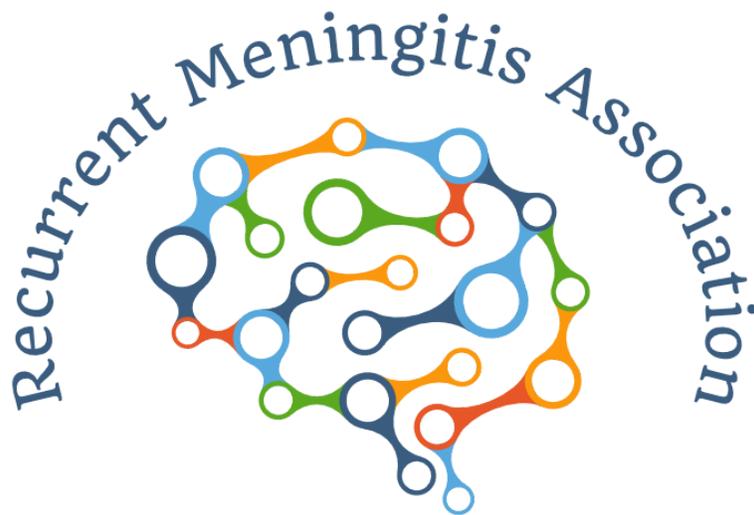


# PROVIDER INFORMATION

## Recurrent Viral Meningitis (Mollaret's)

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### **What is Recurrent Viral Meningitis (Mollaret's)?**

Recurrent viral meningitis (Mollaret's Meningitis) is a rare form of recurrent meningitis believed to be caused by herpes viruses and other closely related viruses.

"Recurrent meningitis is defined by at least two episodes of meningitis with associated CSF pleocytosis with no symptoms between episodes. Recurrent meningitis was first described in the 1940s by physician-scientist Pierre Mollaret, who noted a handful of cases of recurrent acute aseptic meningitis with CSF showing evidence of lymphocytic and

mononuclear pleocytosis. This was later attributed to HSV-2 infection. The condition was later named Mollaret meningitis after him and the “Mollaret cells” he identified, although it is now known that many of the infectious and noninfectious etiologies of chronic meningitis can occur in a fluctuating pattern consistent with a recurrent meningitis. While triggers for recurrent viral meningitis are unclear, significant risk factors should be investigated in those who present with recurrent bacterial meningitis, including host factors such as anatomic defects that provide a nidus for bacterial CNS invasion (eg, skull-base defects, neural tube defects) and acquired and congenital immunodeficiencies that predispose individuals to recurrent ear, nose, and throat infections. Likewise, recurrent meningitis due to fungi or parasites should trigger an investigation for an underlying immunocompromised state or ongoing environmental exposures. This should go beyond testing for HIV and should include evaluation of T-cell and B-cell profiles, complement levels, IgG subclass quantification, and screening for rheumatologic conditions. Recently an association between acute meningoencephalitis infection and positive paraneoplastic antibodies in recurrent meningitis cases was identified, although further studies are required to determine the significance of autoimmune antibodies in recurrent meningitis.”

For quick access to medical articles related to this disease, please visit the medical article search on our website at <https://recurrentmeningitis.org/search>.

*All information contained in this document is provided as information only and is not a substitute for medical advice.*

Our patient registry will be live the end of 2018 and we hope to have the first results from that available the end of 2019.

## Patient Perspective

In surveys of our members in 2018, the reported causative viruses from patient diagnosis were (in order of most to least common):

1. Herpes Simplex Virus - Type 2 (HSV-2/HHV-2)
2. Unknown
3. Herpes Simplex Virus - Untyped
4. Herpes Simplex Virus - Type 1 (HSV-1/HHV-1)
5. Varicella Zoster Virus (HHV-3)

## Diagnosis

In those surveys the reported methods of diagnosis were (in order of most to least common):

1. Lumbar puncture (with and without PCR)
2. Medical History
3. Blood test
4. Physical Exam

Lumbar puncture with polymerase chain reaction (PCR) is the most widely used method for confirming recurrent viral meningitis to date. Both documented in literature and from our experience, the most beneficial time frame to get an accurate result is 24-48 hours after symptom onset without any treatment for the virus. If treatment is given, then the odds of getting a positive result diminish significantly.

There are also many different terms for this disease in the medical community. The name originally used was Mollaret's meningitis after Pierre Mollaret, but current trends in the medical field are moving away from individuals' names toward more descriptive names for a particular disease. The current name for this disease in ICD-11 is "Benign Recurrent Meningitis". The current names for other types of meningitis are herpes simplex meningitis, varicella meningitis, zoster meningitis, etc. Additionally, some of the most common diagnostic terms given to members within our organization include:

- Mollaret's meningitis
- Recurrent aseptic meningitis
- Recurrent meningitis
- Benign recurrent aseptic meningitis
- Recurrent benign lymphocytic meningitis
- Recurrent benign aseptic meningitis
- Benign recurrent meningitis
- Benign recurrent endothelial meningitis
- Benign Multirecurrent Endothelioleukocytal Meningitis

As you can see, eliminating differences in diagnostic terminology may clarify some confusion surrounding this disease.

### Long-Term Effects

Contrary to research which describes this disease as “self-limiting”, we have found that recurrent viral meningitis can be very disabling. In our 2018 survey, in which we asked members how recurrent meningitis affects their lives, only 38% of respondents said their presentation of the disease was truly recurrent with full recovery after each episode, 30% reported chronic symptoms of meningitis, and 27% report experiencing both chronic and acute forms.

