



## Review Article

### Meningeal Irritation : A Review

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#### Abstract

Cases of meningeal irritation are prevalent worldwide and much infectious and non-infectious aetiology exist for this condition. Sub-arachnoid haemorrhage (SAH), central nervous system sarcoidosis(neuro-sarcoidosis), systemic lupus erythematosus (SLE), drugs and chemicals are the non-infectious causes of meningeal irritation. But much is focused on infectious causes because infection of the central nervous system (CNS) is a medical emergency. The clinical constellation of fever, headache and neck-stiffness is diagnostic of meningitis. Other clinical findings like Kernig's sign, Brudzinski's sign and extensor plantar responses support the diagnosis of meningitis and / or meningo-encephalitis. The clinical onset of sudden severe headache, vomiting and unconsciousness is diagnostic of SAH. Neck rigidity, positive Kernig's sign and sub-hyaloid haemorrhage on fundoscopic examination support the diagnosis. However, diagnosis of meningitis and its treatment is very much important and critical in particular. A patient presenting with fever and unconsciousness with no substantial pre-existing illness eg. HTN, DM, endocrinopathy and/ or history of traveling from a malarial epidemic area should be differentially considered meningo-encephalitis for once at least.

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#### Introduction

Cases of meningeal irritation are prevalent worldwide and many infectious and non-infectious aetiologies exist for this condition.<sup>1</sup> Sub-arachnoid haemorrhage (SAH), central nervous system sarcoidosis(neuro-sarcoidosis), systemic lupus erythematosus (SLE), drugs and chemicals are the non-infectious causes of meningeal irritation. But much is focused on infectious causes because infection of the central nervous system (CNS) is a medical emergency<sup>2</sup>. Acute meningitis

encompasses a great majority of morbidity and mortality. Of these, acute bacterial meningitis (ABM) is being the most destructive CNS infection and at least 30 countries have reported serious outbreaks of ABM in the recent years.<sup>3,4</sup> The incidence of ABM is between 3 and 5 per 100,000 people per year and it causes a death toll of more than 2,000 per year even in the United States<sup>5</sup>. The case fatality rate in paediatric patients ranges from 10% to as high as 20% and it may be even upto 50% while that in adult is about 25% as

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- Enterovirus (Echo virus, Coxsackie virus, Polio virus etc.)
- Mumps
- Measles
- Varicella zoster
- Epstein Barr virus
- Cytomegalo virus
- Human immunodeficiency virus (HIV)
- Lymphocytic choriomeningitis virus etc.

### 3. Fungal meningitis

### 4. Protozoal meningitis

- Cryptococcus neoformans
- Histoplasma capsulatum
- Candida albicans etc
- Toxoplasma gondii<sup>23</sup>
- Entamoeba histolytica<sup>24</sup>
- Naegleria fowleri etc.<sup>25</sup>

Other less common but not the least important causes are:

- Cerebral malaria<sup>26</sup> and
- Enteric fever<sup>27,28</sup>.

### Pathophysiology

Inflammation of meninges is the basic pathology in producing the signs of meningeal irritation. The pathologic hallmark of ABM is an exudate in the sub-arachnoid space, where as perivascular lymphocytic infiltration as well as astrogliosis and gliosis are prominent findings in viral meningitis and for meningo-encephalitis<sup>4,29</sup>. Most bacterial meningitis are haematogenous in origin; only a few cases occur from trauma usually involving basal fracture. Bacterial IgA-protease plays vital role in invading host tissues. Later on SA space inflammation occurs and the resultant cytokines (eg. IL-1, TNF etc) impairs BBB. For viral infections haematogenous route is the commonest route, the other being peripheral intra-neuronal route. Olfactory tract may be one of the routes for Herpes simplex virus (HSV).

Following infection, there is inflammation of small and medium-sized subarachnoid blood vessels with leucocytic infiltration. Haemorrhagic cortical infarction as well as brain oedema (vasogenic, cytotoxic, interstitial or combined factors) occur with rise in intra-cranial pressure<sup>4</sup>.

This increase in ICP may cause life-threatening cerebral herniation.

### Presentations

Meningeal irritation presents with features of meningismus caused by reflex spasm of paravertebral muscles. Cervical muscles spasm produces neck-stiffness while lumbar muscles spasm manifests as positive Kernig's sign<sup>30,31</sup>. Patients may present with the meningitic syndrome: a classical triad of headache, neck stiffness and fever<sup>32</sup>. This is found in more than 85% of patients. But their absence does not rule out the diagnosis signs of meningeal irritation as these are not obvious in children<sup>4</sup>. Other presentations include lethargy, confusion, unconsciousness, seizures, CNS dysfunction (Gaze paraesis, hemiparesis, visual field defect etc.).

