Irritable Bowel Syndrome (IBS)

Definition:
Irritable Bowel Syndrome is a chronic episodic medical condition characterized by abdominal pain or discomfort and altered bowel habits in the absence of detectable organic disease. It may present with diarrhea and/or constipation, thus it is often sub-grouped according to stool form: diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), IBS-M (mixed diarrhea and constipation), and IBS-A (alternating diarrhea and constipation). It is part of the spectrum of Functional Gastrointestinal (GI) Disorders.

Epidemiology and Economics:
- IBS has worldwide prevalence rates of 9%-23% in the general population and accounts for up to 40% of diagnoses made by gastroenterologists
- It has a net female predominance, i.e., a female-to-male ratio up to 4:1 in clinic setting, with a female predominance also in greater symptom severity
- Its age distribution is unclear; some studies report a higher prevalence in the young and a decrease with age, others find no age influence
- IBS has a large impact on quality of life (QOL) with consequent high direct and indirect healthcare costs (up to 30 billion dollars in the USA).

Pathophysiology:
- The pathophysiology of IBS is still incompletely known, but is probably complex and multifactorial.
- One issue is whether pain is secondary to gut motility abnormalities or to disturbances in sensory processing (visceral hyperalgesia) or both.
- Multiple patterns of abnormal intestinal motility have been described in IBS, but no single motility disturbance is pathognomonic of the syndrome or has a predictable relationship with pain perception.
- In contrast, an increased sensitivity to painful stimuli at gut level is clearly a key feature of IBS, though the anatomic sites, physiologic derangements, cellular mediators and molecular mechanisms* are incompletely understood. It is still debated if the hyperalgesia is primarily arising in the central nervous system or is, at least at the beginning, triggered by a peripheral (infectious) factor [initial peripheral sensitization followed by central sensitization].
- The role of a genetic predisposition is controversial.

* among specific molecules possibly involved in pain pathogenesis of IBS, serotonin (5-HT) has received most attention as it is an important player in the normal peristaltic reflex of the gut and can also sensitize visceral nociceptors and facilitate transient receptor potential family V receptor 1 (TRPV1) function.

Diagnostic Criteria:
- IBS diagnosis is at present performed based on Rome III criteria *, i.e.:
  - Recurrent abdominal pain or discomfort of at least 3 days/month in the last 3 months associated with 2 or more:
    - Improvement with defecation and
    - Onset associated with a change in frequency of stool and
    - Onset associated with a change of form (appearance of stool)

  *Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.
- Alarm symptoms (e.g., weight loss, fever, rectal bleeding, steatorrhea, lactose/gluten intolerance) suggest the possibility of structural disease, such as colon cancer, inflammatory bowel disease, malabsorption disorders (e.g., celiac sprue) but do not necessarily negate a diagnosis of IBS.
Clinical Features and Instrumental Findings:

- The onset of IBS is usually precipitated by disruption of gastrointestinal function secondary to infection, dietary factors, lifestyle changes or psychological stress [IBS patients report a higher prevalence of sexual, physical and emotional abuse compared to healthy individuals].

- The spontaneous pain is described as a cramping, aching abdominal sensation whose severity ranges from mild and intermittent to severe and continuous. It can be precipitated by meals and improved by defecation. In female patients it is influenced by the menstrual cycle, with an increase immediately before and during menses. The abdominal painful areas typically enlarge with the progression of the disease. Abdominal pain is also evoked by intestinal transit (e.g., postprandial colonic contractions, unnoticed by controls) and endoscopic procedures.

- Clinical symptoms associated with abdominal pain are: fatigue, muscle and joint pain, pelvic pain, headache, sleep and sexual disturbance, affective dysfunction, bladder urgency.

- A number of clinical conditions occur more frequently in IBS than in the general population (comorbidities):
  - Psychiatric Disorders (prevalence: 40%-90% in IBS patients)
  - Fibromyalgia Syndrome (prevalence: 31.6% in women with IBS)
  - Recurrent/Chronic Pelvic Pain (prevalence of dysmenorrhea: 50% in women with IBS)
  - Chronic Fatigue Syndrome, Interstitial Cystitis, Back Pain, Temporomandibular Joint Pain, Headache

- IBS patients have abnormal reactivity to noxious stimuli at both visceral and somatic levels.
  1. Lower than normal pain thresholds to mechanical and electrical stimuli of the gut in the majority of cases [visceral hyperalgesia]
  2. In somatic abdominal areas of pain referral, lower than normal pain thresholds in skin, subcutis and muscle; In somatic areas outside sites of pain referral, lower than normal pain thresholds in subcutis and muscle; controversial results in skin, with normal, higher than normal or lower than normal pain thresholds (thermal, mechanical, electrical stimuli)

- Brain Neuroimaging. Observations from brain imaging in IBS suggest a compromised activation of pain inhibition circuits including those of the cortico-pontine circuit but increased activation of limbic and paralimbic circuits that may be related to pain facilitation.

Prognosis and Treatment:

- IBS typically lasts for the entire life of the patient, though a mild control of the symptoms can be achieved through treatment.

- Treatment is typically multimodal. It involves: dietary factors (careful analysis of potential food triggers); traditional pharmacologic therapy (including bulking agents, antispasmodics, tricyclic antidepressants and other psychotropic agents, and laxatives), serotonergic agents [5-HT3 receptor antagonists, 5-HT4 receptor agonists, combination 5-HT4 agonist and 5-HT3 antagonist]; antidepressants; behavioral and psychological therapy.

References:


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