aureus abscesses. While an inpatient he complained of headaches and nausea and developed a low grade pyrexia and meningism. Brain CT was normal. Lumbar puncture disclosed a high opening pressure (19 cm CSF), 133 white blood cells/µl, predominately lymphocytes, a raised protein (1.61g/l), and a low CSF/blood glucose ratio (1.7/6.1). A sample of 0.5 ml CSF was sent to a British referral laboratory and PCR for *M tuberculosis* was negative. Twenty four hours later, because of increasing confusion and agitation, treatment with intravenous acyclovir, antituberculous chemotherapy (600 mg rifampicin, 300 mg isoniazid, 2 g pyrazinamide, and 10 mg pyridoxine daily), and dexamethasone was commenced. Clinically he showed signs of improvement and was discharged home 2 weeks later on the above treatment. A repeat lumbar puncture 4 weeks later showed similar results. A CSF PCR for *M tuberculosis* was again negative although a fully sensitive *M tuberculosis* grew 12 weeks later from the first sample on Lowenstein-Jensen slopes.

The second patient was a 21 year old Kenyan woman living in the united Kingdom for 3 years. She presented with a 3 month history of photophobia and occipital headaches. She had no other systemic symptoms. She had had peritoneal tuberculosis diagnosed at the age of 6 years during laparotomy for an appendicectomy and had received antituberculous medication for 1 month only. On examination she had mild neck stiffness and a partial left third cranial nerve palsy. Brain CT was normal. Lumbar puncture results showed a high opening pressure (15cm CSF), 90 white blood cells/µl, predominantly lymphocytes, a raised protein concentration (1.62 g/l), and a low CSF/blood glucose ratio. At the same referral laboratory CSF PCR for *M tuberculosis* was negative but culture after 8 weeks grew a fully sensitive organism. Despite the negative PCR antituberculous therapy was started empirically. After 2 months of treatment her symptoms had resolved although a partial third nerve palsy remains.

Adequate volumes of both patients' CSF (0.5 ml) were sent to our referral laboratory where the samples were spun and PCR performed using three primer sets and appropriate controls.[5–7] The assay included primers for the target IS6110, an insertion sequence normally present in multiple copies in the *M tuberculosis* genome, which has been used successfully for the detection of *M tuberculosis* in CSF.[2 4] Multiple primer sets were used as this is thought to increase the probability of detecting target DNA within a specimen.

Recent studies suggest that CSF PCR for *M tuberculosis* is more sensitive than culture in cases of clinically suspected tuberculous meningitis that responded to empirical treatment.[2–4] Some authors have even suggested the usefulness of serial CSF PCR in assessing the efficacy of treatment.[4 8] False negatives and positives are rarely reported in the literature and unless these results are critically reviewed patients could, tragically, have treatment prematurely stopped or be started on prolonged antituberculous chemotherapy. False negatives occurred in two studies, in which reported CSF PCR sensitivities were 32% and 85%.[2 3] In one study 6.1% of CSF specimens received from patients with no evidence of tuberculous meningitis were falsely PCR positive.[3] These results also show that sensitivity and specificity can vary when different assays and laboratories are used. Claims that PCR can detect 1–10 *M tuberculosis* organisms "in vitro" seems not to be the case in clinical samples such as CSF.

In the two patients presented above adequate volumes and repeated samples of CSF were assayed using suitable primers and appropriate controls at a British referral laboratory. Results for these two patients show the dangers of overreliance on CSF PCR when tuberculous meningitis is clinically suspected.

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False negative polymerase chain reaction on cerebrospinal fluid samples in tuberculous meningitis

There have been few studies in the literature concerned solely with the use of the polymerase chain reaction (PCR) to identify *Mycobacterium tuberculosis* DNA directly from CSF.[1–4] These studies suggest that in some cases, PCR may be more sensitive than culture; however, in the largest study, performed by Nguyen *et al*,[3] specimens from seven patients who were culture positive for *M tuberculosis* were not positive by PCR. The study did report on 22 culture negative, PCR positive patients, suggesting that PCR can be more sensitive than culture. Studies comparing PCR with culture of *M tuberculosis* using other clinical specimens, particularly respiratory specimens, have reported that PCR may be less sensitive than culture for the detection of *M tuberculosis*[5–9] and that the low sensitivity correlated with low colony counts on culture.[5] Dalovisio *et al*[6] also reported that multiple specimens may be required to improve the sensitivity of the test in some patients. In the two cases described above, colonies were seen after incubation for 12 and 8 weeks on LJ slopes, suggesting a low inoculum.

The PCR has been reported to detect the equivalent of 1–10 mycobacteria in in vitro testing. However, lower sensitivity is found with clinical specimens.[5 6] The low sensitivity of PCR may be the result of inhibitors of PCR present in the reaction, poor lysis of mycobacteria, and the uneven distribution of mycobacteria in clinical specimens.[5 6]

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A novel mutation of the myelin P_0 gene segregating Charcot-Marie-Tooth disease type 1B manifesting as trigeminal nerve thickening

Charcot-Marie-Tooth disease (CMT) is the most common type of hereditary peripheral neuropathy. It is classified into two types based on pathological and electrophysiological findings: type 1 and type 2. CMT type 1 gene loci have been mapped to chromosome 17 (CMT1A), chromosome 1 (CMT1B),[1] another unknown chromosome, (CMT1C) and the X chromosome (CMTX). CMT1B is a rare form of CMT1 associated with mutations of the myelin protein zero (P_0) gene. Mutations in the P_0 gene have recently