Regarding specific experiences, our members were asked to list their long-term symptoms which they felt could be attributed to the onset of recurrent meningitis. Listed below are the most commonly reported symptoms (in order of most to least common).

1. Memory problems
2. Fatigue
3. Headache
4. Concentration issues
5. Brain Fog
6. Balance Issues
7. Sensitivity to sound
8. Eyesight changes
9. Dizziness

10. Nerve pain in extremities

More research is needed to fully elucidate the long-term effects of recurrent meningitis.

### **Medical Treatments**

Medications most used to treat this disease are Acyclovir and Valacyclovir. Most commonly, when patients present with severe symptoms, either IV Acyclovir is administered or a PICC line is inserted and the patient is instructed to treat at home for two weeks. Outside of active infection, many of our members follow long-term Acyclovir and Valacyclovir regimens in order to suppress viral reactivation. Recent research suggests success by treating with Indomethacin as well.<sup>2</sup> Additionally, because some patients have negative reactions to the antivirals, Lysine and other supplements have been helpful in managing symptoms.

### **Natural/Alternative Treatments**

The most common helpful non-invasive treatments used by our members are (in order):

1. Avoidance of stress
1. Extra sleep
2. Massage

The most common supplements used by our members are (in order):

1. Lysine
2. Magnesium
3. Vitamin C
4. Vitamin B12

## Active Research<sub>3</sub>

Currently, Research is being performed at Aarhus University in Denmark that hopes to better understand the cause of recurrent viral meningitis. Below is information provided by the investigators:

*Identification of novel innate immunodeficiencies in patients with HSV-2 Mollaret's meningitis*

**Dr. Alon Schneider Hait, M.D, Ph.D fellow**

**Supervision: Prof. Trine H. Mogensen**

Department of Infectious diseases, AUH

Department of Biomedicine, Faculty of Health

Aarhus, Denmark

"...In this study, we hypothesize that an inborn genetic defect in the patient's DNA can explain at least part of the disease pathway, by causing the host to react inappropriately to the viral invasion, or to be unable to suppress viral replication in case of reactivation. We believe that differential susceptibility to HSV-2 CNS recurrent infections is explained by host genetics, and in particular mutations found in genes encoding innate immune molecules involved in type I interferon (IFN) production...

In the end of the study, we will publish and disseminate all information gathered regarding our patients, and if novel genetic defects leading to susceptibility to Mollaret' meningitis will be found, we will act to recognize MM as PID (primary immunodeficiency disease) by the scientific and medical communities."

Full update can be found here: <https://recurrentmeningitis.org/2018-q2-research-update/>

## Differential Diagnosis of Recurrent Meningitis<sup>4</sup>

### Causes

#### Autoimmune Diseases

- Behçet's disease
- Granulomatosis with polyangiitis
- Rheumatoid arthritis
- Sarcoidosis
- Sjögren's syndrome
- Systemic lupus erythematosus
- Vogt-Koyanagi-Harada syndrome

#### Benign Tumors

- Craniopharyngioma
- Dermoid cyst
- Epidermoid cyst

#### Infections

- Bacteria
  - Escherichia coli
  - Haemophilus influenzae
  - Neisseria meningitidis
  - Staphylococcus aureus
  - Streptococcus pneumoniae
- Fungi
  - Blastomyces dermatitidis
  - Candida species
  - Coccidioides immitis
  - Cryptococcus neoformans
  - Histoplasma capsulatum
- Parasites

- Echinococcosis species
- Strongyloides stercoralis
- Toxoplasma gondii
- Viruses (Mollaret's)
  - Herpes simplex virus 1 (HSV-1)
  - Herpes simplex virus 2 (HSV-2)
  - Epstein-Barr virus (HHV-4)

### Malignant Neoplasias

- Leptomeningeal metastasis of solid tumors
- Leukemic meningitis
- Lymphomatous meningitis

### Medications

- Antibiotics
  - Amoxicillin
  - Cephalosporins
  - Ciprofloxacin
  - Trimethoprim-sulfamethoxazole
- Anticonvulsants
  - Carbamazepine
  - Lamotrigine
- Chemotherapeutic drugs
  - Cetuximab
  - Intrathecal chemotherapy
- Immunosuppressive agents
  - Azathioprine
  - IVIG
  - Methotrexate
  - TNF inhibitors
    - Adalimumab
    - Etanercept
    - Infliximab

- Etc.
- Non-steroidal anti-inflammatory agents (NSAIDs)
  - Diclofenac
  - Ibuprofen
  - Naproxen
  - Sulindac

## Other Considerations

- Chronic Meningitis<sub>1</sub>

For additional information visit <https://recurrentmeningitis.org>.

## Endnotes

1. CONTINUUM (MINNEAP MINN) 2018;24(5, NEUROINFECTIOUS DISEASE):1298–1326.  
[https://journals.lww.com/continuum/Fulltext/2018/10000/Chronic\\_Meningitis.6.aspx](https://journals.lww.com/continuum/Fulltext/2018/10000/Chronic_Meningitis.6.aspx)
2. <https://www.omicsonline.org/open-access/mollaret-meningitis-with-a-high-level-of-cytokines-in-csf-successfullytreated-by-indomethacin-2155-9562-1000464.pdf>
3. <https://recurrentmeningitis.org/2018-q2-research-update/>
4. Rosenberg, J. & Galen, B.T. Curr Pain Headache Rep (2017) 21: 33.  
<https://doi.org/10.1007/s11916-017-0635-7>