

Borrelia burgdorferi IgG & IgM Ab Index in Serum and CSF

Specimen Type	Serum and CSF	
Specimen Volume	Serum: 3 mL CSF: 2 mL	
Collection	Serum:	Collect blood in red top tube with no additives or tiger top tube. Let clot for 30 minutes. Centrifuge at 3000 rpm for 10 minutes. Separate serum from cells and transfer to a transport tube. Freeze immediately.
	CSF:	Collect by lumbar puncture. Centrifuge at 3000 rpm for 10 minutes. Remove any cells from lumbar collection. Freeze immediately.
Minimum Volume	Serum: 0.5mL CSF: 0.5 mL	
Handling	Serum and CSF: Ship Frozen on dry ice.	
Rejection Criteria	<ul style="list-style-type: none"> • Microbially contaminated specimens. • Hemolyzed specimens. • Specimens outside of listed stability. 	
Stability	See Below.	
Methodology		
Reference Range		
Turnaround Time	Up to 7 business days.	
CPT Codes	See Below.	
Clinical Significance	<p>Lyme borreliosis, caused by the tickborne spirochete <i>Borrelia burgdorferi</i>, often leads to nervous system abnormalities. Major clinical findings of the neurological manifestation of acute Lyme neuroborreliosis (LNB) include painful meningoradiculitis with inflammation of the nerve roots and lancinating, radicular pain (Bannwarth's syndrome), lymphocytic meningitis, and various forms of cranial or peripheral neuritis. Patients with Lyme neuroborreliosis sometimes show pleocytosis, alterations in the blood-cerebrospinal fluid (CSF) barrier manifested by an elevated ratio of albumin in CSF to albumin in serum, and intrathecal production of <i>B. burgdorferi</i>-specific antibodies. The latter is considered the best indicator for Lyme neuroborreliosis. In both American and European patients with meningeal involvement and in European patients with encephalomyelitis, intrathecal production of antibodies against <i>B. burgdorferi</i> can be demonstrated, provided that multiple antibody isotypes are measured. However, this finding is inconsistent in American patients with subtle central nervous system symptoms or with late neurologic manifestations of Lyme neuroborreliosis. Levels of antibody to <i>B. burgdorferi</i> in CSF and serum must account for passive diffusion of immunoglobulin G (IgG) antibodies across the blood-CSF barrier. The CSF/serum ratio of titers to <i>B. burgdorferi</i> may be compared with the ratio of albumin in CSF to albumin in serum.</p>	

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Cerebrospinal fluid is secreted by the choroid plexuses, around the cerebral vessels and along the ventricles of the brain. It fills the ventricles and cistern, bathes the spinal cord, and is reabsorbed into the blood through the arachnoid villi. CSF exchange is rapid, exchanging about 4 times a day. More than 80% of CSF protein content originates from the plasma by ultrafiltration through the walls of the capillaries in the meninges and choroid plexuses; the remainder originates from intrathecal synthesis. Because CSF is mainly an ultrafiltrate of plasma, lower molecular-weight plasma proteins, such as albumin, predominate. No protein with a molecular weight greater than IgG is normally present in routinely detectable concentrations.

The permeability of the blood-CSF barrier to plasma proteins is increased by high intracranial pressure due to brain tumor, intracerebral hemorrhage, traumatic injury, or inflammation due to bacterial or viral meningitis, encephalitis, poliomyelitis. Striking elevations occur in bacterial meningitis, with smaller elevation occurring in the other inflammatory diseases.

Demonstration of increased intrathecal synthesis of immunoglobulins, particularly IgG, has great importance in the diagnosis of demyelinating diseases of the CNS, especially multiple sclerosis.

B. burgdorferi Index Calculations

NOTE: The calculations of B burgdorferi IgG and IgM Antibody Index Ratio are intended to assist in the diagnosis of neuroborreliosis. These calculations are only meaningful in cases where the B. burgdorferi IgG or IgM antibodies in CSF are elevated.

This formula estimates the amount of IgG that is produced intrathecally.

