Evidence Based Approach to Management of IBS

ACG position statement January 2009

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TOPICOS SELECTOS EN MEDICINA INTERNA

Departamento de Medicina Interna UPR

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Functional Bowel Disorders

Definition

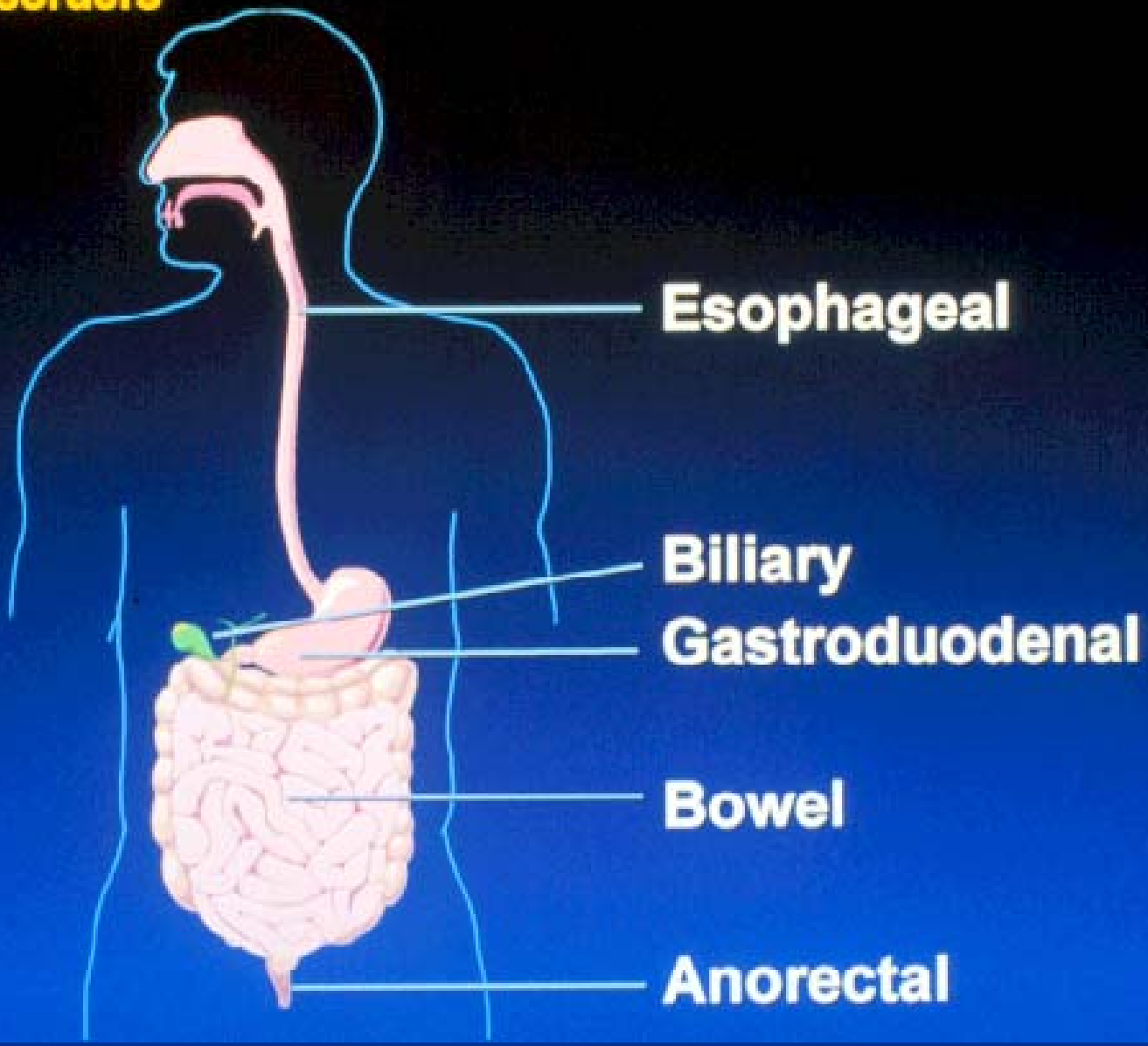
- "A variable combination of chronic or recurrent gastrointestinal symptoms

  (attributed to the pharynx, esophagus, stomach, biliary tree, small or large intestine, or anorectum)

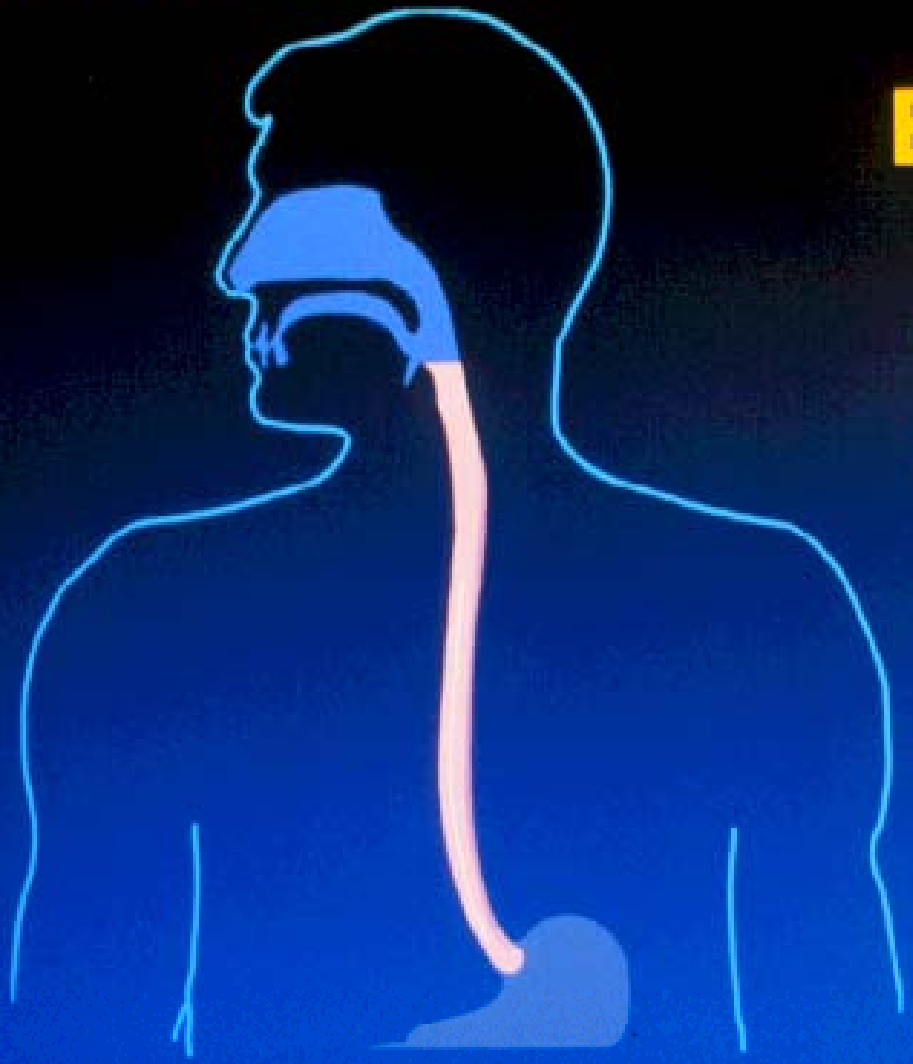
  not explained by structural or biochemical abnormalities."

