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HEPATIC CHANGES FOLLOWING INFECTIOUS DISEASES OF THE CENTRAL NERVOUS SYSTEM: MECHANISMS, PATTERNS, AND CLINICAL IMPLICATIONS

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ABSTRACT

Infectious diseases of the central nervous system (CNS)—including bacterial meningitis, viral encephalitis, tuberculous meningitis, and neuroinvasive systemic infections—do not remain confined to the brain and meninges. They frequently trigger systemic inflammation, neuroendocrine stress responses, hemodynamic instability, and therapeutic exposures that collectively reshape hepatic physiology. The liver, as an immune-metabolic “gatekeeper,” responds to CNS infection through acute-phase signaling, altered bile acid transport, microcirculatory changes, mitochondrial stress, and immune-cell trafficking. Clinically, these processes can manifest as transient transaminase elevation, sepsis-associated cholestasis, mixed hepatocellular–cholestatic patterns, steatosis during prolonged critical illness, and drug-induced liver injury (notably during anti-tuberculous therapy). This article synthesizes current mechanistic evidence for the brain–liver axis, describes the most typical biochemical and morphological patterns of hepatic change after CNS infections, and proposes a practical IMRAD-style approach to evaluation and monitoring. The key message is that post-CNS-infection hepatic abnormalities are often multifactorial: inflammation-driven bile transporter dysfunction, hypoxic–ischemic stress, immune-mediated injury, and medication toxicity may co-occur. Recognizing these patterns can prevent unnecessary invasive procedures, improve antimicrobial/adjunctive therapy safety, and support early detection of clinically significant liver dysfunction.

Keywords: Central nervous system infection; meningitis; encephalitis; sepsis-associated cholestasis; liver injury; brain–liver axis; cytokines; drug-induced liver injury; tuberculous meningitis; bile acid transport.

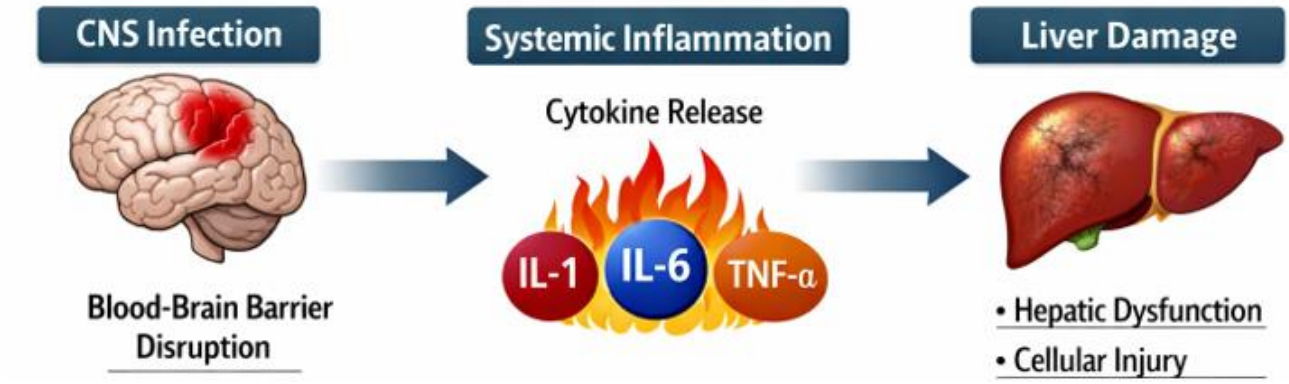

Figure 1. Conceptual pathway linking CNS infection to systemic inflammation and downstream liver injury (cytokine-driven hepatocellular dysfunction and cellular damage).

