Tuberculous Meningitis

Definition
Tuberculous meningitis (TBM) is a chronic infection of the meninges caused by *Mycobacterium tuberculosis*.

Pathogenesis
Dissemination of bacilli to the meninges and brain occurs as a complication of the primary infection, or as a complication of an existing TB lesion (tuberculoma, miliary TB) or reactivation of a latent TB focus.

Meningeal infection is then caused when a parameningeal caseous focus ruptures into the brain/spinal substance and subarachnoid space. A severe inflammatory response is elicited by mycobacterial components. A thick exudate, phlebitis, arteritis, thrombosis, infarction and obstruction of CSF flow are common findings.

Complications include raised intracranial pressure, cerebral oedema, inappropriate antidiuretic hormone (ADH) secretion, hydrocephalus, brain infarcts, hemi- or quadriplegia, convulsions, deafness, blindness, mental retardation and other neurological sequelae.

Diagnostic criteria
Early diagnosis and treatment improves the prognosis.

Clinical:

- History of contact with tuberculosis (not always present).
- Onset may be gradual with vague complaints of headache, irritability, weight loss and drowsiness.
- Examination may reveal signs of meningeal irritation, signs of raised intracranial pressure, convulsions, cranial nerve palsies, localising signs (such as hemipareses), altered level of consciousness or coma and choroidal tubercles.
- Degree of involvement is classified into 3 stages. Prognosis relates to the stage of the disease.

Stage 1: Non-specific signs, signs of meningeal irritation, conscious, rational, no focal neurological signs, no hydrocephalus.
Stage 2: Confusion and/or focal neurological signs.
Stage 3: Stupor, delirium, coma and/or neurological signs (hemiplegia).

Investigations:
It is often not possible to diagnose TBM on a single CSF examination. Often introduction of antibiotics misleads the findings.

Lumbar puncture is hazardous if the patient has a focal neurological deficit or if fundoscopy shows papilloedema. In these circumstances, a C.A.T. brain scan is helpful, if available. Otherwise, it may be safer to start presumptive treatment with anti TB drugs when there are ample historical and clinical more evidences rather than risk lumbar puncture.

- CSF findings: May vary depending on the stage. Protein is markedly raised, glucose is moderately low, chloride is low and lymphocytes usually predominate. CSF adenosine deaminase may be raised (> 7 units/L). Gram stain is negative and acid-fast bacilli are seldom found. A bromide partition test may be helpful. (CSF bromide partition test ratio < 1.6). Bacilli may be cultured from the CSF but may take up to 4–6 weeks.

- A Mantoux test if negative a BCG enhanced reaction test, and chest X-ray should always be done.
- A CT scan of the brain may be helpful.

Treatment objectives

- Early diagnosis and treatment.
- Eradication of the mycobacteria.
- Prevention and early treatment of complications.
- Symptomatic and supportive treatment.
- Education of parents and caregivers. BCG vaccine to newborn babies.

Treatment guidelines

	Management	Comments
Non-drug treatment	Monitor neurological status on a regular basis. Attend to nutritional status. Nasogastric feeding is usually needed initially. CSF shunting procedures or repeated lumbar punctures may be needed as part of the management of hydrocephalus. Monitor liver function. Most of the drugs used are hepatotoxic.	All patients need physiotherapy Follow-up at clinic/hospital is essential. Rehabilitative measures.
Drug treatment 2-month initial phase:	Rifampicin + isoniazid (INH) + pyrazinamide + streptomycin Rifampicin, oral, 20 mg/kg/24 hours as a single daily dose. Isoniazid, oral, 20 mg/kg/24 hours as a single daily dose. Pyrazinamide, oral, 40 mg/kg/24 hours as a single daily dose; maximum 2 g per 24 hours. Streptomycin: 20-40mg/kg/24 hours as a single daily IM dose.	
4-month continuation phase:	Discontinue pyrazinamide. Continue with rifampicin, isoniazid and using the doses above.	
Steroids:	Prednisone, oral, 2–4 mg/kg/24 hours in 3 divided doses for 4–6 weeks. Then taper to stop over 14–21 days.	
Hydrocephalus:	Acetazolamide, oral, 100 mg/kg/24 hours in 3 divided doses; maximum 1 g/day. AND Furosemide, oral, 1–2 mg/kg/24 hours as a single daily dose for at least 4–6 weeks.	Refer non- communicating hydrocephalus for ventriculo- peritoneal shunt urgently.
Convulsions:	Diazepam, slow IV, 0.2–0.3 mg/kg, to control acute seizures. Maintenance: Phenobarbital, oral, 5–10 mg/kg/24 hours	

	in 2 divided doses, until the patient is free of convulsions for 14 days. Taper to stop over 1 week.	
Raised intracranial pressure or cerebral oedema:	Elevate head of bed + 15 degrees. Maintain $Paco_2$ at 28–30 mmHg; intubate and ventilate if necessary. Mannitol, IV, 1g/kg administered over 1 hour. (Do not repeat.) Furosemide, IV, 1 mg/kg. (Do not repeat.) Avoid fluid overload. Limit total daily fluid intake (IV + oral) not to exceed the maintenance requirements for age.	Treat severe cerebral oedema/increased intracranial pressure if there is an acute deterioration of the level of consciousness. 1 kPa = 7.5 mmHg; 1 mmHg x 0.133 = 1 kPa Evidence that fluid restriction is beneficial is inconclusive.