



## *Psychiatric Manifestations of Various Infections and their Importance*

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### **Abstract**

*Many infections can lead to psychiatric manifestations in man. This can occur through multiple pathways that involve several neurotransmitters. Common examples are CNS toxoplasmosis and other infections that can lead to schizophrenia-like manifestations in animals as well as man. Direct CNS invasion may also be a risk factor. It may also cause psychiatric manifestations. These factors have been discussed in this review.*

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### **Historical Background**

The link between infections and mental disorders has been investigated since the 1880s. In 1887, through observing his own patients, Julius Wagner-Jauregg, Nobel Laureate and a leading psychiatrist, published a paper concluding that fever could cure psychoses and discussed infecting patients to induce fever as a therapeutic intervention [1]. Epidemics and pandemics throughout history suggest that infections could trigger various mental disorders and influence the course of mental health and infectious disorders. During the influenza epidemic in 1890, Emil Kraepelin,

a key founder of modern psychiatric classification, described 11 patients who presented with psychiatric symptoms ranging from depressed mood, cognitive deterioration, involuntary movements, paranoia, hallucinations, and delirium [2]. During the Spanish flu in 1918, Karl A. Menninger linked influenza with neuropsychiatry through observations in 100 patients with influenza [3]. The COVID-19 pandemic has also revealed a link between COVID-19 infection and mental disorders. A cohort-based study of adults with COVID-19 infections demonstrated that those with schizophrenia (SCZ) had a 2.5-fold increased risk for

mortality, even after controlling for cardiovascular disease, diabetes, smoking, obesity, age, sex, and race [4]. On the other hand, among patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with 6 other health events; this risk was independent of known physical health risk factors for COVID-19 [5]. These studies highlighted the link between mental disorders and the immune system and supported Kraepelin, who rightly postulated that the immunological defense and adaptation system should be made a major focus in psychiatric research.

Historically, infectious causes of psychiatric symptoms were considered in conditions like neurosyphilis, which in the pre-antibiotic era frequently led to psychosis and personality changes. Similarly, encephalitis lethargica reported in the early 20th century was linked with a variety of psychiatric symptoms, including catatonia and mood disturbances. Studies have disclosed that approximately 25% to 40% of individuals with untreated syphilis infection might in the end develop tertiary disease, including psychiatric disorder, even though this might take up to 30 years after the initial infections [6].

In modern medicine, the expanding knowledge of neuroimmunology and microbiota-gut-brain interactions has renewed interest in the psychiatric outcomes of infections.

## Introduction

The complex relationship between infections and psychiatric disorders has been recognized for centuries. However, it remains much unappreciated in both clinical and research scenario. Infections, particularly those affecting the central nervous system (CNS), can manifest with a plethora of psychiatric symptoms. These symptoms often precede or outlast the resolution of the infection, contributing significantly to morbidity and often leading to misdiagnosis or delayed treatment.

Understanding the psychiatric consequences of infections is crucial for timely diagnosis, effective treatment, and holistic patient care. This article reviews the psychiatric manifestations of infections,

explores the mechanisms behind them, and emphasizes their clinical importance.

## Mechanisms Linking Infections to Psychiatric Symptoms

Several biological mechanisms explain how infections lead to psychiatric manifestations:

### Direct CNS Invasion

- Some pathogens cross the blood-brain barrier and directly infect CNS tissue (like Herpes Simplex Virus, HIV, *Toxoplasma gondii*) [7].
- This invasion may result in encephalitis or meningitis, presenting with hallucinations, agitation, or cognitive disturbances.

### Neuroinflammation

- Systemic infections trigger the release of pro-inflammatory cytokines (like IL-1, IL-6, TNF-alpha) [8].
- These cytokines can alter neurotransmitter systems, neuroplasticity, and brain function, contributing to depression, anxiety, and even psychosis [9].

### Autoimmune Mechanisms

- Post-infectious immune responses may attack brain tissue (e.g., PANDAS—Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections) [10].
- Conditions like anti-NMDA receptor encephalitis often follow viral infections and present with acute psychiatric symptoms.

### Microbiota-Gut-Brain Axis

- Infections disrupting gut microbiota can influence brain function via neural, immune, and hormonal pathways.

This interaction has been implicated in mood disorders and schizophrenia. Beneficial gut bacteria release GABA and serotonin which cause relaxation and contentment [11]. Any disruption may thus alter mood and happiness.

### Immuno-Psychiatric Interface

The complex relationship between the immune system and the CNS is the key factor in the etiology of psychiatric disorders in the context of infectious diseases. Dysregulated immunological responses, characterized

by aberrant cytokine production, microglial activation, and T-cell infiltration, can trigger psychiatric symptoms through neurotoxic effects on synaptic function and neurotransmitter metabolism [12]. Chronic immunological activation, often associated with chronic infection or systemic inflammation, significantly exacerbates mental morbidity by perpetuating neuroinflammatory processes and impairing neuroplasticity [12]. Moreover, the bidirectional communication between the immune and neuroendocrine systems plays a crucial role in defining the clinical course of psychiatric disorders, influencing stress responsivity, mood control, and cognitive function in patients with infectious diseases [12]. This highlights the need for a comprehensive understanding of the relationships between immunological dysregulation and psychiatric disease, as it is essential for developing targeted immunomodulatory medicines and tailored interventions that aim to restore CNS homeostasis and improve mental health outcomes.

## Common Infections with Psychiatric Manifestations

### Viral Infections

#### Herpes Simplex Virus (HSV)

- HSV-1 encephalitis is notorious for causing acute psychosis, memory loss, and personality changes.
- Even after treatment, cognitive and psychiatric symptoms may persist.