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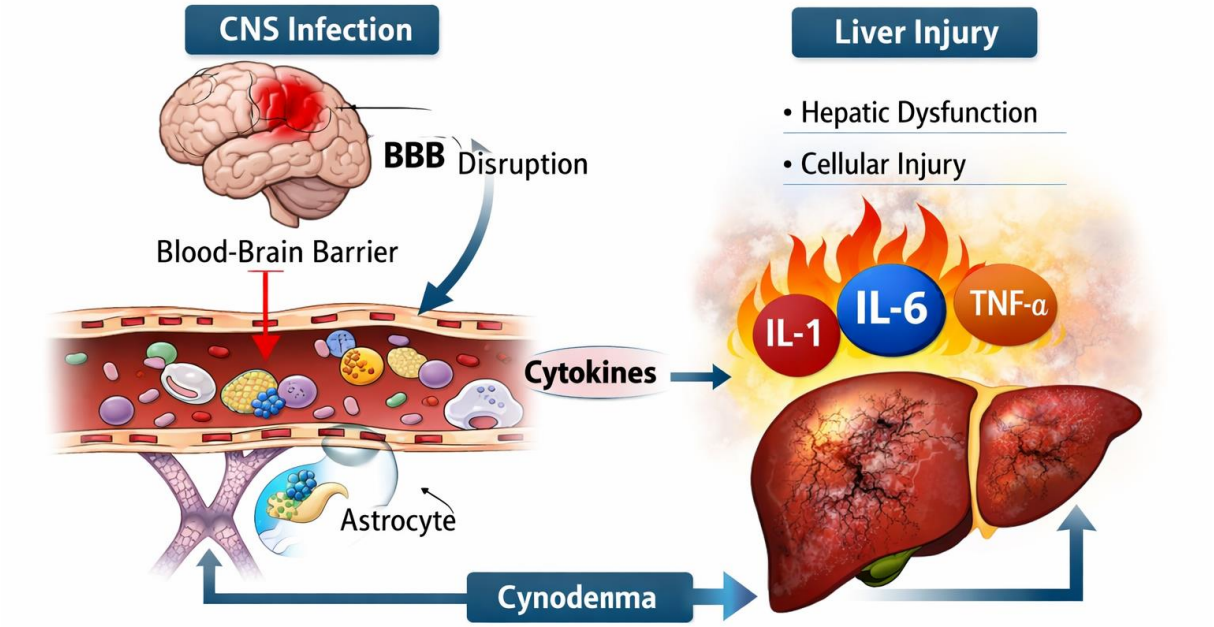
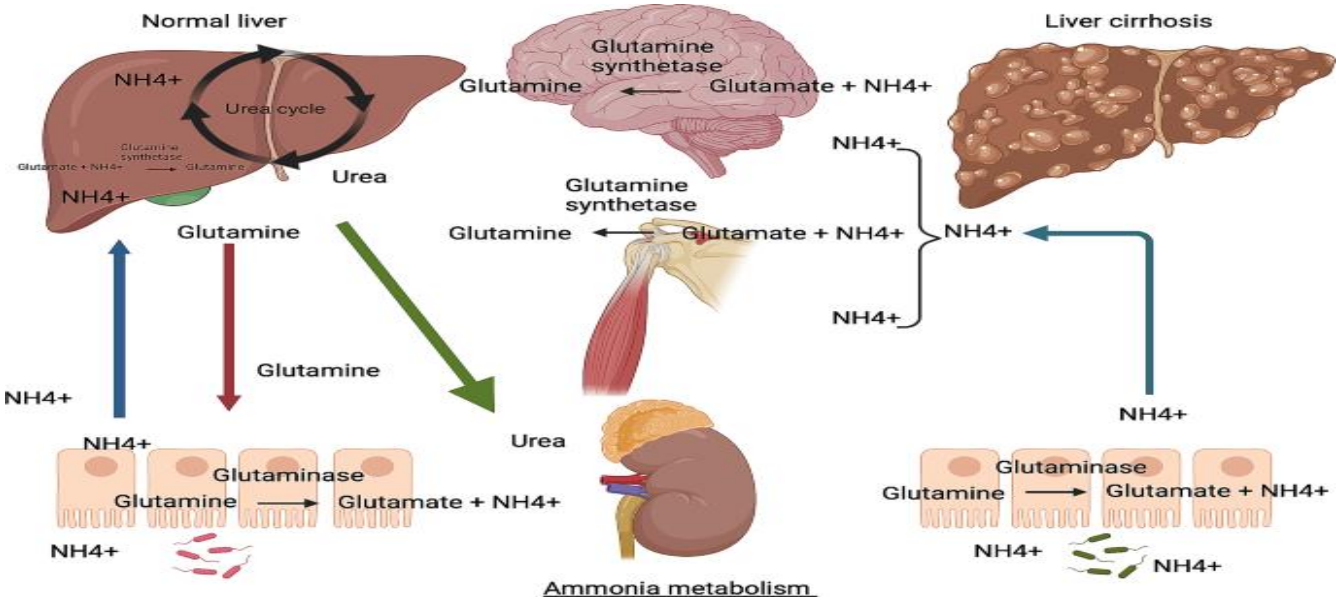


