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## **Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options.**

[Konturek PC](#), [Brzozowski T](#), [Konturek SJ](#).Department of Medicine, Thuringia Clinic Saalfeld, Teaching Hospital of the University Jena, Germany. [pkonturek@thueringen-kliniken.de](mailto:pkonturek@thueringen-kliniken.de)

### **Abstract**

Stress, which is defined as an acute threat to homeostasis, shows both short- and long-term effects on the functions of the gastrointestinal tract. Exposure to stress results in alterations of the brain-gut interactions ("brain-gut axis") ultimately leading to the development of a broad array of gastrointestinal disorders including inflammatory bowel disease (IBD), irritable bowel syndrome (IBS) and other functional gastrointestinal diseases, food antigen-related adverse responses, peptic ulcer and gastroesophageal reflux disease (GERD). The major effects of stress on gut physiology include: 1) alterations in gastrointestinal motility; 2) increase in visceral perception; 3) changes in gastrointestinal secretion; 4) increase in intestinal permeability; 5) negative effects on regenerative capacity of gastrointestinal mucosa and mucosal blood flow; and 6) negative effects on intestinal microbiota. Mast cells (MC) are important effectors of brain-gut axis that translate the stress signals into the release of a wide range of neurotransmitters and proinflammatory cytokines, which may profoundly affect the gastrointestinal physiology. IBS represents the most important gastrointestinal disorder in humans, and is characterized by chronic or recurrent pain associated with altered bowel motility. The diagnostic testing for IBS patients include routine blood tests, stool tests, celiac disease serology, abdominal sonography, breath testing to rule out carbohydrate (lactose, fructose, etc.) intolerance and small intestinal bacterial overgrowth. Colonoscopy is recommended if alarming symptoms are present or to obtain colonic biopsies especially in patients with diarrhoea predominant IBS. The management of IBS is based on a multifactorial approach and includes pharmacotherapy targeted against the predominant symptom, behavioural and psychological treatment, dietary alterations, education, reassurance and effective patient-physician relationship. When evaluating for the stress-induced condition in the upper GI tract, the diagnostic testing includes mainly blood tests and gastroscopy to rule out GERD and peptic ulcer disease. The therapy for these conditions is mainly based on the inhibition of gastric acid by proton pump inhibitors and eradication of *Helicobacter pylori* infection. Additionally, melatonin an important mediator of brain gut axis has been shown to exhibit important protective effects against stress-induced lesions in the gastrointestinal tract. Finally, probiotics may profoundly affect the brain-gut interactions ("microbiome-gut-brain axis") and attenuate the development of stress-induced disorders in both the upper and lower gastrointestinal tract. Further studies on the brain-gut axis are needed to open new therapeutic avenues in the future.

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