#### HIV/AIDS

- HIV-associated neurocognitive disorder (HAND) includes apathy, depression, and dementia.
- Psychiatric symptoms may be early signs of CNS involvement.

#### SARS-CoV-2 (COVID-19)

- A wide range of neuropsychiatric symptoms have been reported in COVID, like anxiety, depression, brain fog, insomnia, and even psychosis.
- These may occur during infection or as part of long COVID.

## Bacterial Infections

### Syphilis

- Neurosyphilis can present with paranoia, mania, or depression.
- Often misdiagnosed due to its protean presentation, it remains a “great imitator.”

### Streptococcal Infections

- In children, Group A Streptococcus or *S. pyogenes* has been associated with PANDAS, characterized by sudden-onset OCD and tics.

### Tuberculosis (TB)

- TB meningitis can cause mood swings, psychosis, and cognitive impairment.
- Chronic TB can also contribute to depression due to systemic inflammation and the stress of illness.

## Parasitic and Fungal Infections

### Toxoplasma gondii

- Linked with schizophrenia and bipolar disorder in epidemiological studies. In animals, it has been seen that rats and mice lose fear of cats when infected with *T. gondii*. Then they roam freely in front of cats which devour them, and thus the life cycle is completed.
- The parasite may influence dopamine regulation in the brain.

### Cryptococcus

- CNS infection in immunocompromised individuals (e.g., HIV patients) can result in hallucinations, confusion, and cognitive decline.

Syndrome	Possible Infectious Causes
Delirium	UTI, pneumonia, sepsis, CNS infections
Depression	HIV, Hepatitis C, COVID-19, TB
Anxiety	COVID-19, Lyme disease, post-viral syndromes
Psychosis	HSV, HIV, NMDA-receptor encephalitis, neurosyphilis
Mania	HIV, TB, neurosyphilis
Obsessive-Compulsive Disorder (OCD)	PANDAS, Lyme disease (caused by <i>Borrelia burgdorferi</i> )
Cognitive Impairment/Dementia	HIV, neurosyphilis, TB meningitis

### Pediatric Considerations

Children are particularly vulnerable to neuropsychiatric consequences of infections due to their developing brains.

- PANDAS and PANS (Pediatric Acute-onset Neuropsychiatric Syndrome) illustrate how infections can cause acute-onset OCD, tics, and mood lability.
- Developmental regression, anxiety, and ADHD-like symptoms may follow viral or bacterial infections.

### Importance of Recognizing Psychiatric Manifestations of Infections

#### Diagnostic Accuracy

- Misdiagnosis as primary psychiatric illness can delay appropriate treatment.
- Atypical presentations (e.g., late-onset psychosis) should raise suspicion for infectious or autoimmune causes.

#### Timely Intervention

- Many infectious causes (e.g., HSV, syphilis) are treatable, and early therapy can prevent long-term damage.
- Recognition of psychiatric symptoms as part of infection can be life-saving.

### Public Health Implications

- Identifying psychiatric sequelae can aid in tracking outbreaks (e.g., post-COVID neuropsychiatric syndromes).
- Neuropsychiatric disability contributes significantly to the global burden of infectious diseases.

### Improved Patient Outcomes

- Integrative care models involving psychiatrists, infectious disease specialists, and neurologists yield better outcomes.
- Mental health support improves adherence to treatment for chronic infections like HIV and TB.

### Challenges in Clinical Practice

#### Lack of Awareness

- Many clinicians overlook infectious causes when evaluating new-onset psychiatric symptoms, especially in adults.

#### Overlapping Symptoms

- Infections often mimic primary psychiatric disorders, making differentiation difficult without high clinical suspicion.

### Limited Access to Diagnostics

Serological and neuroimaging tests may be expensive or unavailable, particularly in low-resource settings.

### Stigma

Both mental illness and infections like HIV or syphilis carry stigma, discouraging patients from seeking help.

### Recommendations and Clinical Approach

#### History and Examination

- Always inquire about recent infections, travel, immune status, substance use, and sexual history.
- Look for constitutional symptoms (fever, weight loss) and neurological signs.

#### Investigations

- CBC, ESR, CRP
- Serology: HIV, VDRL/RPR, Lyme, HSV, EBV, Toxoplasma
- CSF analysis (if CNS infection suspected)
- Brain imaging (MRI > CT)
- Autoimmune panel if indicated

#### Multidisciplinary Approach

- Collaboration between psychiatry, infectious diseases, neurology, and immunology improves diagnostic accuracy and management.

#### Early Intervention

- Treat both the infection and the psychiatric symptoms concurrently.
- Consider psychotropics carefully—interactions with antimicrobials and immune status should guide choices.
- Second Generation Antipsychotics- to treat psychosis.
- Antidepressants And Anxiolytics- to treat mood symptoms and anxiety.
- Psychotherapy- Cognitive behavior therapy, Supportive therapy, Psychoeducation.

### Conclusion

The psychiatric manifestations of infections are diverse, clinically significant, and often under-recognized. From delirium in systemic infections to chronic depression in HIV or acute psychosis in

encephalitis, the spectrum is broad and impactful. Given the treatable nature of many underlying infections, early identification of psychiatric symptoms as potential red flags is vital. Integrating psychiatric evaluation into infectious disease care, and vice versa, not only improves outcomes but also reflects the complexity and interconnectedness of human health. As we move forward in a post-pandemic world with a growing awareness of the brain-immune axis, understanding these intersections is more relevant than ever.

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