

## CLINICAL SPECIFICATIONS

### BLOOD-BRAIN BARRIER PROTEINS (saliva)

#### Function:

The blood brain barrier (BBB) is a physical barrier formed by the arrangement of endothelial cells and tight junctions that line the capillaries which supply blood to the brain. The tissue proteins of the BBB are also present in the enteric nervous system (ENS). The complex ENS network resides in the wall of the gastrointestinal tract, the myenteric plexus and the submucosal plexus.<sup>1</sup> The ENS controls aspects of gut function, including motility, microvascular circulation, epithelial secretion of fluid, ions and bioactive peptides and intestinal barrier function.<sup>2</sup>

#### Associated With:

Individuals training for professional sports (saliva)<sup>3</sup>  
 Inflammatory bowel disease (saliva)<sup>4</sup>  
 Traumatic brain injury (serum)<sup>5</sup>

#### Known Cross-Reactions:

#### Clinical Significance:

Salivary antibodies to BBB proteins in an indication of a cross-reactivity between an orally exposed antigen and BBB proteins of the enteric nervous system or intestinal tight junction proteins. Repeated head trauma and traumatic brain injury (TBI) associated with accidents and some sports, such as football or hockey, have also been shown to damage the BBB and the astrocytes.<sup>6</sup> TBI is a multifaceted pathology involving excitotoxicity, free radical formation, brain swelling, and the entry of locally produced molecules such as cytokines, chemokines, and other molecules.<sup>5</sup> Within hours of TBI, increased intestinal permeability<sup>7</sup> Reviewed in <sup>8</sup> has been shown and TBI can lead to chronic gastrointestinal dysfunctions.<sup>7</sup> Salivary levels of BBB proteins have been used soon after birth in asphyxiated newborns to identify infants at risk of neurological disorders.<sup>9</sup> Although not the ideal biomarker, BBB proteins in saliva can be seen in patients with inflammatory bowel disease.<sup>4</sup> Persons with salivary BBB protein antibodies must protect and support gut and brain barriers.

#### Suggested Reading:

1. Badizadegan et al. Presence of intramucosal neuroglial cells in normal and aganglionic human colon. *Am J Physiol Gastrointest Liver Physiol*, 2014; 307:G1002-1012.
2. Savidge et al. Starring roles for astroglia in barrier pathologies of gut and brain. *Lab Invest*, 2007; 87:731-736.
3. Michetti et al. Saliva S100B in professional sportsmen: high levels at resting conditions and increased after vigorous physical activity. *Clin Biochem*, 2011; 44(2-3):245-247.
4. Manolakis et al. Calprotectin, calgranulin C, and other members of the S100 protein family in inflammatory bowel disease. *Digest Dis Sci*, 2011; 56(6):1601-1611.
5. Vojdani. Brain-reactive antibodies in traumatic brain injury. *Funct Neurol Rehabil Ergon*, 2013; 3(2-3):173-181.
6. Marchi et al. Consequences of repeated blood-brain barrier disruption in football players. *PLoS ONE*, 2013; 8(3):e56805.
7. Kharrazian. Traumatic brain injury and the effect on the brain-gut axis. *Altern Ther Health Med*, 2015; 21(suppl3):28-33.
8. Bansal et al. Traumatic brain injury and intestinal dysfunction: uncovering the neuro-enteric axis. *J Neurotrauma*, 2009; 26:1353-1359.
9. Gazzolo et al. Neurological abnormalities in full-term asphyxiated newborns and salivary S100B testing: the "Cooperative Multitask against Brain Injury of Neonates" (CoMBINe) international study. *PLoS ONE*, 2015; 10(1):e0115194.