Local (Loc) IgG/IgM Synthesis

The formula for Local IgG/IgM synthesis is used to calculate the minimum amount of Local IgG or IgM synthesis in the CNS, using empirically derived correction factors to account for the loss of molecular size selectivity by the BBB. Similar to the IgG/IgM Index, Local IgG/IgM Synthesis has high diagnostic sensitivity and a low false positive rate; however, in the presence of BBB impairment, it has an increased rate of false negative results. Values for Local IgG/IgM Synthesis above the upper limit of normal in a patient with an increased IgG/IgM Index provides strong evidence for increased intrathecal IgG/IgM synthesis.

Albumin Ratio

The Albumin Ratio calculates the degree of permeability of the blood brain barrier (BBB) by the measurement of albumin in the CSF and serum. An index of less than 9 is considered consistent with an intact barrier. Values 9 to 14 are interpreted as slight impairment; 14 to 30 as moderate impairment; 30 to 100 as severe impairment, and exceeding 100 indicates a total breakdown of the barrier.

The IgG Index is calculated from the albumin and IgG concentrations in serum and CSF using the formula $\text{Index} = (\text{IgG CSF} / \text{IgG ser}) / (\text{Alb CSF} / \text{Alb ser})$. Normally the index is ≤ 0.7 . Values greater than 0.7 are considered evidence of increased CSF IgG synthesis.

IgG Synthesis Rate

Similar to albumin, IgG enters the CSF from the serum. Unlike albumin however, IgG can also be produced intrathecally. Thus, an altered CSF:serum IgG ratio can result from a damaged BBB and/or increased local IgG production. The formula for calculating IgG synthesis rate uses constants that correct for the average normal serum:CSF ratios of IgG and albumin (i.e., 369 and 230, respectively), the molecular weight ratio (i.e., 0.43) of these 2 proteins, and the daily production of CSF volume (i.e., the factor, 5). The formula is based on the concept that, in conditions in which BBB damage occurs, the degree of increased permeability of the BBB to albumin is directly proportional to the degree of increased permeability to IgG. By subtracting from the CSF IgG concentration, the amount of IgG due to entry into the CSF from the serum when the BBB has normal permeability and when its permeability is increased, this formula estimates the amount of IgG that is produced intrathecally. Unfortunately, this formula has the greatest tendency to yield falsely elevated results in conditions of BBB impairment. Therefore, this tendency must be kept in

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mind when interpreting values for IgG synthesis rate.

$$\{IgG_{csf} - (IgG_{ser}/369) - [(Alb_{csf} - (Alb_{ser}/230))] \times (IgG_{ser}/Alb_{ser}) \times 0.43\} \times 5.$$

Test Name	Methodology	Reference Range	Units	CPT Code	Stability
Borrelia burgdorferi IgG Antibodies Index Ratio	CALC	< 1.0	N/A	N/A	N/A
Borrelia burgdorferi IgM Antibodies Index Ratio	CALC	< 1.0	N/A	N/A	N/A
IgG (loc)	CALC	< .10	mg/dL	N/A	N/A
IgG Index	CALC	< .70	N/A	N/A	N/A
CNS IgG Synthesis Rate	CALC	< 3.3	mg/24 hr	N/A	N/A
IgM (loc)	CALC	< .010	mg/dL	N/A	N/A
IgM Index	CALC	< .10	N/A	N/A	N/A
Albumin Index Ratio	CALC	< 9.0	N/A	N/A	N/A
IgG Total CSF	Immunoturbidimetry	≤ 8.84	mg/dL	82784	Frozen for 2 weeks
IgG Total Serum	ELISA	540 to 1423	mg/dL	82784	Frozen for 2 months
IgM Total CSF	NEPH	0.0-0.6	mg/dL	82784	Frozen for 2 months
IgM Total Serum	NEPH	52 - 217	mg/dL	82784	Frozen for 2 months
Albumin CSF	NEPH	10.4 – 43.2	mg/dL	82042	Frozen for 2 months
Albumin Serum	NEPH	3700 - 5100	mg/dL	82040	Frozen for 2 months
Borrelia burgdorferi IgG Antibodies CSF	EIA	< 0.09	Index	86618	Frozen for 5 months
Borrelia burgdorferi IgG Antibodies Serum	EIA	< .80	Index	86618	Frozen for 5 months
Borrelia burgdorferi IgM Antibodies CSF	EIA	≤ 0.06	Index	86618	Frozen for 5 months
Borrelia burgdorferi IgM Antibodies Serum	EIA	< .80	Index	86618	Frozen for 5 months