Rome criteria, 1990

Functional GI Disorders



Functional GI Disorders



Esophageal

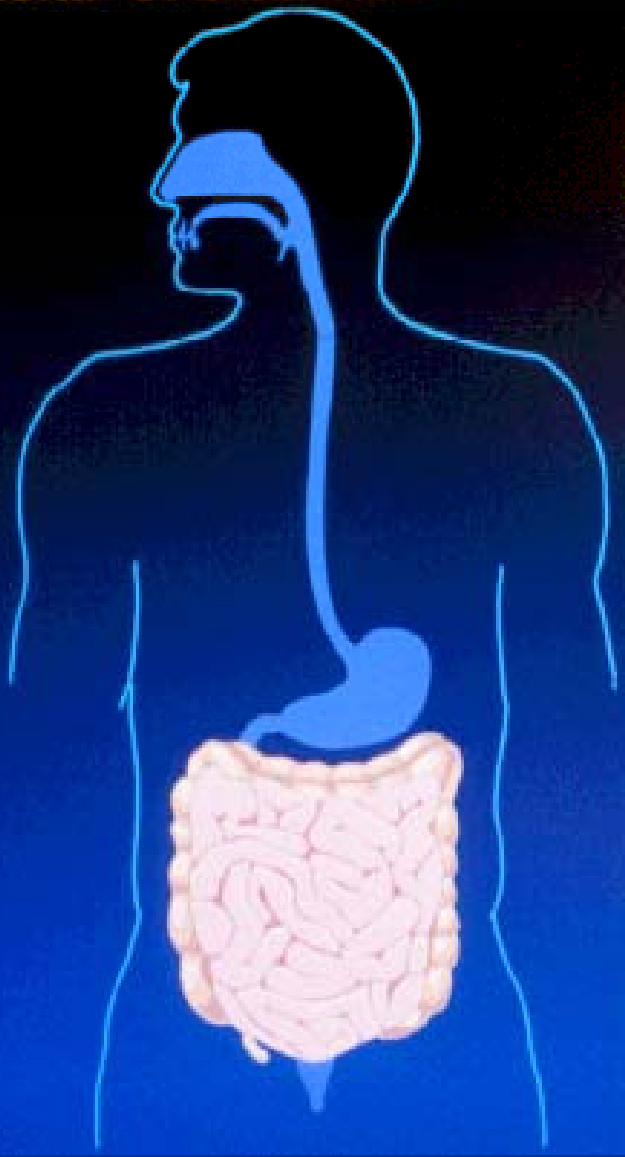
- Globus
- Rumination syndrome
- Functional chest pain
- Functional heartburn
- Functional dysphagia

Functional GI Disorders

Gastroduodenal

- Functional dyspepsia
- Aerophagia

Functional GI Disorders



Bowel

- Irritable bowel syndrome
- Functional abdominal bloating
- Functional constipation
- Functional diarrhea

Functional Abdominal Pain

Functional GI Disorders

Biliary

- Gallbladder dysfunction
- Sphincter of Oddi dysfunction

Functional GI Disorders

Anorectal

- Functional incontinence
- Functional anorectal pain
  - Levator ani syndrome
  - Proctalgia fugax
- Dyschezia

Irritable Bowel Syndrome

IBS - Diagnostic criteria

- Definition: abdominal pain or discomfort that occurs in association with altered bowel habits over a period of at least 3 months
- Various criteria useful for diagnosis
  - Manning sens 77% spec 89%
  - Rome I sens 71% spec 85%
  - Rome II not evaluated
  - Rome III not evaluated

Manning Criteria

- Abdominal pain:
  - with looser stools
  - with more frequent BMs
  - eased after BMs
- Abdominal distention
- Mucus
- Incomplete evacuation

IBS - Diagnosis

Rome Criteria I

Symptoms >3 months

Abdominal pain/discomfort

- Relieved with defecation and/or
- With change in stool frequency and/or
- With change in stool consistency

+

Two or more at least 1/4 of the time

- Δ in stool frequency
- Δ in form
- Difficult passage
- Mucous
- Bloating

Rome II (1999)

- Irritable Bowel Syndrome can be diagnosed based on at least 12 weeks (which need not be consecutive) in the preceding 12 months, of *abdominal discomfort or pain that has two out of three of these features*:
  1. Relieved with defecation; and/or
  2. Onset associated with a change in frequency of stool; and/or
  3. Onset associated with a change in form (appearance) of stool

Rome III (2006)

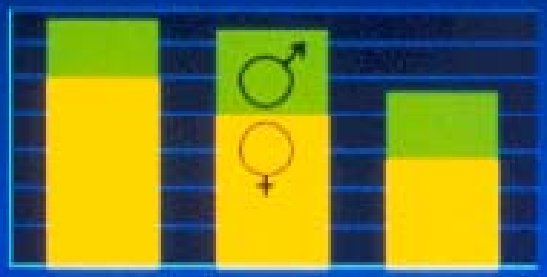
- Same as Rome II except : The time frame for a diagnosis now originates at six months prior to clinical presentation and diagnosis and must be currently active (i.e., meet criteria) for three months.
- This time frame is less restrictive than Rome II

IBS: Burden of Illness

- 7%-10% of people have IBS worldwide
- IBS-D and IBS-M more prevalent than IBS-C
- More common:
  - Women (1.5X)
    - Key component of Gulf War syndrome
  - Lower socioeconomic groups
  - Younger than 50 yrs of age
- Significant impairment in quality of life and work productivity

IBS - Epidemiology

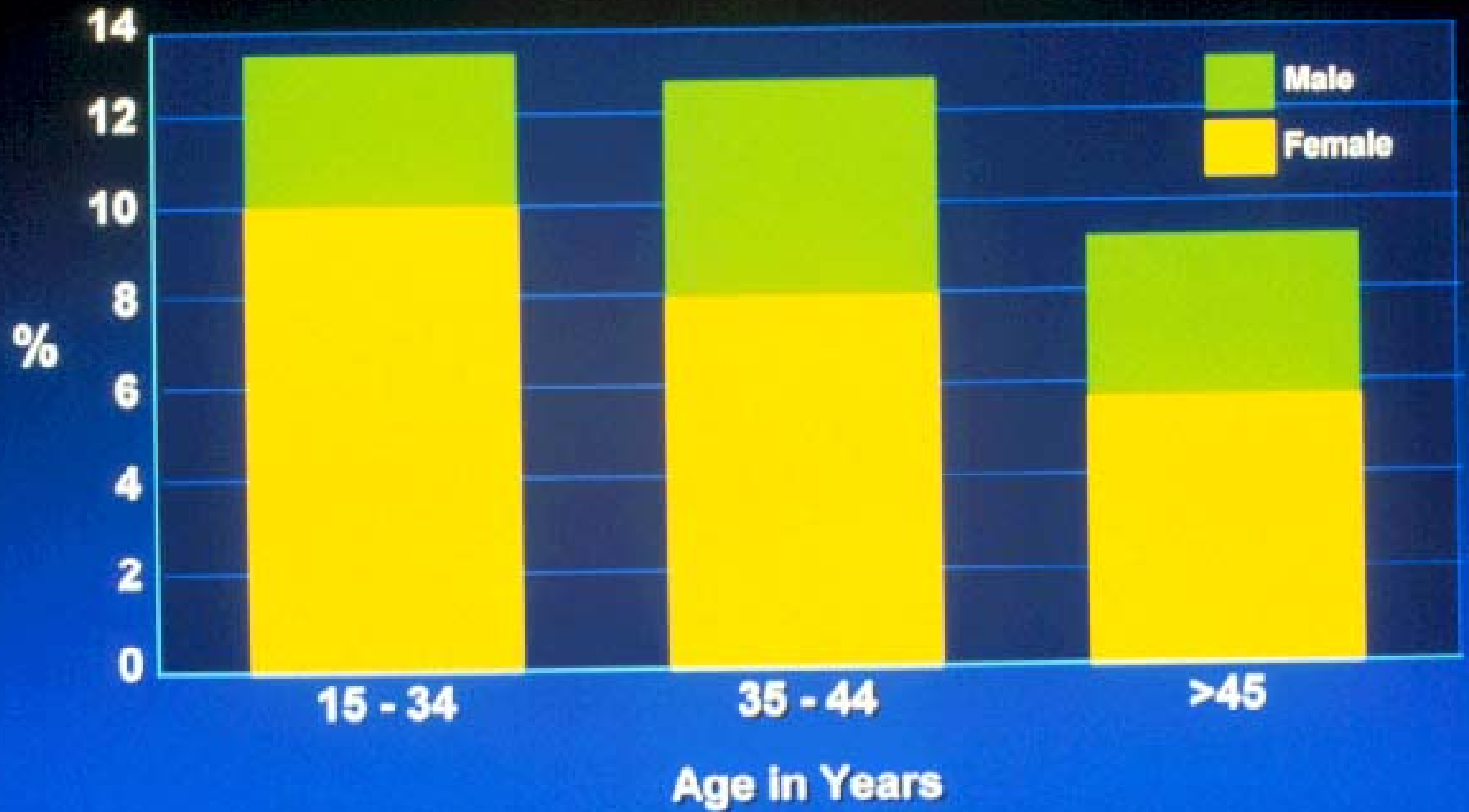
- Up to 15% of population
  - Females > males
    Younger > older
    - 2/3 do not seek health care
      - Sociocultural factors affect M.D. visits



