Irritable Bowel Syndrome (IBS)

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Plan of lecture

- Etiology, pathogenesis of **Irritable Bowel Syndrome (IBS)**;
- IBS diagnosis;
- IBS treatment;

Irritable Bowel Syndrome (IBS) [1]

- Irritable bowel syndrome is characterized by recurrent abdominal discomfort or pain with at least two of the following characteristics: relation to defecation, association with a change in frequency of stool, or association with a change in consistency of stool (Irritable Bowel Syndrome By Stephanie M. Moleski. MSD publication [1] https://www.merckmanuals.com/professional/gastrointestinal-disorders/irritable-bowel-syndrome-ibs/irritable-bowel-syndrome-ibs)

IBS etiology and pathogenesis [1]

The cause of irritable bowel syndrome (IBS) is unknown. No anatomic cause can be found on laboratory tests, x-rays, and biopsies. Emotional factors, diet, drugs, or hormones may precipitate or aggravate gastrointestinal symptoms. Historically, the disorder was often considered as purely psychosomatic. Although psychosocial factors are involved, IBS is better understood as a combination of physiologic and psychosocial factors.

Physiologic factors:

A variety of physiologic factors seem to be involved in IBS symptoms. These factors include:

- Altered intestinal motility
- Increased intestinal sensitivity (visceral hyperalgesia)
- Various genetic and environmental factors

IBS etiology and pathogenesis **[1]**

- Visceral hyperalgesia refers to hypersensitivity to normal amounts of intraluminal distention and heightened perception of pain in the presence of normal quantities of intestinal gas; it may result from remodeling of neural pathways in the brain-gut axis. Some patients (perhaps 1 in 7) have reported their IBS symptoms began after an episode of acute gastroenteritis (termed postinfectious IBS). A subset of patients with IBS has autonomic dysfunctions. However, many patients have no demonstrable physiologic abnormalities, and, even in those who do, the abnormalities may not correlate with symptoms.
- Constipation may be explained by slower colonic transit, and diarrhea may be explained by faster colonic transit. Some patients with constipation have fewer colonic high amplitude-propagated contractions, which propel colonic contents over several segments. Conversely, excess sigmoid motor activity may retard transit in functional constipation.

IBS etiology and pathogenesis **[1]**

- Postprandial abdominal discomfort may be attributed to an exaggerated gastro-colonic reflex (the colonic contractile response to a meal), the presence of colonic high amplitude-propagated contractions, visceral hyperalgesia, or a combination of these factors. Fat ingestion may increase intestinal permeability and exaggerate hypersensitivity. Ingestion of food high in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (collectively called FODMAPs) are poorly absorbed in the small intestine and may increase colonic motility and secretion.

IBS etiology and pathogenesis [1]

- Hormonal fluctuations affect bowel functions in women. Rectal sensitivity is increased during menses but not during other phases of the menstrual cycle. The effects of sex steroids on gastrointestinal transit are subtle. The role of small-bowel bacterial overgrowth in IBS is controversial.
- Psychologic distress is common among patients with IBS, especially in those who seek medical care. Some patients have anxiety disorders, depression, or a somatization disorder. Sleep disturbances also coexist.

IBS etiology and pathogenesis **[1]**

- However, stress and emotional conflict do not always coincide with symptom onset and recurrence. Some patients with IBS seem to have a learned aberrant illness behavior (ie, they express emotional conflict as a gastrointestinal complaint, usually abdominal pain). The physician evaluating patients with IBS, particularly those with refractory symptoms, should investigate for unresolved psychologic issues, including the possibility of sexual or physical abuse. Psychosocial factors also affect the outcome in IBS.

Symptoms and Signs [1]

- Irritable bowel syndrome tends to begin in adolescence and the 20s, causing bouts of symptoms that recur at irregular periods. Onset in late adult life is less common. Symptoms of IBS rarely rouse the sleeping patient. Symptoms are often triggered by food or by stress.
- Patients have abdominal discomfort, which varies considerably but is often located in the lower abdomen, is steady or cramping in nature, and is related to defecation.

