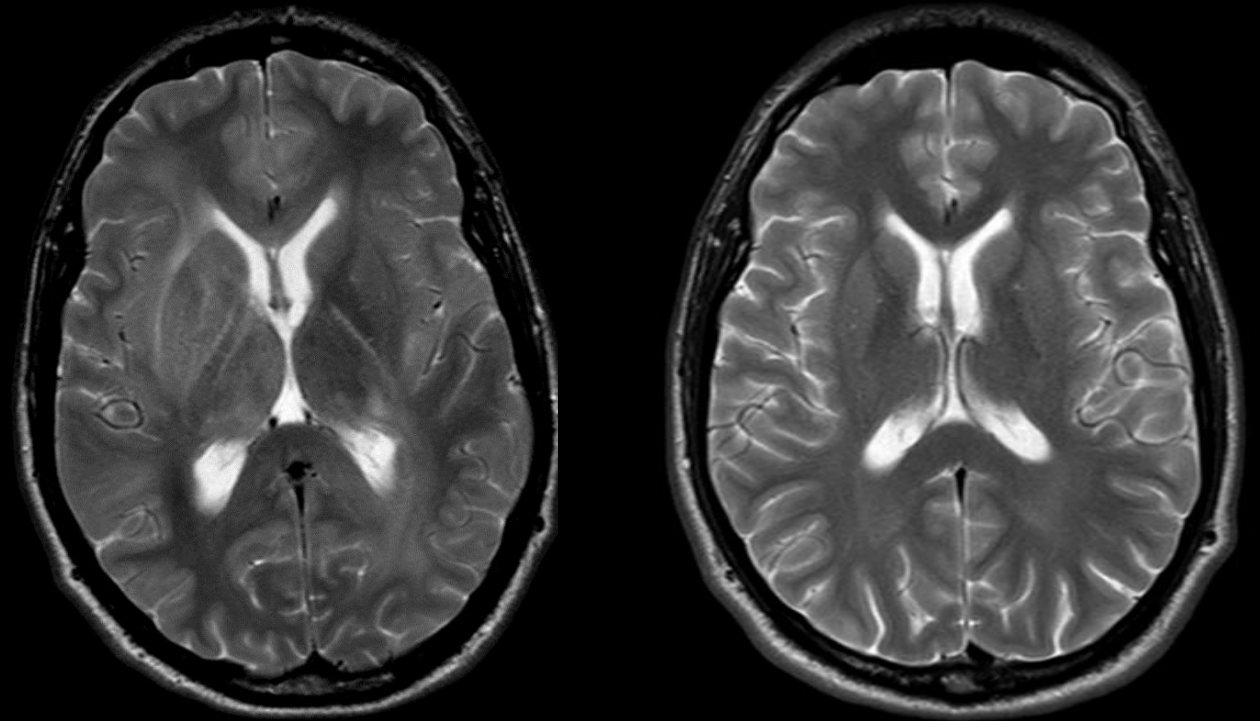
Protein 5.5 g/l protein

CSF HIV RNA 2128158 copies/ml

Serum HIV RNA 7358 copies/ml

Other viral PCR studies negative

Unmatched OCB's in CSF



His MRI at presentation and then after compliance with ART is below. The MRI on the left shows significant swelling and white and grey matter signal change and this is an IRIS-type HIV encephalopathy with an inflammatory response to HIV in the CNS as described above and was treated with steroids and after compliance on ART the scan on the right shows resolution of the signal change. This is similar to a CD8 encephalitis.

Cryptococcal meningitis

- Mortality and adverse neurologic sequelae from HIV-associated cryptococcal meningitis (HIV-CM) remains high due to raised intracranial pressure (ICP) complications
- high opening pressure occurs in more than 50% of HIV-CM patients
- Repeated lumbar puncture with CSF drainage and external lumbar drainage might be required in the management of these patients
- Significant neurological decline can occur if elevated CSF pressures are inadequately managed
- medical management, serial lumbar punctures, external lumbar and ventricular drain placement, and either ventricular or lumbar shunting may be needed

CSF biomarkers

- Despite significant research efforts directed towards a better understanding of the mechanisms underlying HIV neuropathogenesis, definitive causal pathophysiology of HAND and thus effective prevention or treatment remain elusive
- Controversies exist as to whether milder forms of memory and cognitive impairments detected on neuropsychometric tests have any true clinical or prognostic significance, and there remains uncertainty as to whether HIV replication (or, indeed, HIV driven neuroinflammation) at primary, or during chronic infection is the cause
- Despite viral suppression in plasma below the limit of detectability, replication may rarely occur within the cerebrospinal fluid (CSF).

- There is growing interest in the field of CSF biomarkers for neuronal injury and associated cognitive impairment in PLWH.
- CSF Neurofilament light chain (NFL) has emerged as a sensitive marker for assessing ongoing axonal damage in HIV infected patients.
- It has previously been found that CSF NFL can predict severe neurocognitive impairment.
- Impairment of BBB with simultaneously raised levels of CSF neopterin and CSF NFL give further support to the existence of neuroinflammation and axonal injury in untreated HIV.
- High levels in treated HIV patients might be important in HAND evaluation

CSF biomarkers in other patients with Alzheimer's Disease

- In PLWH who have significant cognitive decline CSF analysis may help diagnose other conditions such as AD when used alongside MRI and PET scanning

- CSF is measured for

CSF TOTAL TAU reference range 146-595pg/ml

CSF A-BETA 1-42 reference range 627-1322pg/ml

CSF TAU/ABETA RATIO reference range <1.00

CSF PHOSPHORYLATED TAU reference range 24-68pg/ml

The analysis of these figures in a study done at the National Hospital for Neurology and Neurosurgery showed that the combination of an A-Beta 1-42 < 450 pg/ml with a Tau AB ratio of >1 and a phosphorylated Tau of >62 gave a sensitivity of 68.5% and a specificity of 86.9% and a diagnosis of Alzheimer's disease.

Conclusions

- Lumbar punctures are a vital part of the neurological evaluation in patients with HIV presenting with OI, HAND, meningitis or encephalitis syndromes
- LPs are safe
- Lowering the CSF pressure in cryptococcal meningitis can be sight saving