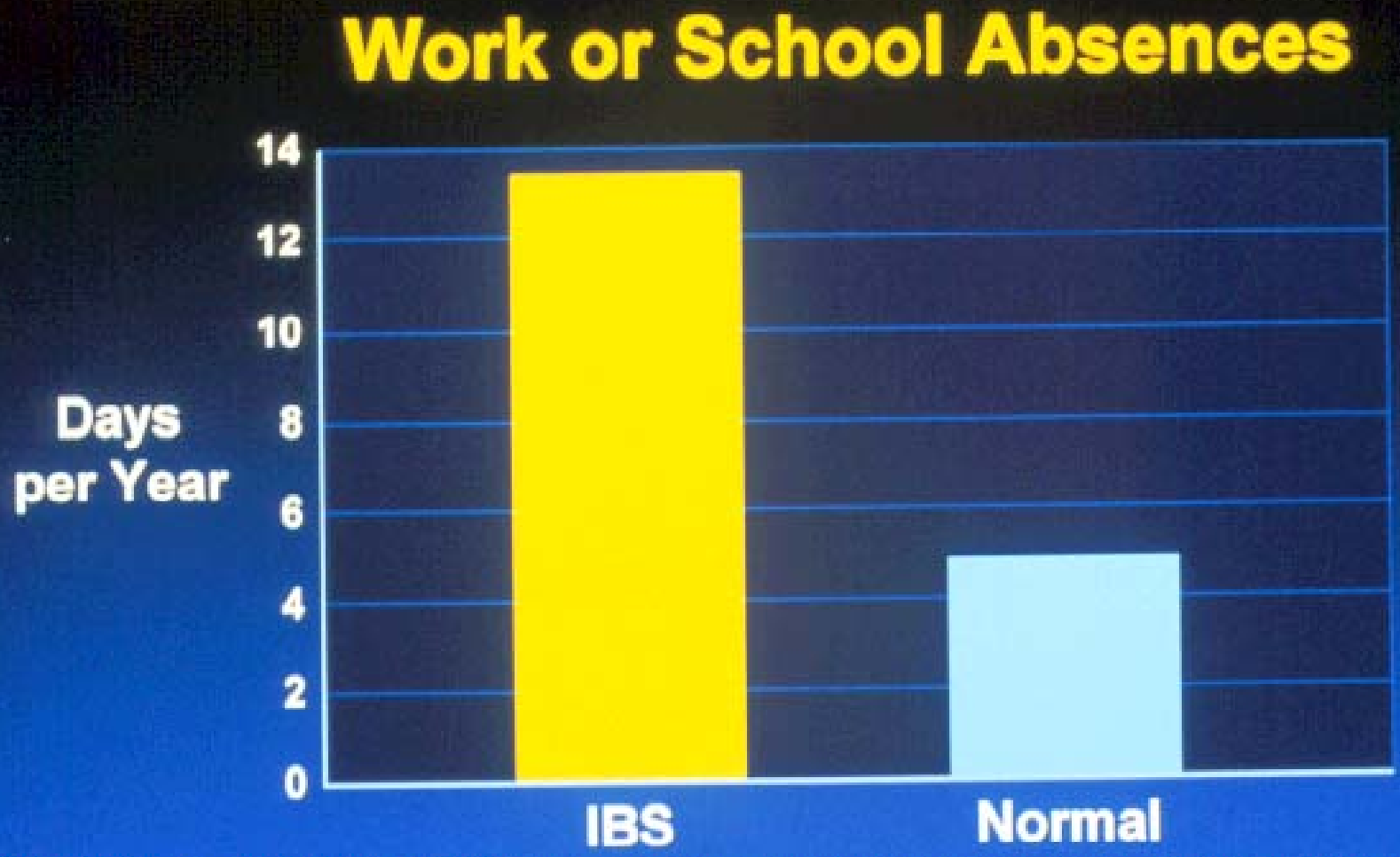
- 12% primary care practice, 28% GI practice
  - >3x work loss, M.D. visits

IBS - Epidemiology

U.S. Prevalence



IBS - Epidemiology



IBS - Diagnosis

Physical
- *Abnormal exam*
- *Fever*
- *Positive occult stool*

Historical
- *Weight loss*
- *Onset in older patients*
- *Nocturnal awakening*
- *Family Hx CA / IBD*

Initial Labs ?
- ↓ *Hgb*
- ↑ *WBC*
- ↑ *ESR*
- *Abnormal chemistry*

Red Flags

Alarm features

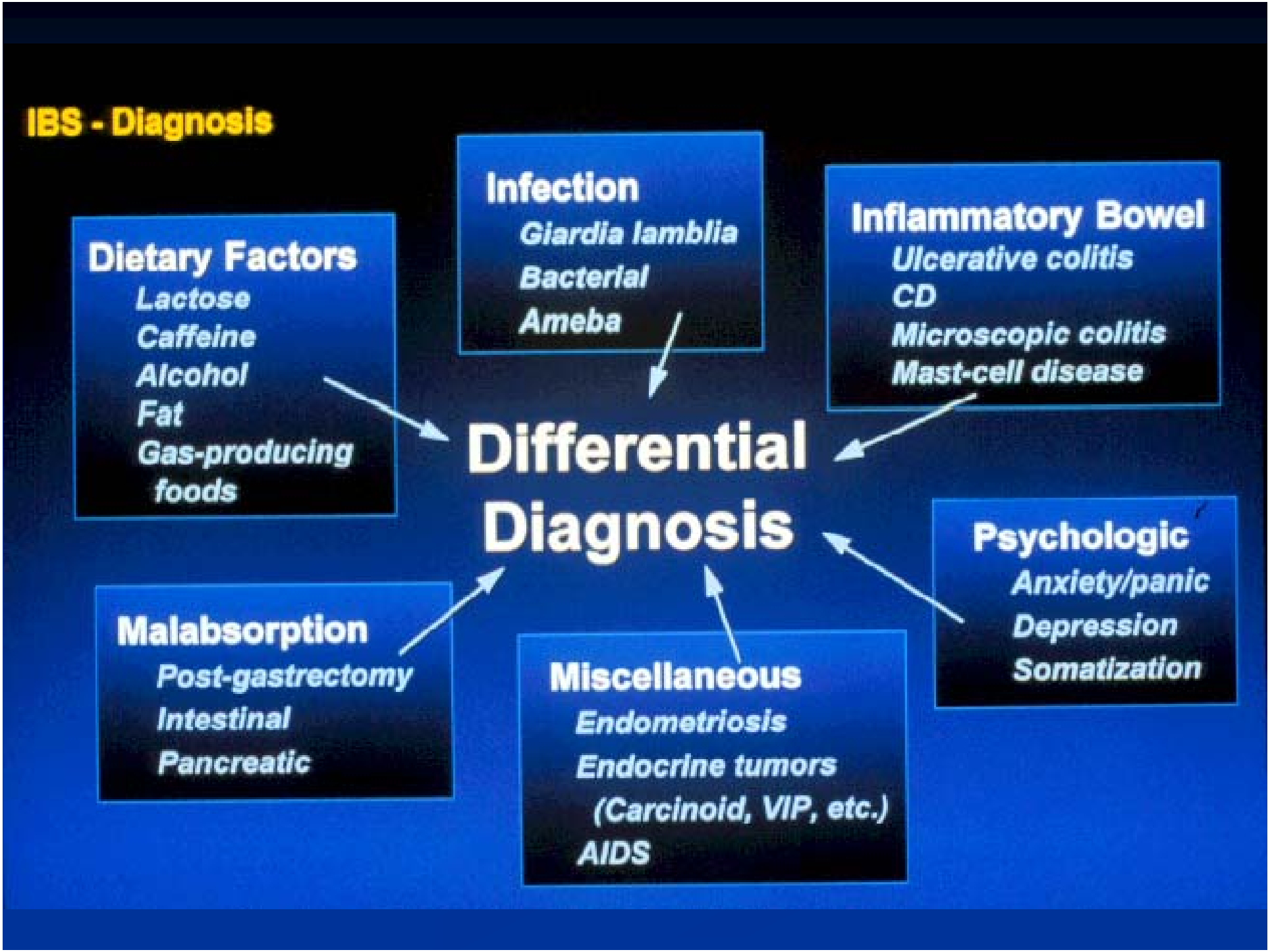
- Increased concern for organic disease
  - Rectal bleeding – poor discrimination
  - Nocturnal symptoms- poor discrimination
  - Anemia - good specificity
  - Weight loss – good specificity
- " the absence of anemia, weight loss, and a familiy hx of colorectal cancer, IBD or celiac sprue should reassure that the diagnosis of IBS is correct."