Symptoms and Signs [1]

- In addition, abdominal discomfort is temporally associated with alterations in stool frequency (increased in diarrhea-predominant IBS and decreased in constipation-predominant IBS) and consistency (ie, loose or lumpy and hard). Pain or discomfort related to defecation is likely to be of bowel origin; that associated with exercise, movement, urination, or menstruation usually has a different cause.

Symptoms and Signs [1]

- Although bowel patterns are relatively consistent in most patients, it is not unusual for patients to alternate between constipation and diarrhea. Patients may also have symptoms of abnormal stool passage (straining, urgency, or feeling of incomplete evacuation), pass mucus, or complain of bloating or abdominal distention. Many patients also have symptoms of dyspepsia. Extraintestinal symptoms (eg, fatigue, fibromyalgia, sleep disturbances, chronic headaches) are common.
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Diagnosis of IBS [1]

- Diagnosis
- • Clinical evaluation, based on Rome criteria
- • Screening for organic causes with basic laboratory tests and sigmoidoscopy or colonoscopy
- • Other tests for patients with red flag findings (eg, rectal blood, weight loss, fever)

Diagnosis of irritable bowel syndrome is based on characteristic bowel patterns, time and character of pain, and exclusion of other disease processes through physical examination and routine diagnostic tests.

Diagnosis of IBS [1]

Red flags

Diagnostic testing should be more intensive when the following red flags are present either at initial presentation or at any time after diagnosis:

- ***Older age***
- ***Fever***
- ***Weight loss***
- ***Rectal bleeding***
- ***Vomiting***

Differential diagnosis [1]

- Because patients with IBS can develop organic conditions, testing for other conditions should also be considered in patients who develop alarm symptoms or markedly different symptoms during the course of IBS. Common illnesses that may be confused with IBS include:
- Lactose intolerance
- Drug-induced diarrhea
- Postcholecystectomy syndrome
- Laxative abuse
- Parasitic diseases (eg, giardiasis)

Differential diagnosis [1]

- Common illnesses that may be confused with IBS include:
- Eosinophilic gastritis or enteritis
- Microscopic colitis
- Small-bowel bacterial overgrowth
- Celiac disease
- Bile acid diarrhea
- Early inflammatory bowel disease

Differential diagnosis [1]

- However, uninflamed colonic diverticula do not cause symptoms, and their presence should not be considered explanatory.
- The bimodal age distribution of patients with inflammatory bowel disease makes it imperative to evaluate both younger and older patients. In patients > 60 with acute symptoms, ischemic colitis should be considered. Patients with constipation and no anatomic lesion should be evaluated for hypothyroidism and hypercalcemia. If the patient's symptoms suggest malabsorption, tropical sprue, celiac disease, and Whipple disease must be considered. Defecatory disorders should be considered as a cause of constipation in patients who report symptoms of difficult defecation.

Differential diagnosis [1]

- Rare causes of diarrhea include hyperthyroidism, medullary cancer of the thyroid or carcinoid syndrome, gastrinoma, and vipoma. However, these causes of diarrhea are typically accompanied by stool volumes > 1000 mL daily, which differentiates them from IBS.

Subjective data: complaints, history of disease[1,3]

Particular attention should be given to the character of the pain, bowel habits, familial interrelationships, and drug and dietary histories. Equally important are the patient's overall emotional state, interpretation of personal problems, and quality of life. The quality of the patient–physician interaction is key to diagnostic and therapeutic efficacy.

The Rome criteria are standardized symptom-based criteria for diagnosing IBS. The Rome criteria require the presence of abdominal pain for at least 1 day/week in the last 3 months along with ≥ 2 of the following ([3] Lacy BE, Mearin F, Chang L, et al: Bowel disorders. Gastroenterology 150:1393–1407, 2016. doi: 10.1053/j.gastro.2016.02.031):

- Pain that is related to defecation.
- Pain is associated with a change in frequency of defecation.
- Pain is associated with a change in consistency of stool.