### Typhoid meningism:

About 2% of the total patients of enteric fever may present with the features of meningism<sup>33</sup>.

### Recurrent Meningitis

A second episode of meningitis due to a different organism from the first one or due to the same organism occurring after more than 3 weeks after the completion of the treatment from the initial episode.

### Chronic Meningitis

It is defined as the chronic inflammation of meninges (pia, arachnoid and dura maters) persisting for longer than 4 weeks associated with a persistent inflammatory response in the CSF (WBC count > 5 cells/mm<sup>3</sup>).

### Investigation and diagnosis

The diagnosis of meningitis is based on a compatible clinical picture, but CSF study is critical to as well as essential in diagnosing it. CSF study includes macroscopic appearance (eg. xanthochromia in SAH), cytology, antigen testing, ELISA, PCR, free amino acid/free fatty acid level by chromatography etc.<sup>34</sup>. Other tests include CT scan/MRI scan of brain, angiography, Widal test, chest skiagram, Montaux test, CBC, blood culture etc. Meningeal biopsy and histopathology may be required in selective cases of non-responder group or patients with abnormal brain scan<sup>35</sup>.

### Treatment

Treatment is given as early as possible. Before starting empirical treatment, CSF should be obtained and if lumbar puncture is to defer for CT Scanning, blood samples should be collected. However, if rashes are seen and clinically meningococcal meningitis is suspected, specific treatment should be started without delay or even without trying to collect CSF since meningococci can be isolated from blood culture even few hours after antibiotic administration.

### Current choice of treatment for acute pyogenic meningitis includes:

Neonates	○ Ampicillin+Cefotaxime or Gentamir
Infants	○ Ampicillin + Cefotaxime
Pre-school children	○ Cefotaxime
Older child & young adults	○ Penicillin G+Cefotaxime or Cefotaxime or Ceftriaxone alone <sup>4</sup> .
Older (>50 years)	○ Ampicillin + Cefotaxime or Ampicillin + Vancomycin <sup>4</sup> .

### Dosages of drugs are as follows:

i) Ampicillin	: 300 mg/Kg/day.
ii) Benzyl penicillin	: 2.4 gm every 4 hourly.
iii) Ceftriaxone	: 30-50mg Kg/day every 12 hourly.
iv) Cefotaxime	: 30-50mg /Kg/day every 6 hourly.
v) Chloramphenicol	: 50mg/Kg /day in 4 divided doses.
vi) Gentamicin	: 5-7mg/ kg/ day in 3 divided doses.
vii) Penicillin G	: 0.6-1.0 ml/ (0.36-6gm) every 4 hourly
viii) Vancomycin	: 15mg /Kg every 8 hourly.

But in short, Ceftriaxone 2gm intravenously/intramuscularly can be given empirically in the adults<sup>36</sup>.

Treatment of viral meningitis and /or meningo-encephalitis is mainly supportive.

### Treatment of Tubercular Meningitis:

Isoniazid (INH), Pyrazinamide (PZA) and Ethionamide are freely distributed in the CSF. For first few months, Rifampicin, Ethambutol and Streptomycin are also distributed in the CSF<sup>33</sup>. Tubercular meningitis is treated with anti-tubercular drugs for at least 9 months and usually includes Rifampicin, Isoniazid (INH) and Pyrazinamide (PZA)<sup>52</sup>.

### Adjunctive therapy :

- i) Short course dexamethasone (first 2- 4 days)
- ii) Mannitol and /or glucorticoids to reduce ICP

iii) Lorazepam, phenytoin etc. to avoid epileptiform seizures.

iv) Plasmapheresis in patients with fulminant meningococcal infection etc.

### Prevention

Haemophilus influenzae type b vaccine (Hib vaccine) can be given to protect neonates as well as children<sup>34</sup>. Vaccine against meningococcus A and B are available. Meningococcal contacts can be given prophylaxis with rifampicin 300mg 12 hourly for 2 days or ciprofloxacin 750 mg daily for 2 days<sup>38</sup>. Contacts of Haemophilus influenzae type b infection can be given ciprofloxacin 750mg daily for 4 days<sup>33</sup>.

### Clinical review of personal series

A hospital based prospective study on Clinico-pathological assessment and prognosis of Meningeal irritation and Meningitis were carried out among the hospitalized patients in medical unit of Rajshahi Medical College Hospital, Rajshahi over a period of one year from November 1999 to October 2000 in a Medicine unit.

