

Additional file 1: Diagnostic evaluation of patients with suspected encephalitis

Step 1 Initial testing, all patients^a

CSF (“study package”):

- Leucocyte count, protein, glucose, albumin
- Virus PCR: enterovirus, HSV1 and 2, VZV
- Microscopy and culture; if treated with antibiotics; bacterial PCR
- Extra CSF stored for additional testing ^{a,b}

Serum (“study package”):

- HIV, EBV, CMV, Parvo B19 virus, Toxoplasmosis, Treponema
- Extra serum stored for additional testing ^{a,b}

Other tests (recommended):

- noseswab (airway viruses, mycoplasma pneumoniae)
- faeces for enterovirus
- vesicles (HSV-/VZV-PCR)



If negative or clinical suspicion of auto- immune encephalitis:

- Encephalitis antibodies in serum and CSF^b
- Paraneoplastic antibodies in serum and CSF^b
- Screening for malignancy (CT scan, tumor markers)



Step 2 If step 1 is negative: repuncture

- repeat PCR analysis of HSV, EV, VZV
- antibody production of HSV, VZV in CSF and serum
- consult infectious disease specialist for further analysis

^a Special indications:

- if travel abroad: discussion with infectious disease consultant and targeted testing depending on destination and incubation period
- if immunocompromised: JC virus, Cryptococcus (antigen detection and PCR), HHV6, listeria monocytogenes, CMV- PCR, EBV-PCR
- Possible tick exposure (seasonal): B burgdorferi antibodies in serum and CSF and Tick borne encephalitis in serum.
- Exposure to TB or travel/ stay in TB endemic areas; CSF smear for acid fast bacilli, CSF mycobacterial culture, MTB PCR for CSF, Quantiferon

^b CSF and serum:

Encephalitis antibodies: NMDAr, AMPAR1 and 2, GABAR1, CASPR2, LGI1, +/- VGKC
Paraneoplastic antibodies: Hu, Ri, Yo, amphiphysin, CRPM5, MA1, Ma2