QUESTION 95
A 30-year-old man is admitted to hospital with a three-day history of headache and fever. In the six hours preceding admission, he has become confused and drowsy and is observed to have focal twitching of the right arm. His temperature is 39.2°C. He is unable to answer questions coherently or follow commands. He has mild neck stiffness. A computed tomography (CT) scan of the brain is normal.

Cerebrospinal fluid (CSF) analysis is as follows:

- white cell count 90 x 10^6/L [<5]
- lymphocytes 80 x 10^6/L [<2]
- neutrophils 10 x 10^6/L [<2]
- protein 0.80 g/L [0.15-0.40]
- glucose 3.2 mmol/L [2.5-4.5]

Herpes simplex encephalitis is suspected and he is started on intravenous aciclovir.

Which one of the following is the most appropriate next investigation to confirm the diagnosis?
A. Cerebral magnetic resonance imaging (MRI).
B. Electroencephalography (EEG).
C. Cerebral positron emission tomography (PET) scanning.
D. Brain biopsy.
E. Polymerase chain reaction (PCR) assay for viral DNA.

Reference: Infectious Diseases A clinical Approach Yung, McDonald, Spelman, Street and Johnson 2001 Page 171-172

Herpes simplex encephalitis
The most common agent responsible for sporadic cases of encephalitis is herpes simplex virus. In adults, almost all infections are due to HSV 1; in neonates, HSV type 2 is almost invariably responsible and follows transmission during delivery. The disease is not seasonal and presents in all age groups. It typically affects the temporal and frontal lobes and almost invariably presents with fever as well as focal signs, especially dysphasia or personality change; two thirds of patients suffer either focal or generalized seizures.

Diagnosis has recently been greatly facilitated by the introduction of CSF PCR into routine clinical use. This is now the diagnostic test of choice and has a greater than 95% sensitivity in competent laboratories when compare to brain biopsy. If suspicion is high and an initial test is negative, the PCR should be repeated after 24-48 hours. Sensitivity is reduced if acyclovir treatment has been used for longer than 24 hours.

EEG has 84% sensitivity and reveals characteristic temporal spike and wave activity. CT is abnormal in 50-75% of patients, while MRI is more sensitive and is the imaging modality of choice if available. Alternative modes of diagnosis include demonstration of intrathecal HSV antibody which becomes detectable 3-10 days following clinical onset and persists for at least 30 days. Simultaneous serum antibody is performed and a serum: CSF ratio of less than 20:1 is suggestive of intrathecal synthesis.

Timely diagnosis is critical as this is one of the few agents causing encephalitis for which effective, non-toxic treatment is available in the form of acyclovir; outcome is heavily dependent on early institution of therapy. Accordingly, any patients with a reasonable suspicion of HSE should be treated with intravenous acyclovir. If presentation is atypical or he patient does not respond to therapy, brain biopsy should be performed since as many as 20% of patients with a typical presentation have an alternative diagnosis, many of which are due to treatable infectious agents.

Answer: E. Polymerase chain reaction (PCR) assay for viral DNA.