Figure 2. CNS infection → BBB disruption → cytokine signaling → liver injury (schematic illustration of the inflammatory cascade).



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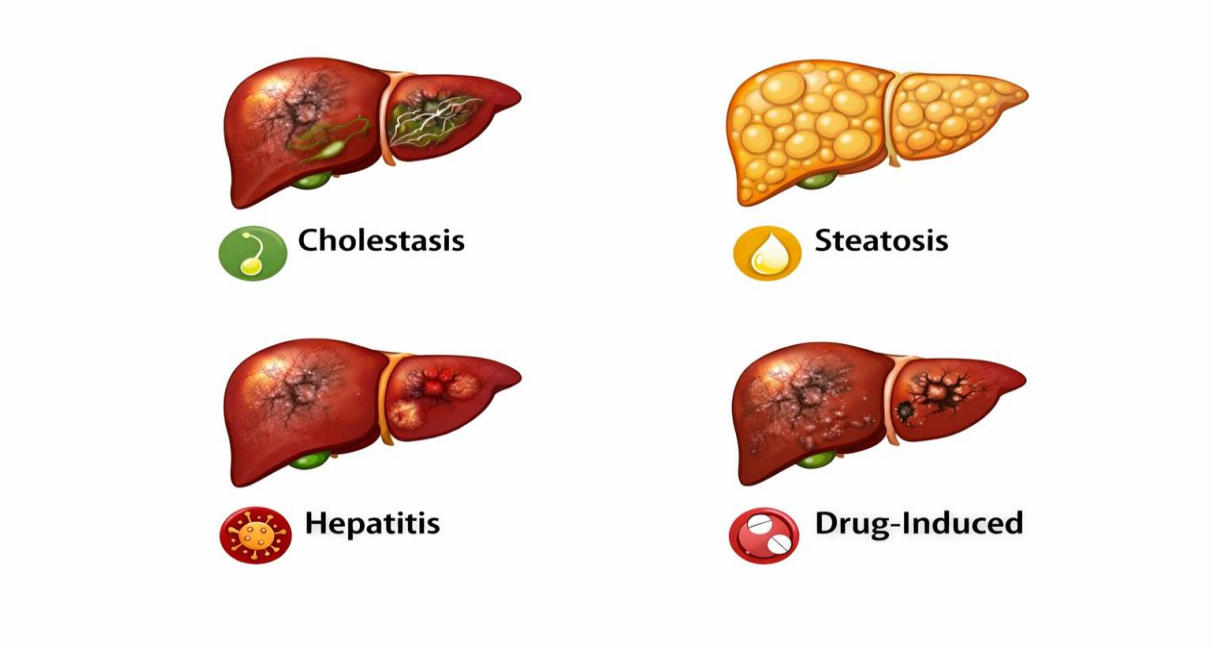

Figure 3. Common post-infectious liver patterns encountered after CNS infections: cholestasis, steatosis, hepatitis-like injury, and drug-induced liver injury (DILI).

