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# LIMBIC ENCEPHALITIS VERSUS LESARGHUS– COMPARING THE SIMILARITIES

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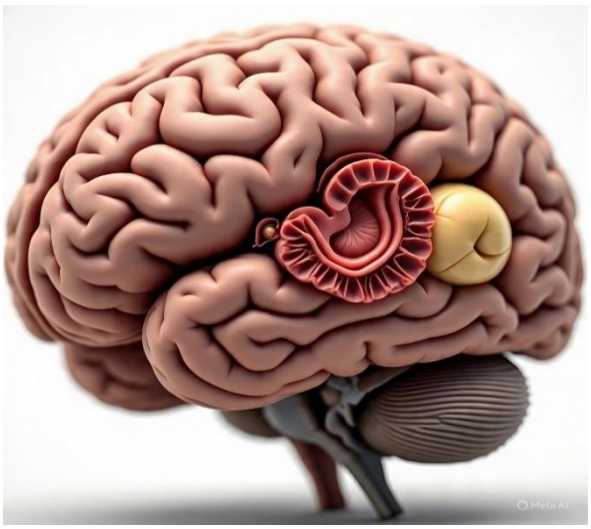
## ABSTRACT
Limbic encephalitis (LE), described in by Brierley et al., (1960) as "it is a rare neurological clinical entity of subacute course that causes neuropsychiatric symptoms where inflammation affects the limbic system, a part of the brain involved in emotions, memory, and behaviour." It's often associated with autoimmune responses or can be paraneoplastic (related to cancer). The condition can present with a variety of symptoms, including memory problems, confusion, seizures, and psychiatric manifestations. In addition to the usual symptoms of encephalitis such as altered consciousness, fever, and focal neurological deficits, limbic encephalitis can present with neuropsychiatric manifestations and seizures. Autoimmune encephalitis is the supraordinate term to LE; this term is often used as a comprise for non-paraneoplastic and paraneoplastic forms. LE can be short-lived and subside quickly upon immunologic therapy; in other instances, it may transgress into epilepsy.
There is a disease mentioned in Unani literature, by the name Lesarghus, classified under sarsam which has signs and symptoms nearly similar to Limbic Encephalitis described in modern medicine. Lesarghus is a chronic condition caused due to ghair tabai Balgham (abnormal phlegm). Continuous fever, Yawning, Loss of memory, continuous sleepy feeling, Lymphadenopathy, Headache, Seizures/spasms & vomiting etc., are usual symptoms of Lesarghus. The purpose of this review is to describe the similarities between Lesarghus & Limbic encephalitis.

**Keywords:** Lesar ghus; Acute Encephalitic Syndrome; Limbic Encephalitis; Autoimmune Encephalitis; Sarsam; Unani Medicine.

## INTRODUCTION
Limbic encephalitis is a form of encephalitis, a disease characterized by inflammation of the brain.[1] Limbic encephalitis is driven by autoimmune mechanisms, wherein the immune system generates antibodies that target components of the central nervous system. The condition may be paraneoplastic—associated with an underlying tumor—or non-paraneoplastic, with no detectable malignancy. [1]. Even though it's called "limbic" encephalitis, the disease usually affects more than just the limbic system. Brain autopsies often show damage in other areas too. [2][3][4]. The initial description of limbic encephalitis was provided by Brierley and colleagues in 1960. The potential

link to underlying malignancy was first reported in 1968, a finding that has since been substantiated by numerous investigators.
The majority of limbic encephalitis cases are associated with an underlying tumor, whether diagnosed or yet to be identified. In tumor-related cases, meaningful recovery is typically dependent on complete tumor removal—a goal that is not always achievable, especially in cases involving malignant or inoperable growths. Limbic encephalitis is further classified based on the specific autoantibody involved in the pathogenesis. The most common subtypes include:
1. **Anti-Hu (ANNA-1)** – Commonly linked to small cell lung carcinoma and often found in paraneoplastic cases.
2. **Anti-Ma2** – Often linked to testicular tumors and predominantly seen in young males.
3. **Anti-NMDAR** – Predominantly affecting young adults and pediatric patients, this antibody is frequently associated with ovarian teratomas and is a key marker in non-paraneoplastic and paraneoplastic limbic encephalitis.
4. **Anti-LGI1** – Primarily affecting older individuals, this antibody is generally not linked to an underlying tumor and is strongly associated with faciobrachial dystonic seizures, often preceding the development of full-blown limbic encephalitis.
5. **Anti-CASPR2** – This antibody is linked to a broad spectrum of neurological presentations, including limbic encephalitis, peripheral nerve hyperexcitability, and Morvan syndrome. It may occur in the context of a paraneoplastic process or as an idiopathic autoimmune disorder.