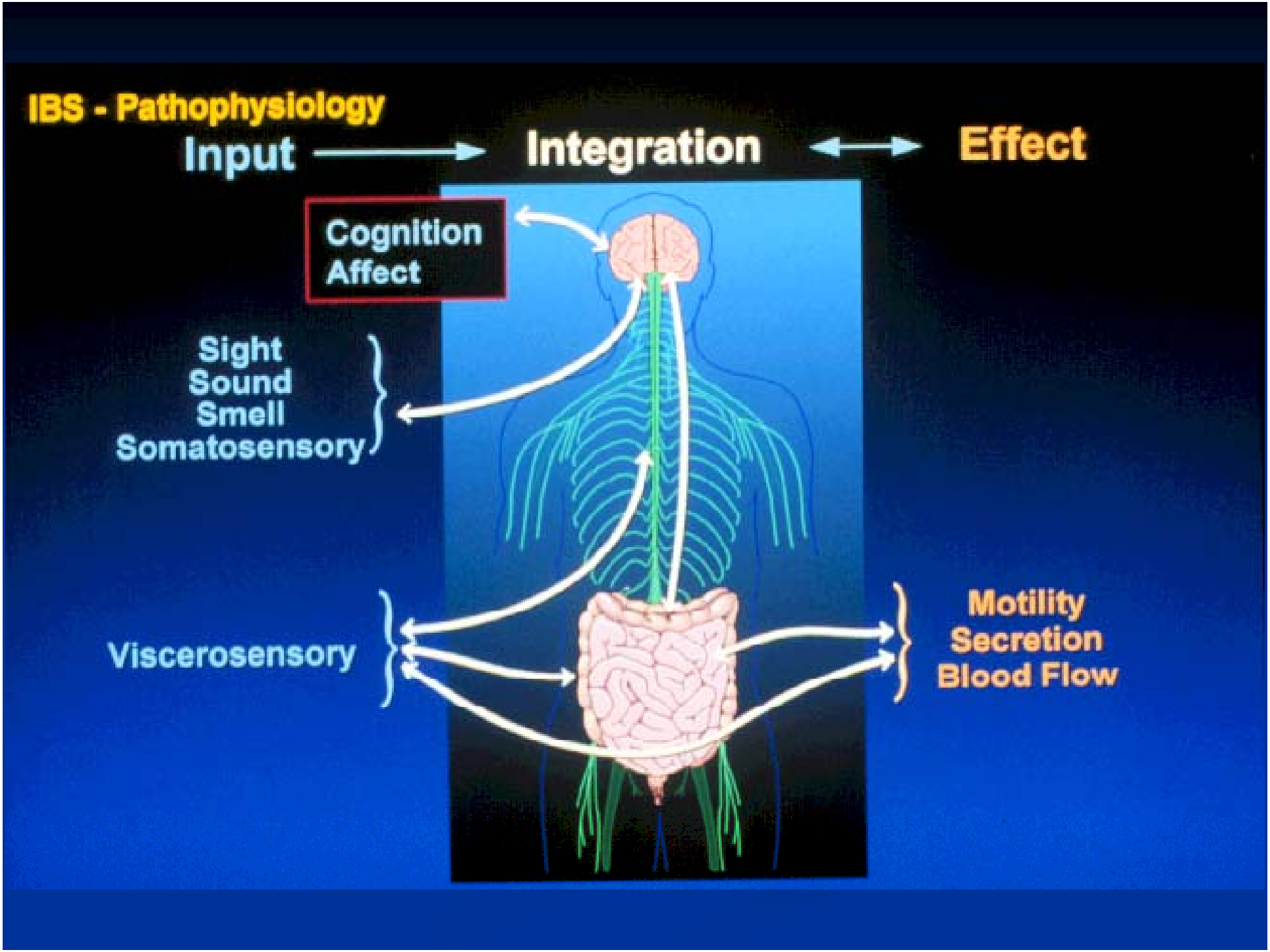
Diagnostic testing – Not recommended

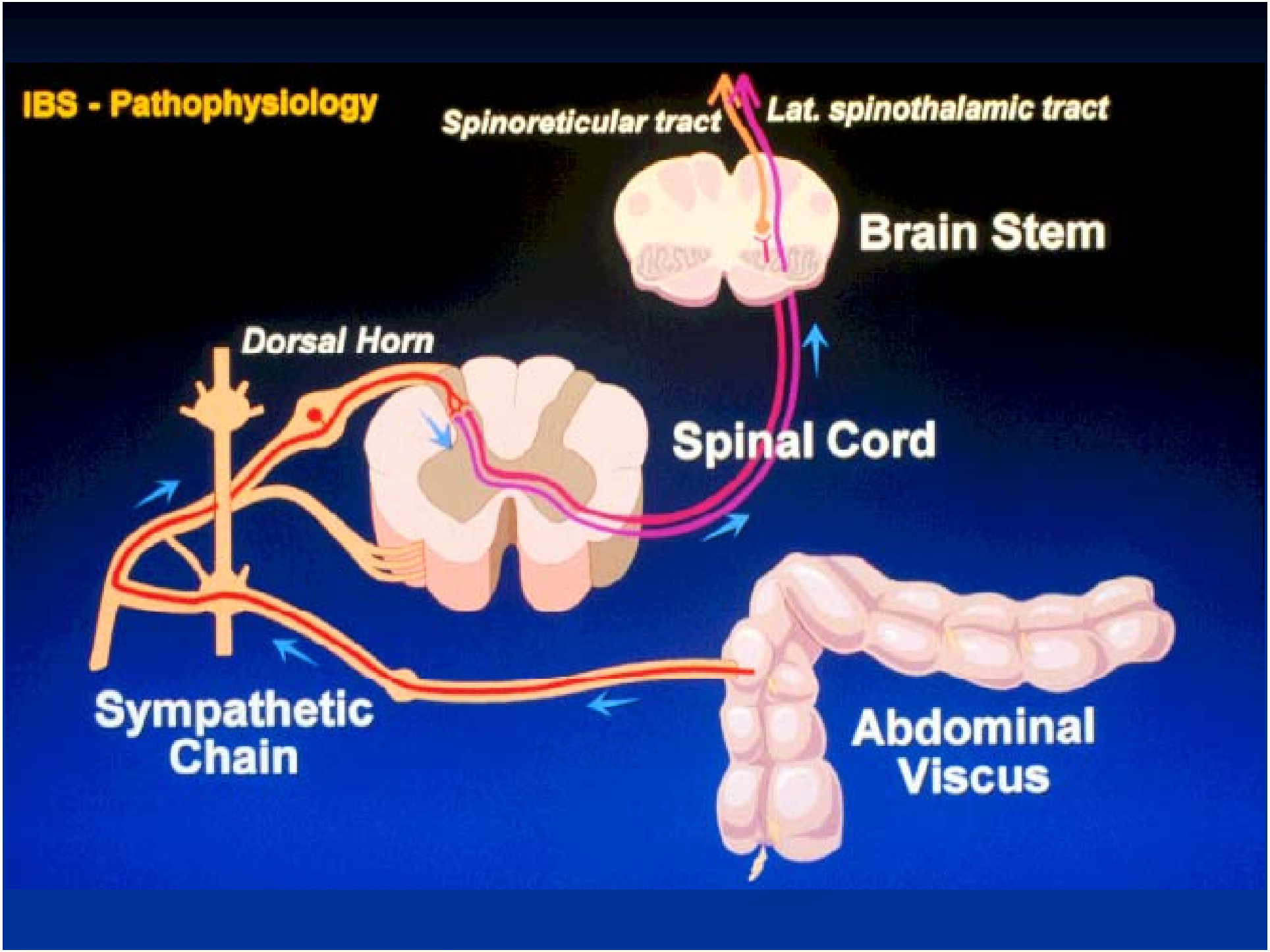
- Routine tests (CBC, chemistries, thyroid, O+P, imaging) in typical IBS with no alarm symptoms
- Testing for small bowel bacterial overgrowth
- Colonoscopy in patients <50 yrs with typical symptoms and no alarm features including family history