INTRODUCTION

CNS infections remain a major cause of acute morbidity worldwide, ranging from rapidly progressive bacterial meningitis to viral encephalitis and chronic infections such as tuberculous meningitis. While the clinical focus naturally centers on neurologic complications—raised intracranial pressure, seizures, cerebral edema, focal deficits, and long-term cognitive outcomes—the systemic "echo" of a CNS infection is increasingly recognized as a determinant of prognosis and therapeutic tolerance. The liver is a primary target of this systemic response because it integrates innate immunity, metabolism, detoxification, bile production, and regulation of circulating inflammatory mediators. Several observations motivate a dedicated discussion of hepatic changes after CNS infections. First, abnormal liver function tests (LFTs) are common during systemic infections and inflammatory states; the liver is frequently involved even when the primary infection is outside the hepatobiliary tract. Second, sepsis and severe inflammation can cause cholestasis through cytokine-mediated impairment of bile formation and transporter function, often producing prominent hyperbilirubinemia with modest transaminase rise. Third, modern concepts of inter-organ communication highlight a brain–gut–liver (and broader brain–liver) axis, where acute brain injury and neuroinflammation can reshape hepatic immune signaling and metabolic outputs, potentially amplifying systemic inflammation and influencing recovery. Fourth, treatment itself—especially prolonged antimicrobial regimens and adjunctive therapies—can contribute to hepatotoxicity. This is particularly relevant in tuberculous meningitis, where first-line anti-tuberculous drugs are hepatically metabolized and may induce clinically meaningful liver injury. The purpose of this article is to present an

METHODS

Design and approach. This article is a narrative, mechanism-to-clinic synthesis structured in IMRAD format. Evidence was integrated from peer-reviewed reviews and guideline resources addressing (a) liver involvement in systemic infection, (b) sepsis-associated cholestasis and transporter-level mechanisms, (c) inter-organ axes connecting brain inflammation to hepatic signaling, and (d) hepatotoxicity considerations in CNS infection therapies, particularly tuberculous meningitis. Search strategy (conceptual). Sources were identified by targeted searches combining

terms for CNS infections (meningitis, encephalitis, tuberculous meningitis) with hepatic outcomes (cholestasis, transaminases, liver injury, bile transporters, hepatotoxicity). Priority was given to authoritative reviews on sepsis-induced cholestasis and infection-related liver involvement, guideline and knowledge platforms for hepatotoxicity management in tuberculosis therapy, and recent reviews describing the brain–liver or brain–gut–liver axis and metabolic crosstalk. Outcome framework. The analysis was organized around four clinically recognizable hepatic outcomes after CNS infection: (1) inflammation-driven cholestasis, (2) hepatocellular injury and sterile inflammatory amplification, (3) metabolic/critical-illness–associated steatosis and dysfunction, and (4) drug-induced liver injury.