**Classification:** Limbic encephalitis can be categorized into two primary types: paraneoplastic, which is associated with an underlying malignancy, and non-paraneoplastic, which is typically related to infections or autoimmune conditions unrelated to cancer.
- Paraneoplastic limbic encephalitis (PNLE) happens when a tumor or cancer causes the immune system to attack the brain. Removing the tumor can sometimes help treat the condition.
- Non-paraneoplastic limbic encephalitis (NPLE), more common than PNLE, is unrelated to cancer and is often linked to infections, autoimmune diseases, or unknown causes. [5].

**LIMBIC SYSTEM** [6]
**Signs and symptoms:** Symptoms develop over days or weeks. Short-term memory problems usually develop slowly and are a main sign of this disease. But they're often missed because more noticeable symptoms—like seizures or severe behavior changes—get more attention.,
- Headache
- Irritability
- Sleep disturbance
- Delusions
- Hallucinations
- Agitation

- Seizures and
- Psychosis

or due to the presence of other symptoms requiring sedation, memory assessment is not feasible in a sedated patient

**Cause:** Limbic encephalitis results from an autoimmune reaction affecting the limbic system. In non-paraneoplastic cases, this reaction is commonly triggered by infections, particularly herpes simplex virus, or by systemic autoimmune conditions. When associated with malignancy, the condition is classified as paraneoplastic limbic encephalitis.

**Diagnosis:** Limbic encephalitis is difficult to diagnose, often leading to delays of several weeks. Key tests, such as CSF autoantibody detection, are not routinely available, and rarer antibodies like NMDAR can only be tested at a few research centers. This contributes to significant delays in diagnosis. Because of overlapping clinical features, many patients are initially misdiagnosed with herpes simplex or HHV-6 encephalitis.

**Diagnostic criteria of Paraneoplastic Limbic Encephalitis:**

**1.** Criteria by Gultekin et al. [8]

a) Histopathological Evidence of Limbic Encephalitis or

**b)** All 4 of the following:

- system Problems like memory loss, seizures, or changes in behavior may signal that the limbic system is affected.
- Neurological symptoms usually precede cancer diagnosis by less than four years.
- A thorough evaluation is essential to exclude other potential causes of limbic encephalopathy, including metastatic disease, infections, metabolic and nutritional disturbances, cerebrovascular insults, and adverse effects of treatment
- At least one of the following:
  - CSF with inflammatory findings
  - MRI FLAIR or T2 uni- or bilateral temporal lobe hyperintensities
  - EEG with epileptic or slow activity focally involving the temporal lobes

**2.** Criteria by the Paraneoplastic Neurological Syndrome Euronetwork (Graus et al.)[9]

a) Subacute onset (days or up to 12 wks) of seizures, short-term memory loss, confusion, and psychiatric symptoms, and

b) Neuropathologic or radiologic evidence (MRI, SPECT, PET) of involvement of the limbic system, and

c) Exclusion of other possible etiologies of limbic dysfunction and

d) Demonstration of a cancer within 5 yr of the diagnosis of neurologic symptoms or the development of classic symptoms of limbic dysfunction in association with a well-characterized paraneoplastic antibody (Hu, Ma2, CV2, amphiphysin, Ri).

**INVESTIGATION**

**Cerebrospinal fluid (CSF):** CSF examination usually shows lymphocytic pleocytosis (<100 cells/μL), mildly elevated protein (<1.5 g/L), normal glucose, increased IgG index, and oligoclonal bands, though it may be normal in patients with anti-VGKC antibodies examination.[10][11][12]

**Neuroimaging:** An MRI of the brain is usually the first and most important test to detect limbic system problems. It often shows brighter areas (T2 signal) in one or both temporal lobes.[13] Serial MRI in limbic encephalitis initially demonstrates acute uni- or bilateral enlargement and FLAIR/T2 hyperintensity of the temporomesial structures. Although these features may persist long term, they typically evolve into temporomesial atrophy in most cases.[14]

**PET-CT** Although not essential, PET-CT may assist in early diagnosis when MRI is negative in suspected cases.[15]

**Neuro-electrophysiology:** EEG usually reveals nonspecific slowing and epileptiform activity, primarily from the temporal lobes**.**

## TREATMENT

Limbic encephalitis is an uncommon neurological condition for which no randomized controlled trials currently exist to guide management. Treatment approaches that have been utilized include intravenous immunoglobulin, plasmapheresis, corticosteroids, cyclophosphamide, and rituximab.[1] Recovery is unlikely if an associated tumor is present unless it is removed. Unfortunately, removal may not be possible when the tumor is malignant and advanced.