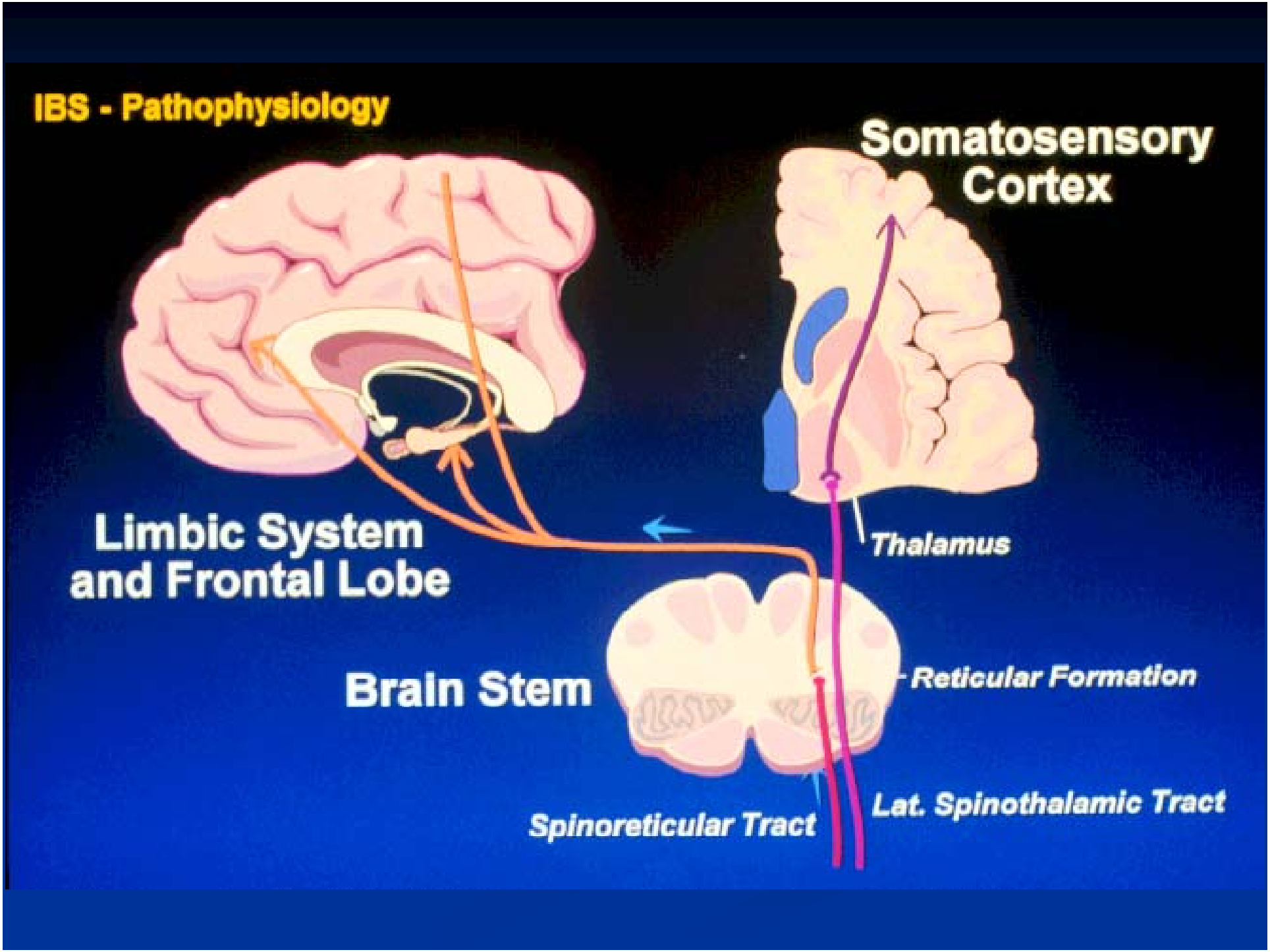
Diagnostic testing - Recommended

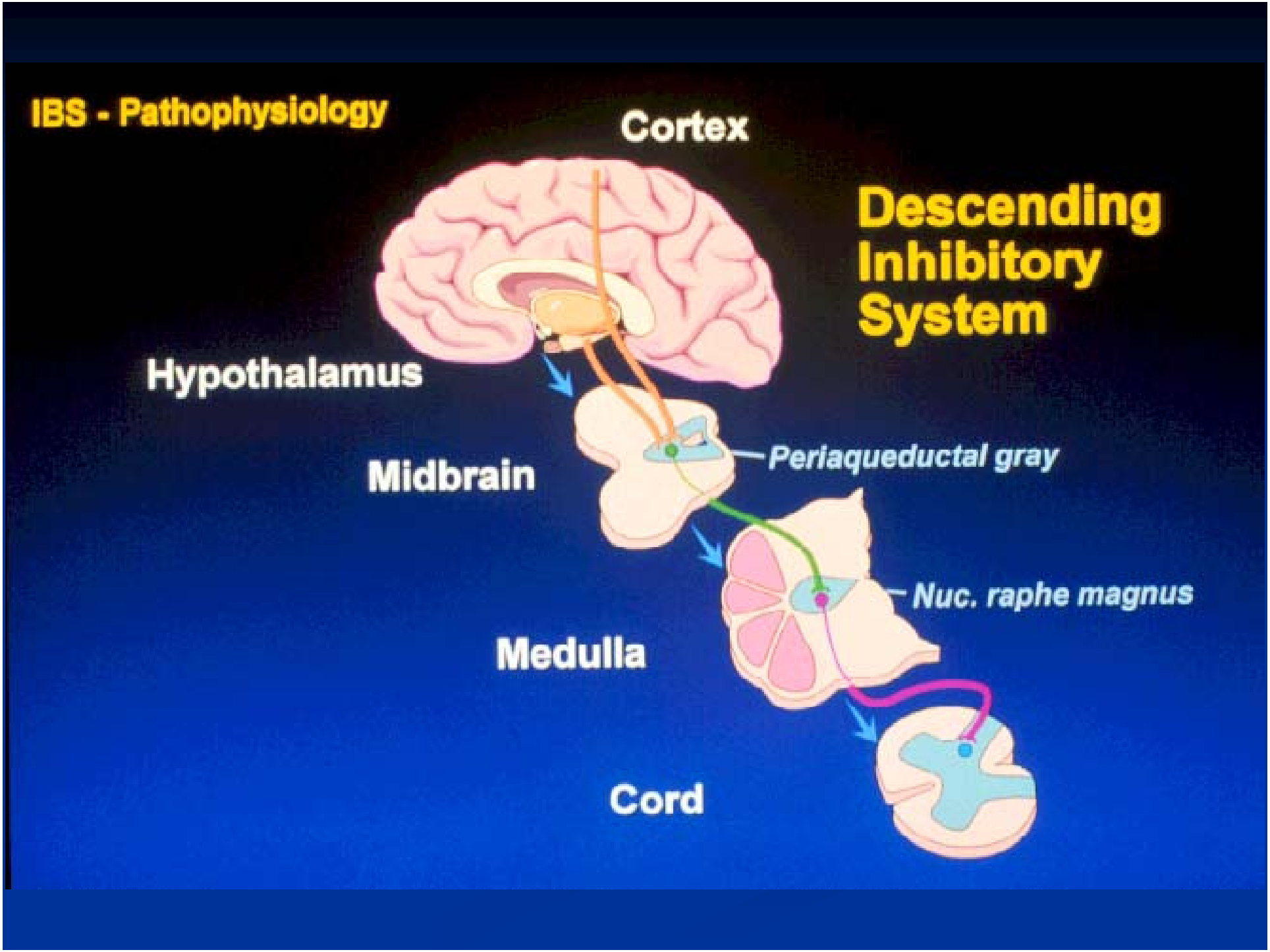
- Celiac sprue testing in patients witn IBS-D or IBS-M
- Lactose hydrogen breath testing if dietary modification does not work and suspicion continues
- Colonoscopy in IBS with alarm features
- Colonoscopy in IBS ≥ 50 yrs (screening)
  - Biopsies if IBS-D to R/O microscopic colitis