The case inclusion criteria were :

- i) Hospital admitted patients in the medical unit with fever, headache and signs of meningeal irritation eg. Neck rigidity, positive Kernig's sign and / or positive Brudzinski's sign.
- ii) Patients of both sexes of thirteen (13) years and above.

The case exclusion criteria were :

- i) Patients who refused lumbar puncture or died before doing lumbar puncture were not included in this study.
- ii) Cases of encephalitis.

One hundred cases (n=100) who clinically presented with features suggestive of meningeal irritation and meningitis were studied with particular reference to age incidence, sex distribution, socioeconomic status, symptoms and signs and results of laboratory tests.

All the patients were above 13 years of age with most of the patients below 50 years of age (69%). Males suffered most in this series (65%) and people of middle and low socioeconomic status were the common sufferers (97%).

Stiff neck was the most common symptom (93%). Other presentations were fever (89%), altered consciousness (72%), headache (62%), vomiting (54%) in order of frequency. Two patients presented with seizures and another two with haemoptysis. Nuchal rigidity was the most common sign (93%). Others were as follows: fever (89%), altered consciousness (72%), positive Kernig's sign (55%) and extensor plantar response in (39%).

CSF were turbid in 3 patients of pyogenic meningitis. Xanthochromia was present in 4 cases of sub-arachnoid haemorrhage. Otherwise CSF were clear and colourless. Spider web's clot formed in 01 sample of CSF in a test tube. CSF glucose was < 60 mg/dl in (29%) cases.

Viral meningitis / meningoencephalitis was the most common cause of meningeal irritation (50%) followed by tubercular meningitis (27%) typhoid meningism (13%), pyogenic meningitis (03%) and sub-arachnoid hemorrhage (04%) in this series.

The patients were treated mostly with parenteral third-generation cephalosporins and dexamethosone and the suspected cases with anti-tubercular drugs with dexamethasone.

Most of the pyogenic meningitis patients started improving by 3<sup>rd</sup> day of treatment, where as the median improvement day was 5 in cases of viral meningitis/ meningoencephalitis. Patients of tubercular meningitis showed start of improvement by 10<sup>th</sup> day after getting anti-tubercular treatment in the most.

Outcome was excellent in viral meningitis and / or meningo-encephalitis and worst in sub-arachnoid haemorrhage. 48 patients out of 50 cases of viral meningitis improved (96%) while only 1 out of 4 patients of sub-arachnoid haemorrhage improved (25%).

The mortality rate was 11% in tubercular meningitis and 19% in cases of pyogenic meningitis while 4% of viral meningitis/ meningoencephalitis patients died.

## Conclusion

Patients with meningeal irritation, especially meningitis often come into in-patient medical units. The clinical consequences of fever, headache and neck-stiffness is diagnostic of meningitis. Other clinical findings like Kernig's sign, Brudzinski's sign and extensor plantar responses all support the diagnosis of meningitis and / or meningo-encephalitis. Among the causes of meningeal irritation, SAH is important one. The clinical constellation of sudden severe headache, vomiting and unconsciousness is diagnostic of SAH. Neck rigidity, positive Kernig's sign and sub-hyaloid haemorrhage on fundoscopic examination support the diagnosis.

But diagnosis of meningitis and its treatment is very much important and critical in particular. A patient presenting with fever and unconsciousness with no substantial pre-existing illness eg. HTN, DM, endocrinopathy and/ or history of travelling from a malarial epidemic area should be differentially considered meningo-encephalitis for once at least.

History is much suggestive in cases of acute bacterial meningitis and viral meningitis and / or meningo-encephalitis. But this may not be true always due to indiscriminate use of antibiotic and anti-pyretics when a physician really fall into a dilemma particularly in cases of tubercular meningitis. A consistent history should arise the suspicion.

Considering the clinical presentation, patient should be taken as a case of acute bacterial meningitis for failure to treat acute bacterial meningitis will cause 100% mortality if the case is not proved to be other wise. And in suspicious cases, lumbar puncture should be done for diagnosis of tubercular meningitis. Still there remains a large group of patients who come with short history of fever, rapid loss of consciousness and signs of meningeal irritation. Their CSF are clear, protein levels raised, but CSF glucose level remains normal. Thick and thin film do not reveal malarial parasites. Empirically they were considered as possible cases of viral meningo-encephalitis. These cases can not be confirmed because of lack of facilities for viral isolation and other laboratory investigations. This requires future exploration.

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