RESULTS

Mechanistic pathways from CNS infection to hepatic dysfunction.Systemic inflammatory signaling and the acute-phase response. CNS infections frequently induce a systemic inflammatory response through cytokine release (e.g., IL-1, IL-6, TNF-α), activation of innate immune pathways, and neuroendocrine stress signaling. The liver is central to the acute-phase response, synthesizing proteins that modulate inflammation and coagulation while simultaneously adapting metabolic pathways to stress. Inflammatory mediators can shift hepatocyte function away from bile formation and xenobiotic processing toward acute-phase protein production, raising susceptibility to cholestasis and metabolic imbalance. Sepsis-associated cholestasis and bile transporter dysfunction. One of the most characteristic hepatic patterns during severe infection is cholestasis that arises from impaired bile formation and bile acid transport rather than mechanical obstruction. Cytokines and endotoxin-driven pathways can downregulate nuclear receptors and transporters involved in bile acid homeostasis, shifting bile acid traffic and promoting intrahepatic bile acid accumulation. Microcirculatory and hypoxic–ischemic stress. Severe CNS infection can be accompanied by shock, vasopressor requirement, hypoxemia, and microvascular dysfunction, all of which can impair hepatic perfusion. Reduced oxygen delivery to hepatocytes promotes mitochondrial stress and hepatocellular injury, potentially increasing AST/ALT. Immune cell trafficking and axis effects. Beyond generalized sepsis biology, inter-organ axis literature suggests that acute brain inflammation can modulate hepatic chemokine production and immune cell recruitment, with potential bidirectional effects: hepatic inflammation can amplify systemic immune responses and may influence immune cell migration relevant to CNS injury. 2) Typical patterns of liver abnormalities after CNS infection Pattern A: Predominant cholestasis (hyperbilirubinemia ± modest ALP/GGT). Patients may show rising total and direct bilirubin with relatively mild aminotransferase elevation. Pattern B: Hepatocellular injury (AST/ALT elevation). This may reflect hypoxic stress, direct inflammatory injury, metabolic dysregulation, or concomitant systemic infection affecting the liver. Pattern C: Mixed cholestatic–hepatocellular changes. Mixed patterns are common because cholestasis and hepatocellular injury mechanisms often overlap during severe illness. Pattern D: Drug-induced liver injury (DILI). Tuberculous meningitis is a high-yield example because standard regimens include hepatically metabolized drugs with known hepatotoxic risk, requiring careful monitoring and structured reintroduction strategies when hepatotoxicity occurs.

3) Morphological correlates (conceptual pathology) Although liver biopsy is rarely indicated solely for transient LFT abnormalities in acute CNS infection, morphological correlates can be inferred: canalicular cholestasis in inflammation-associated cholestasis; necroinflammatory foci in hepatocellular injury; steatosis in prolonged critical illness; and variable necrosis or cholestasis in DILI. 4) Practical evaluation and monitoring Baseline assessment should include ALT, AST, ALP, GGT, total/direct bilirubin, INR, albumin, and medication history. Trend-based interpretation is crucial: rapid bilirubin rise with modest ALT/AST in severe infection supports inflammation-mediated cholestasis, while disproportionate ALT/AST elevations with rising INR heighten concern

for significant hepatocellular injury or DILI. When anti-tuberculous therapy is used, guideline-informed hepatotoxicity management and stepwise reintroduction are recommended.

DISCUSSION

Hepatic changes after CNS infections are rarely attributable to a single cause. The liver integrates immune sensing, bile acid signaling, and metabolic adaptation; therefore neuroinfection-driven systemic inflammation can produce cholestasis through transporter downregulation while simultaneously exposing hepatocytes to hypoperfusion, oxidative stress, and immune-cell–mediated injury. Inter-organ axis concepts add another layer, suggesting that neuroinflammation may reshape hepatic immune signaling and create feedback loops that worsen organ dysfunction. Clinically, LFT abnormalities should be interpreted as potentially expected but still actionable findings. Recognizing sepsis-associated cholestasis can prevent unnecessary biliary interventions when imaging does not support obstruction. Vigilance for DILI is essential in regimens known for hepatotoxicity, particularly in tuberculous meningitis, where structured reintroduction strategies help balance infection control with hepatic safety. Even after neurologic stabilization, hepatic changes can influence rehabilitation and medication tolerance. Persistent cholestasis may impair nutrition, and unresolved hepatocellular injury may constrain drug options. Future prospective studies focused on meningitis and encephalitis should quantify the prevalence of distinct LFT patterns, link them to severity and therapies, and explore biomarkers connecting neuroinflammation to hepatic transporter dysfunction.

CONCLUSION

Hepatic changes following infectious diseases of the central nervous system are common, clinically meaningful, and typically multifactorial. Dominant drivers include systemic inflammation with cytokine-mediated bile transporter dysfunction, microcirculatory and hypoxic stress causing hepatocellular injury, inter-organ axis signaling, and drug-induced liver injury—especially during prolonged anti-infective regimens such as those used for tuberculous meningitis. Recognizing characteristic laboratory patterns and interpreting them in context enables safer pharmacotherapy, reduces unnecessary procedures, and supports integrated, organ-protective management.

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