Physical examination [1]

- Patients generally appear to be healthy. Palpation of the abdomen may reveal tenderness, particularly in the left lower quadrant, at times associated with a palpable, tender sigmoid. A digital rectal examination, including a test for occult blood, should be done on all patients. In women, a pelvic examination helps rule out ovarian tumors and cysts or endometriosis, which may mimic IBS.

Testing [1]

- The diagnosis of IBS can reasonably be made using the Rome criteria as long as patients have no red flag findings, such as rectal bleeding, weight loss, and fever, or other findings that might suggest another etiology.

Testing [1]

- Many patients with IBS are overtested; however, complete blood count, biochemical profile (including liver tests), serologic markers for celiac disease (tissue-transglutaminase IgA with an IgA level), stool examination for infection (in patients with diarrhea predominance), thyroid-stimulating hormone and calcium for patients with constipation, and flexible sigmoidoscopy or colonoscopy should be considered. In patients presenting with chronic diarrhea, fecal calprotectin or fecal lactoferrin should be the first-line tests to screen for inflammatory bowel disease. Chronic diarrhea should also prompt testing for Giardia. An antigen test or a polymerase chain reaction test for Giardia is recommended.

Testing [1]

- During flexible fiberoptic proctosigmoidoscopy, introduction of the instrument and air insufflation frequently trigger bowel spasm and pain. The mucosal and vascular patterns in IBS usually appear normal. Colonoscopy is preferred for patients > 50 to exclude colonic polyps and tumors. In patients with chronic diarrhea, particularly older women, mucosal biopsy can rule out possible microscopic colitis.

Testing [1]

- Additional studies (such as ultrasonography, CT, barium enema x-ray, upper gastrointestinal esophagogastroduodenoscopy, and small-bowel x-rays) should be undertaken only when there are other objective abnormalities.

Testing [1]

Patients with IBS may subsequently develop additional gastrointestinal disorders, and the clinician must not summarily dismiss their complaints. Changes in symptoms (eg, in the location, type, or intensity of pain; in bowel habits; in constipation and diarrhea) and new symptoms or complaints (eg, nocturnal diarrhea) may signal another disease process.

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- Other symptoms that require investigation include fresh blood in the stool, weight loss, very severe abdominal pain or unusual abdominal distention, steatorrhea or noticeably foul-smelling stools, fever or chills, persistent vomiting, hematemesis, symptoms that wake the patient from sleep (eg, pain, the urge to defecate), and a steady progressive worsening of symptoms. Patients > 40 are more likely than younger patients to develop an intercurrent physiologic illness.

Treatment [1]

Treatment:

- ***Support and understanding***
- ***Normal diet, avoiding gas-producing and diarrhea-producing foods***
- ***Increased fiber intake and hydration for constipation***
- ***Drug therapy directed at the dominant symptoms***

Therapy is directed at specific symptoms. An effective therapeutic relationship is essential for effectively managing IBS. Patients should be invited to express not only their symptoms but also their understanding of their symptoms and the reasons prompting a visit to the health care practitioner (eg, fear of serious disease). Patients should be educated about the disorder (eg, normal bowel physiology and the bowel's hypersensitivity to stress and food) and reassured, after appropriate tests, about the absence of a serious or life-threatening disease. Appropriate therapeutic goals (eg, expectations regarding the normal course or variability in symptoms, adverse effects of drugs, the appropriate and available working relationship between the physician and the patient) should be established.

Treatment [1]

- Finally, patients can benefit by being actively involved in the management of their condition. When successful, this can enhance the patient's motivation to adhere to treatment, foster a more positive physician–patient relationship, and mobilize the coping resources of even the most chronically passive patients. Psychologic stress, anxiety, or mood disorders should be identified, evaluated, and treated. Regular physical activity helps relieve stress and assists in bowel function, particularly in patients with constipation.

Treatment, diet [1]

- In general, a normal diet can be followed. Meals should not be overly large, and eating should be slow and paced. Patients with abdominal distention and increased flatulence may benefit from reducing or eliminating beans, cabbage, and other foods containing fermentable carbohydrates.