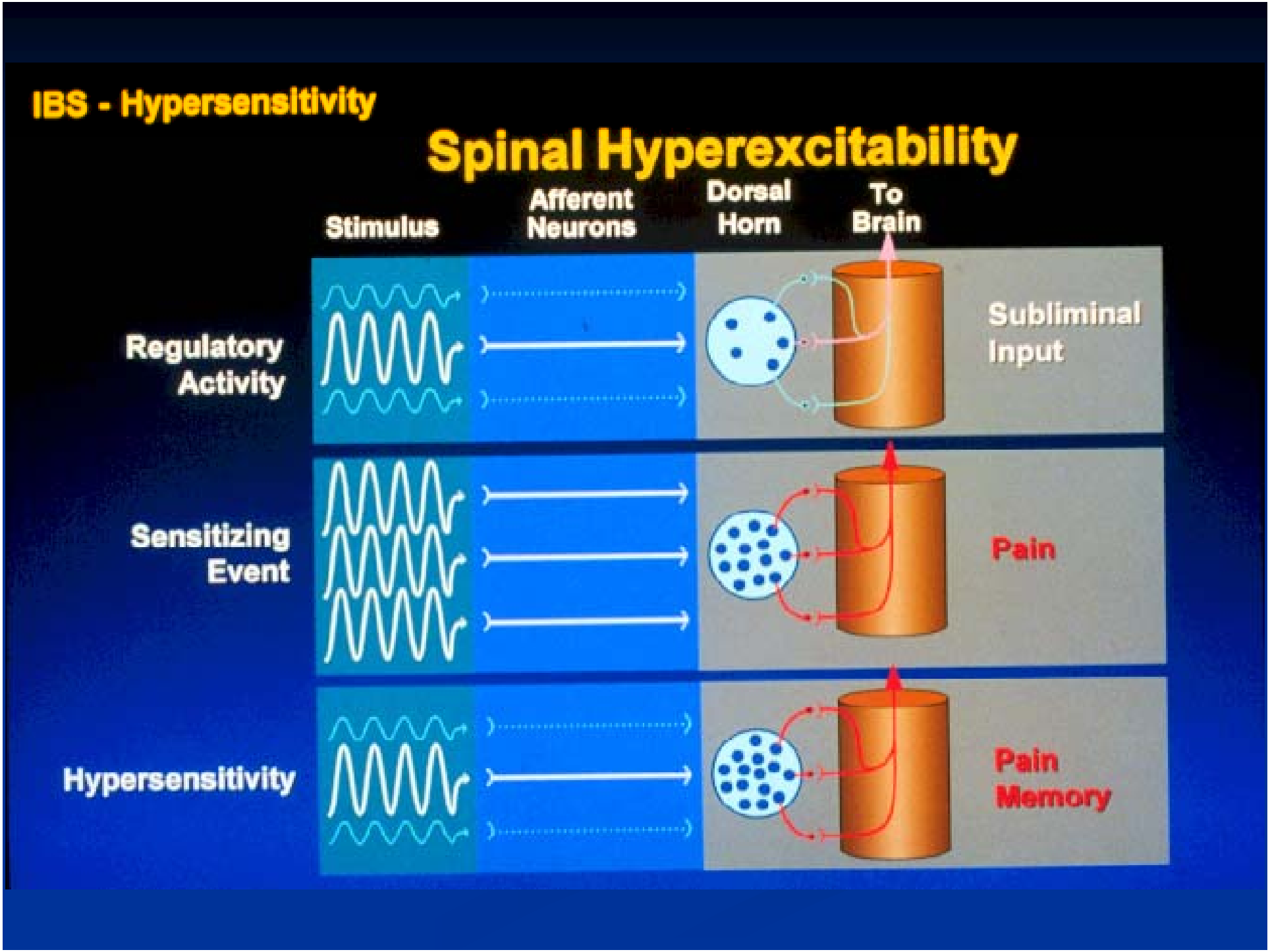

IBS - Diagnosis
Infection
Giardia lamblia
Bacterial
Ameba
Inflammatory Bowel
Ulcerative colitis
CD
Microscopic colitis
Mast-cell disease
Dietary Factors
Lactose
Caffeine
Alcohol
Fat
Gas-producing foods
Differential Diagnosis
Psychologic
Anxiety/panic
Depression
Somatization
Malabsorption
Post-gastrectomy
Intestinal
Pancreatic
Miscellaneous
Endometriosis
Endocrine tumors
(Carcinoid, VIP, etc.)
AIDS

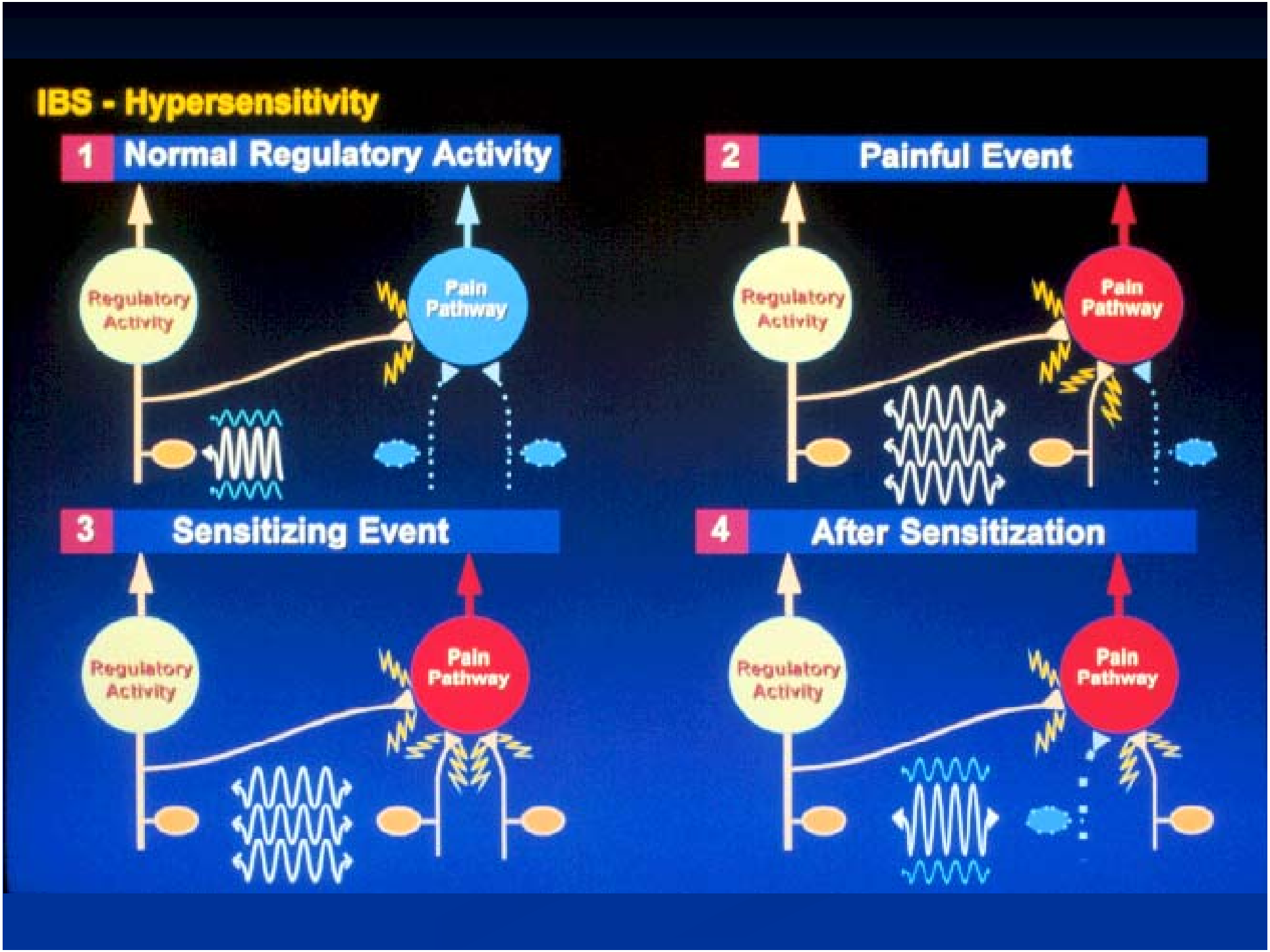

IBS - Pathophysiology
Input
Integration
Effect
Cognition
Affect
Sight
Sound
Smell
Somatosensory
Viscerosensory
Motility
Secretion
Blood Flow


IBS - Pathophysiology
Spinoreticular tract
Lat. spinothalamic tract
Brain Stem
Dorsal Horn
Spinal Cord
Sympathetic Chain
Abdominal Viscus


IBS - Pathophysiology
Somatosensory Cortex
Limbic System and Frontal Lobe
Thalamus
Brain Stem
Reticular Formation
Spinoreticular Tract
Lat. Spinothalamic Tract


IBS - Pathophysiology
Cortex
Descending Inhibitory System
Hypothalamus
Midbrain
Periaqueductal gray
Nuc. raphe magnus
Medulla
Cord

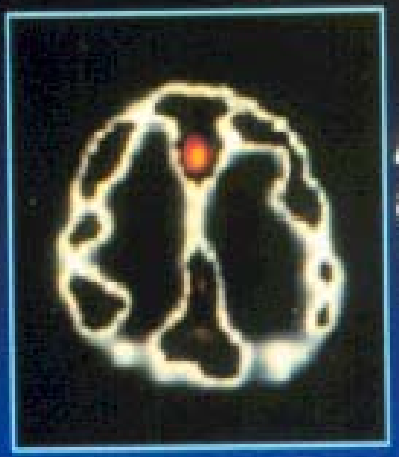

IBS - Hypersensitivity
Spinal Hyperexcitability
Stimulus
Afferent Neurons
Dorsal Horn
To Brain
Regulatory Activity
Subliminal Input
Sensitizing Event
Pain
Hypersensitivity
Pain Memory