The algorithms for treatment of LE are based on either case reports or small case series. Despite the limited data and no randomized controlled trial evidence, the current clinical experience suggests the following three general principles:

- Removal and/or treatment of tumour (if known),
- Immunotherapy, and
- The treatment(s) should start as early as possible.

**Removal and/or treatment of tumour:** The identification and removal of a tumour is the most important measure to improve or stabilize paraneoplastic. However, as many as 30–40% of the patients with paraneoplastic LE do not have any detectable antibodies associated with a tumour. Therefore, all patients with LE should be screened for underlying tumours. Screening techniques for tumours can include the following: (1) physical examination, (2) computed tomography (CT) of the thorax, abdomen and pelvis, (3) mammography of women and (3) ultrasonography, b-HCG and AFP to screen for testicular tumours in men.

## LESARGHUS [16]

Lesarghus is a type of Sarsam (meningitis) among its four types;

**Classification of Sarsam**- according to humour involved

- Faranitus (due to abnormal blood)
- Faranitus khalis (due to abnormal bile)
- Lesarghus (due to abnormal phlegm)
- Sarsame sauda (due to abnormal sauda)
- Classification of Sarsam-according to severity

**Haad (acute) –** Faranitus & Faranitus khalis

**Muzmin (chronic)-** Lesarghus & Sarsame saudavi

**Acute meningitis:** Faranitus- it is produced by the ghair tabai dam (abnormal blood). Faranitus affects the brain tissue or meninges or both. According to Ibn Sina, Faranitus present only in the meninges. This name is given because it interrupts the intellect and thinking.

**Faranitus khalis:** it is due to ghair tabai safra (abnormal bile), the symptoms of this disease are more prominent, because of Hiddate safra (sozish).

**Chronic meningitis**

- Lesarghus - due to ghair tabai Balgham (Abnormal Phlegm)
- Sarsam e Saudavi - due to ghair tabai sauda (Abnormal Black bile)

In case the brain tissue and meninges both are involved, the symptoms are as follow.

- Present in all age group but child is more prone to develop this.
- It is also due to injury of brain tissue.
- Amraaze jaubah (middle ear disease).
- Inflammation of the cranium.

Lesarghus is a Greek word and is a special type of encephalitis. Because of Ghair tabai balgham, it is named Lesarghus, which means a disease of forgetfulness. According to Sabit bin Qurrah and Ibn Sarafiyoon, Lesarghus is produced by ghair tabai balgham which accumulates in anterior part of the brain after infection.

**According to Sabit bin Qurrah, Ibn Sarafiyoon, and Ibn Sina -**
"Lesarghus is a phlegmatic type of inflammation that occurs in the brain, which is located inside the skull. It typically affects the pathways (or routes) of the brain, rather than the membrane, brain substances, or specific areas of the brain." (limbic encephalitis).
**Cause:** Balgham ghair tabai (Abnormal/Morbid Phlegm)

- According to Ibn Sina "lesar ghus us warm e balghami ko kehte hai jo khopri ke andar paida hota hai aur yeh warm aam taur se dimag ke majari (rasto) main hota hai, na ki dimaghi pardo (meninges), dimaghi batoon, ya khas dimagh me" [16]

**Symptom:**

- Continuous fever
- Yawning
- Loss of memory
- Patient sleeps continuously
- Lymphadenopathy
- Headache
- Seizures/spasms
- Vomiting.
- The patient lives in between the status of sleep and wakefulness.
- Modern science proves that now a days it is almost discussed in the case of limbic encephalitis.
- It resembles with sleeping sickness, which is commonly reported in Africa
- The movement of the eyelids and tongue becomes restricted.
- Complaints start with the fever.
- Fever persists for up to a month, then fever subsides, followed by pain in the feet and lymphadenopathy, which leads to → anaemia