Treatment, diet [1]

- Reduced intake of sweeteners (eg, sorbitol, mannitol, fructose), which are constituents of natural and processed foods (eg, apple and grape juice, bananas, nuts, raisins), may alleviate flatulence, bloating, and diarrhea. Patients with evidence of lactose intolerance should reduce their intake of milk and dairy products. Patients can try reducing their intake of the aforementioned food categories one at a time and noting the effect on their symptoms, or they can try a low-FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet, which restricts all of the aforementioned food categories. In addition, a low-fat diet may reduce postprandial abdominal symptoms.

Treatment, diet [1]

- Patients should be encouraged to drink more fluids. Dietary fiber supplements may soften stool and improve the ease of evacuation. Psyllium hydrophilic mucilloid with two glasses of water may be used. However, excessive use of fiber can lead to bloating and diarrhea, so fiber doses must be individualized. Occasionally, flatulence may be reduced by switching to a synthetic fiber preparation (eg, methylcellulose).

Drug Therapy [1]

- Drug therapy is directed toward the dominant symptoms. Anticholinergic drugs (eg, hyoscyamine 0.125 mg orally 30 to 60 minutes before meals) may be used for their antispasmodic effects.
- In patients with constipation-predominant IBS (IBS-C), the chloride channel activator lubiprostone 8 mcg or 24 mcg orally twice a day and the guanylate cyclase C agonists linaclotide 72 mcg, 145 mcg, or 290 mcg orally once a day or plecanatide 3 mg orally once a day may be helpful. Polyethylene glycol laxatives have not been well-studied in IBS. However, they have been shown to be effective for use in chronic constipation and for bowel lavage before colonoscopy and are thus frequently used for IBS-C. Prucalopride is a highly selective serotonin receptor agonist that is approved for chronic constipation.

Drug Therapy [1]

- In patients with diarrhea-predominant IBS (IBS-D), oral diphenoxylate 2.5 to 5 mg or loperamide 2 to 4 mg may be given before meals. The dose of loperamide should be titrated upward to reduce diarrhea while avoiding constipation. Rifaximin is an antibiotic that has been shown to relieve symptoms of bloating and abdominal pain and to help decrease looseness of stools in patients with IBS-D. The recommended dose of rifaximin for IBS-D is 550 mg orally 3 times a day for 14 days. Alosetron is a 5-hydroxytryptamine (serotonin) 3 (5HT3) receptor antagonist that may benefit women with severe IBS-D refractory to other drugs. Because alosetron has been associated with ischemic colitis, its use in the US is under a restricted prescribing program. Eluxadoline has mixed opioid receptor activity and is indicated for treatment of IBS-D; however, because of the risk of pancreatitis, it cannot be used in patients who have had a cholecystectomy, have sphincter of Oddi dysfunction, have liver disease, or drink more than 3 alcoholic drinks a day.

Drug Therapy [1]

- For many patients, tricyclic antidepressants (TCAs) help relieve symptoms of diarrhea, abdominal pain, and bloating. These drugs are thought to reduce pain by down-regulating the activity of spinal cord and cortical afferent pathways arriving from the intestine. Secondary amine TCAs (eg, nortriptyline, desipramine) are often better tolerated than parent tertiary amines (eg, amitriptyline, imipramine, doxepin) because of fewer anticholinergic, sedating antihistaminic, and alpha-adrenergic adverse effects. Treatment should begin with a very low dose of a TCA (eg, desipramine 10 to 25 mg orally once a day at bedtime), increasing as necessary and tolerated up to about 100 to 150 mg orally once a day.
- Selective serotonin reuptake inhibitors are sometimes used in patients with anxiety or an affective disorder, but studies have not shown a significant benefit for patients with IBS and they may exacerbate diarrhea.

Drug and Psychological Therapy [1]

- Preliminary data suggest that certain probiotics (eg, Bifidobacterium infantis) alleviate IBS symptoms, particularly bloating. The beneficial effects of probiotics are not generic to the entire species but specific to certain strains. Certain aromatic oils (carminatives) can relax smooth muscle and relieve pain caused by cramps in some patients. Peppermint oil is the most commonly used agent in this class.
- Psychologic therapies - Cognitive-behavioral therapy, standard psychotherapy, and hypnotherapy may help some IBS patients.