IBS - Hypersensitivity
1 Normal Regulatory Activity
Regulatory Activity
Pain Pathway
2 Painful Event
Regulatory Activity
Pain Pathway
3 Sensitizing Event
Regulatory Activity
Pain Pathway
4 After Sensitization
Regulatory Activity
Pain Pathway

IBS - Physiology

Regional Cerebral Activation with PET Scan

Rectal distension



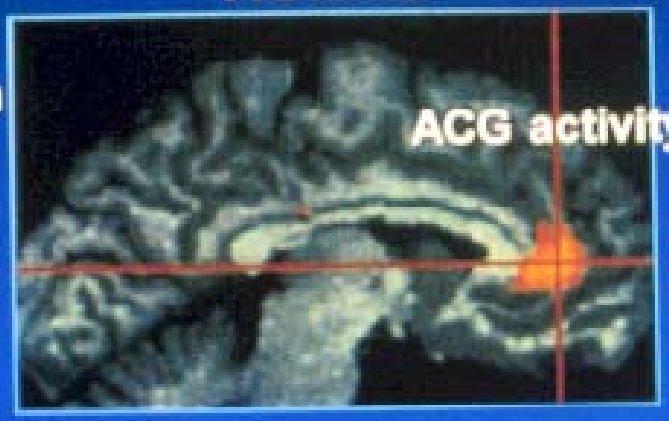
ACG activity

No ACG activity

Normal

IBS

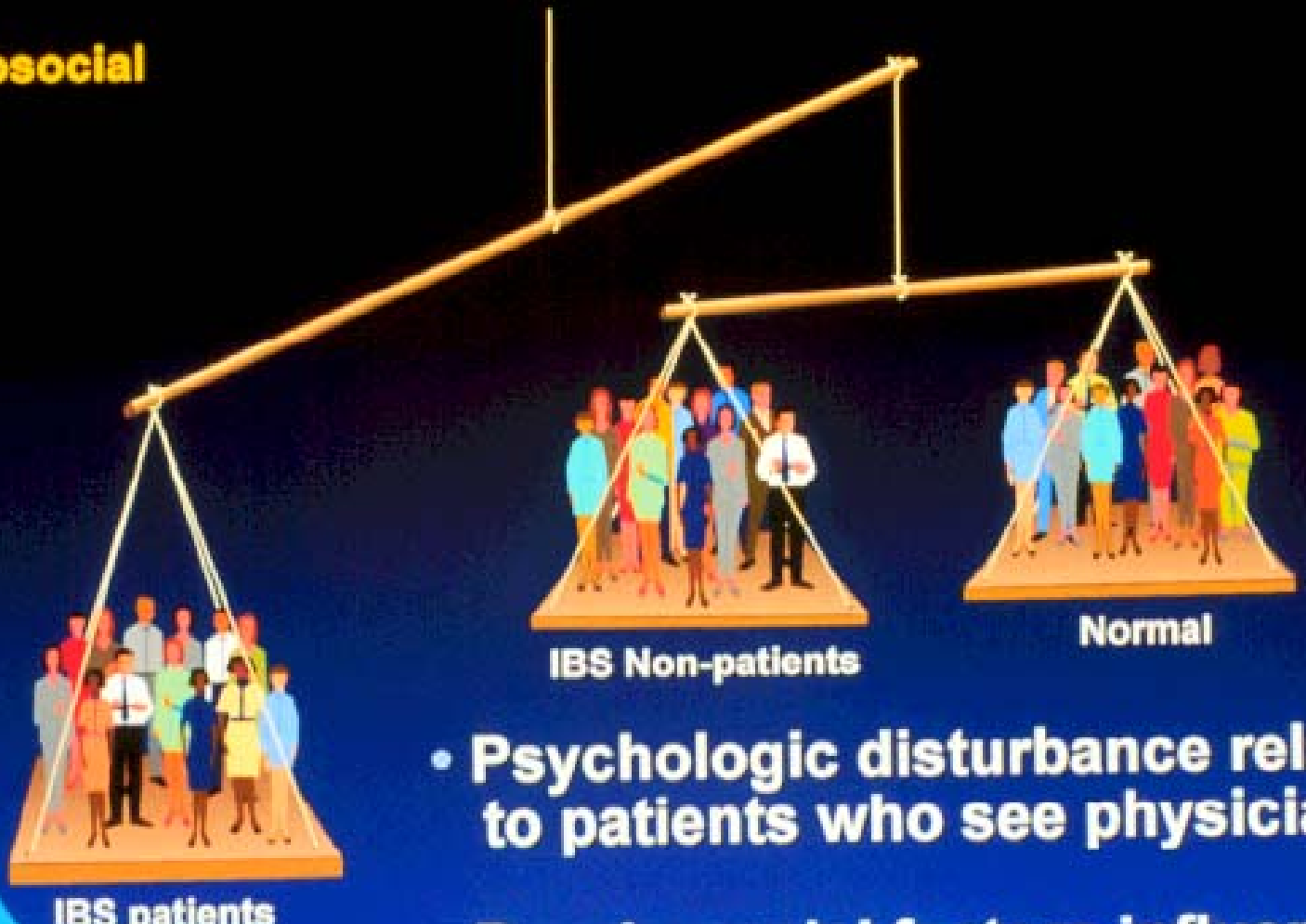
Anticipation of rectal distension



ACG activity

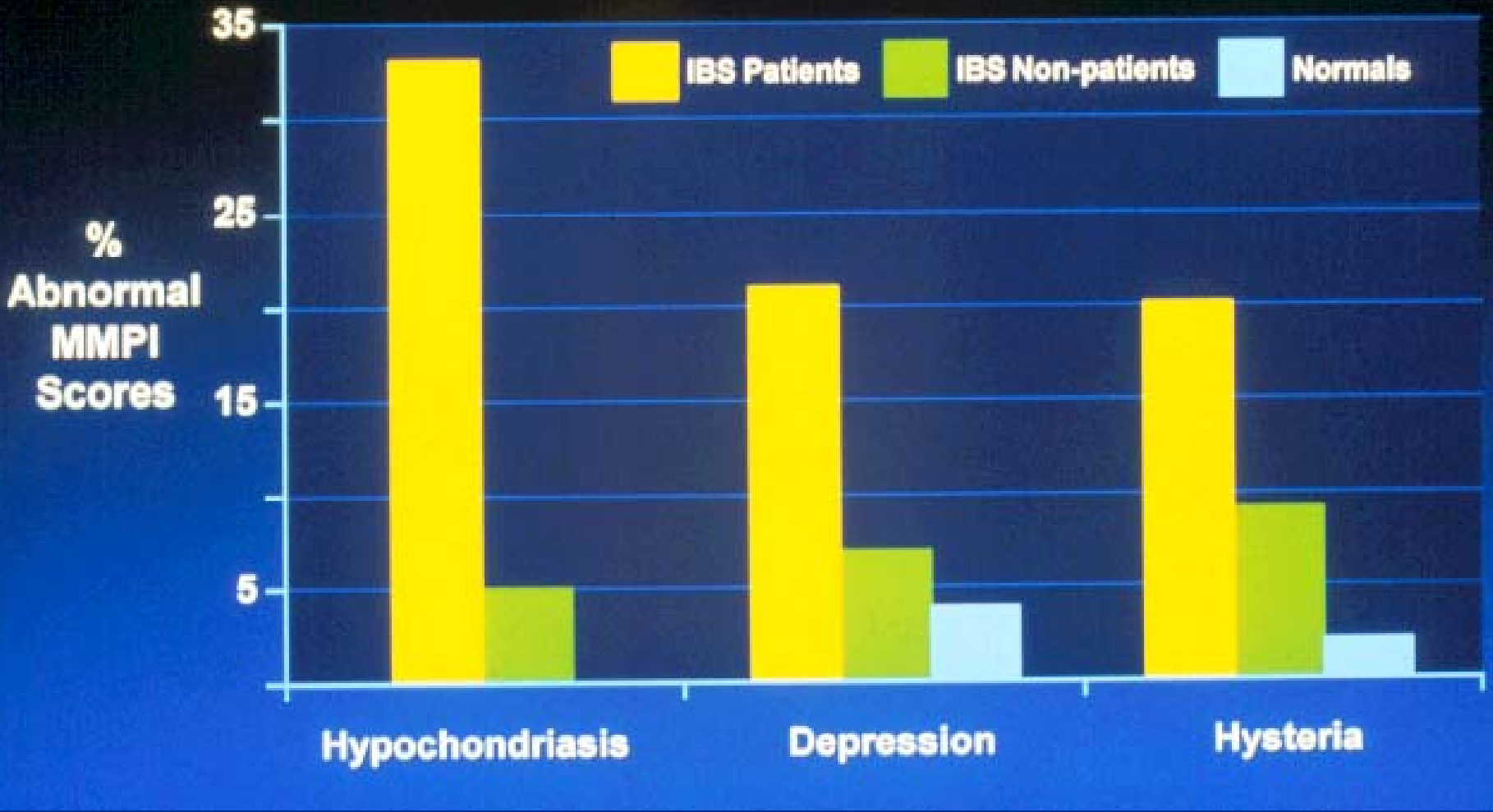
Prefrontal activity

IBS - Psychosocial

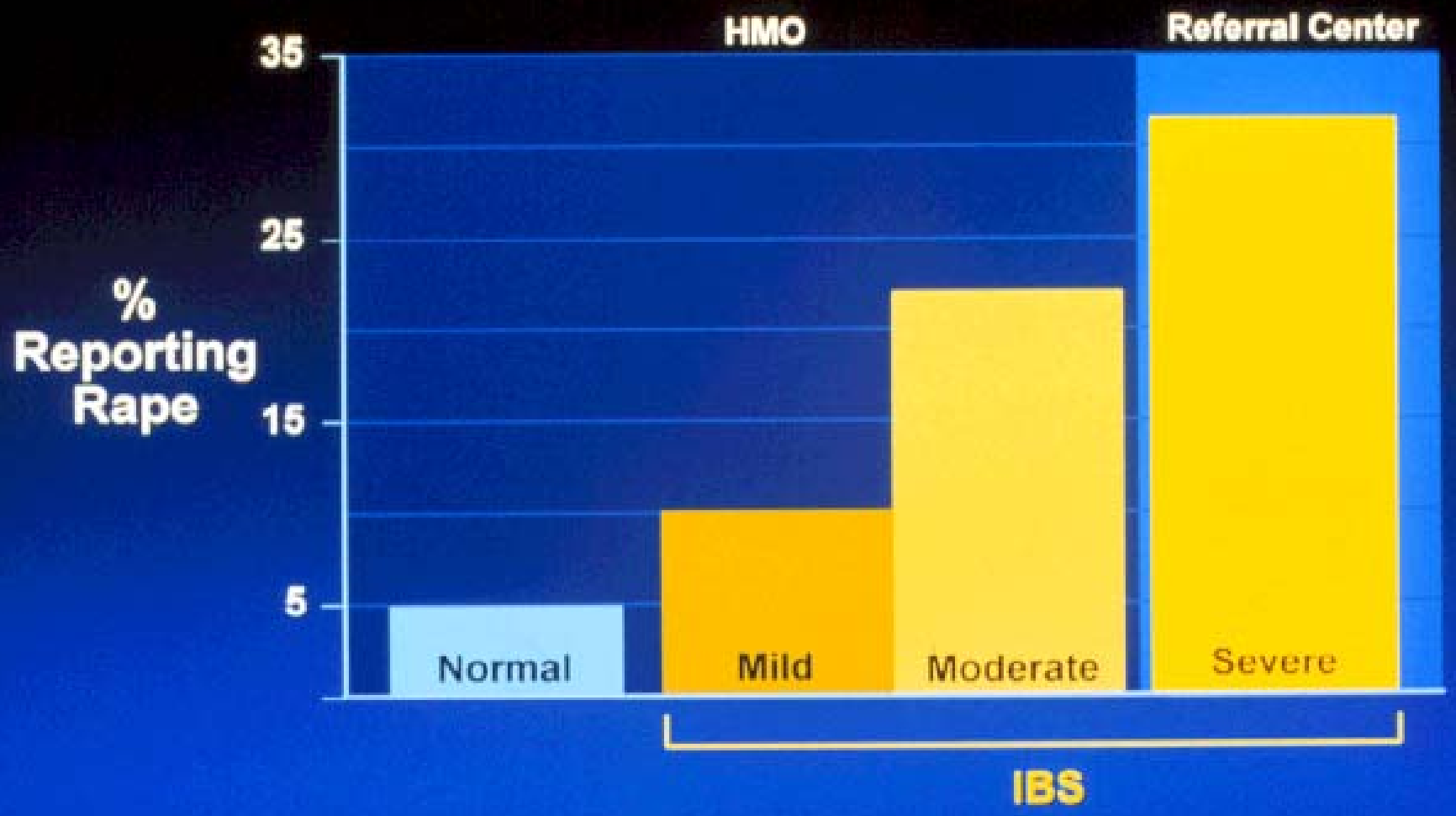


- Psychologic disturbance relates to patients who see physicians
- Psychosocial factors influence health care seeking

IBS - Patients and Non-patients



IBS and Abuse



IBS - Treatment

Placebo Response Rate

Author	Drug	Placebo Response (%)	p<.05
Piai '81	Prifinium	33	yes
Milo '80	Domperidone	34	yes
Page '81	Dicyclomine	54	yes
Heefner '78	Desipramine	60	equivocal
Myren '82	Trimiprimine	67	no
Longstreth '81	Metamucil	71	no
Fielding '81	Timolol	73	no
Fielding '80	Trimebutine	88	no

IBS - Physician Patient Relationship

Treatment Guidelines

- Identify concerns
- Explain basis for symptoms
- Reassure
- Cost effective evaluation
- Involve patient
- Provide continuity
- Set realistic limits

Diet and IBS

- 60% patients believe that certain foods exacerbate symptoms
- Not enough evidence that food allergy testing or exclusion diets are effective in treating IBS

Fiber and laxatives in IBS-C

- Psyllium is moderately effective
- Calcium polycarbophil may be effective
- Wheat and corn bran not more effective than placebo – not recommended
- PEG laxative improves stool frequency but not abdominal pain

Antispasmodics in IBS

- Certain antispasmodics may provide short term relief of abdominal pain/discomfort in IBS
  - Hyoscine
  - Peppermint oil
- Evidence of long term efficacy not available

Antidiarrheals in IBS

- Loperamide effective for the control of diarrhea