**Management of Lesarghus** [16][17][18][19][20]

- **Diet:** Aabe Moong, moong ki khichree
- **Huqna:** the formulation having bekhe krafs + bekhe kibr + bekhe badyaan + pudina + bekhe izkhar used as enema.
- **Munzij-Mushil Therapy**:

o **Munzije Balgham:** Gule banafsha (7gm) + Maveez munaqqa (9 pieces) + Bekhe kasni (7gm) + Gauzaban (5gm) + Tukhme khatmi (5gm) - neem koob + hot water, and use with Khamira banafsha for 7-10 days.

o **Mushile balgham:** Barge sana (7mg) + Maghze khayar shambar (4gm) + Tamar hindi (4gm) + Zanjabeel (5gm) + Sheer khasht (20ml) + Sheerae maghze badam sheerein (5 pieces) – used for 3-4 days. One dose of Habbe Ayarij.

- **Takmeed wa Taskheen:** For purpose of fomentation on scalp, firstly removed the hairs and apply Mung bread (one side baked) and/or Murg or Kabootar (after removing intestine) as a whole and tied over scalp.
- **Moqawwiyat:** Kushta Khubsul hadeed (200 mg) + Kushta Marjan Jawahar wala (200 mg) + Dawaul Misk Motadil 2 gm.

| **Management of Lesarghus** | |
|---|---|
| Diet | Mung ka pani, mung ki khichree |
| Huqna | Preparation having Bekhe krafs + Bekhe kibr + Bekhe badyaan + pudina + Bekhe izkhar is advised for this purpose. |
| Munzije Balgham | Gule banafsha (7gm) + Maveez munaqqa (9pcs) + Bekhe kasni (7gm) + Gauzaban (5gm) + Tukhme khatmi (5gm) - Neem kub + hot water - with Khamira banafsha for 7-10 days. |
| Mushile balgham | Bbarg e sana 7 mg + maghz e khayar shambar 4 gm + Tamare hindi 4 gm+ zanjabeel 5gm+ sheer khahst 20 ml+ sheera e maghz e badam sirin 5pices- 3-4 day |
| Habbe ayarij | One dose |
| Takmeed wa Taskheen | For this purpose, fomentation on scalp (after removal of hairs) and application of Moong ki roti (one side baked), local application of fresh meet of chicken or pigeon (after removing of intestine). |
| Muqawwiyat | Kushta Khubsul Hadeed (200mg) + Kushta Marjan Jawahar wala (200mg) + Dawaul Misk Motadil (2gm). |

**Comparison of Lesarghus and Limbic Encephalitis**

| **Lesarghus** | | **Limbic Encephalitis** | |
|---|---|---|---|
| Auto Immunity | + | Auto Immunity | + |
| Inflammation Of Limbic System | + | Inflammation Of Limbic System | + |
| Headache | + | Headache | + |
| Insomnia | + | Sleep Disturb | + |
| Seizure | + | Seizure | + |
| Irritability | + | Irritability | + |
| Fever | + | Fever | + |
| Vomiting | + | Vomiting | + |
| Loss of consciousness or coma | + | Loss of consciousness or coma | + |
| Short Term Memory Loss | + | Short Term Memory Loss | + |

## CONCLUSION

Limbic encephalitis was once considered a rare disorder with a very poor prognosis. While it was thought that LE was always related to a neoplasm, several reports have been published in recent years describing different forms of LE that are associated with different antibodies. These forms of LE are not always associated with ‘well-characterized classical’ antibodies or a neoplasm. Current evidence demonstrates that LE is an autoimmune disorder that consists of a spectrum of autoimmune diseases.

Therefore, LE may be unrelated to a neoplasm in many cases, and some cases of LE show a good response to immunotherapy. By the above discussion we have also reached at the conclusion that the symptoms of Lesarghus in unani medicine is actually similar to limbic encephalitis in modern science. For the treatment of Lesarghus, Unani medicine has recommended a wide variety of herbs (single, compound and in combination of Regimenal therapy). Other recommended regimens include tabreede raas, mushil, huqna, lakhlakha, mushil-munzij therapy, massage/dalk, nutool, pashoya, zimad, takmeed, and taskheen. Dietary supplements, improved living conditions, lifestyle changes, and plenty of rest are also important. As these are the natural and safest methods, should must be applied accordingly in the treatment of Lesarghus by the Unani physician after well testing in real time situation, they must be re-validated through continuous and rigorous trial.

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**CONFLICT OF INTEREST**

Nill

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