- Not effective in reducing pain, bloating or global symptoms in IBS

Antibiotics in IBS

- Rifaximin, a non absorbable antibiotic, is effective for the treatment of bloating and diarrhea
  - Improves general well being
  - 400 mg po bid/tid
- Metronidazole – 1 report
- Clarithromycin – no improvement

Probiotics in IBS

- Lactobacillus alone – no improvement
- Bifidobacteria and certain combo's – some improvement

$5HT_3$ receptor antagonists in IBS

- Alosetron is effective in improving abdominal pain, urgency, global symptoms and diarrhea associated complaints in men and women with IBS-D
- Concern for safety due to constipation and ischemic colitis (1.7 cases per 1000 patient-years)
- Regulated by a prescription program by FDA and manufacturer
  - For practical purposes, not available

$5HT_4$ (serotonin) receptor agonists in IBS

- Tegaserod removed from the market in March 2007
  - Increased cardiovascular events
- Effective in treatment of abdominal pain, bloating, and constipation in IBS-C and IBS-mixed

C-2 chloride channel activators in IBS

- Lubiprostone effective in improving abdominal pain/discomfort, straining, constipation in women with IBS-C

Antidepressant agents in IBS

- TCA and SSRI improve abdominal pain and increase well being in IBS
  - Lower doses than for depression (TCA)
- Theoretically, TCA more effective for IBS-D and SSRI more effective for IBS-C

Psychological therapies in IBS

- Cognitive therapy, dynamic psychotherapy and hypnotherapy all effective in IBS
- Relaxation therapy not effective in IBS

Herbal therapies and Acupuncture in IBS

- Chinese herbal mixtures appear to show a benefit
- Highly variable components and purity
- Significant concerns about liver toxicity
- The efficacy of acupuncture is uncertain

Emerging therapies in IBS

- Peripheral acting agents
  - Chloride secreting agents
  - Calcium channel blocker
  - Opioid receptor ligands
  - Motilin receptor agonists
- Peripheral and central agents
  - Serotonergic agents
  - Corticotropin RH antagonists
  - Autonomic modulators