Irritable Bowel Syndrome: A Post-infectious Syndrome

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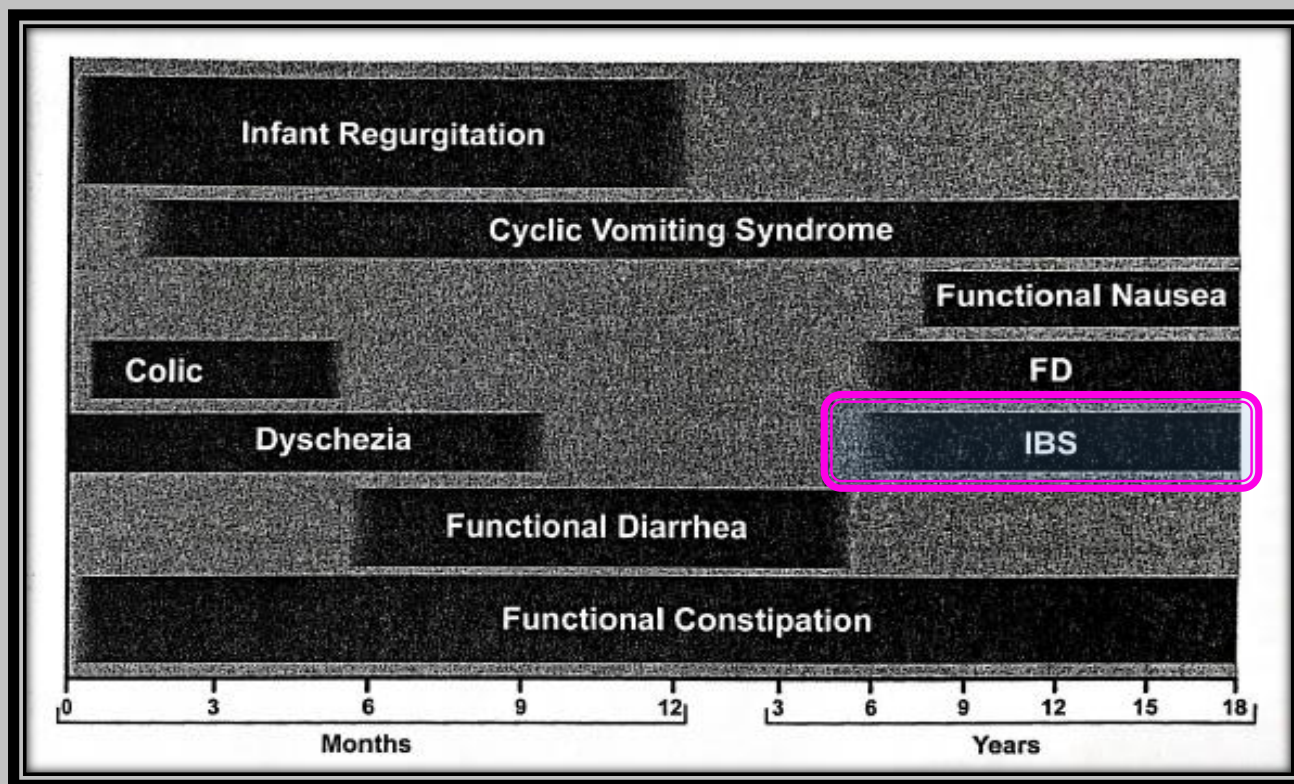# DISCLOSURE: Conflicts of Interest

- None

IBS, a Post-infectious Syndrome

- Perspectives Setting: FGIDs

- Pathophysiology of IBS

- Epidemiology of IBS and PI-IBS

- Risk Factors for PI-IBS

- Clinical Manifestations

- Diagnostic Approach

- Management Strategies

Irritable Bowel Syndrome (H2b)
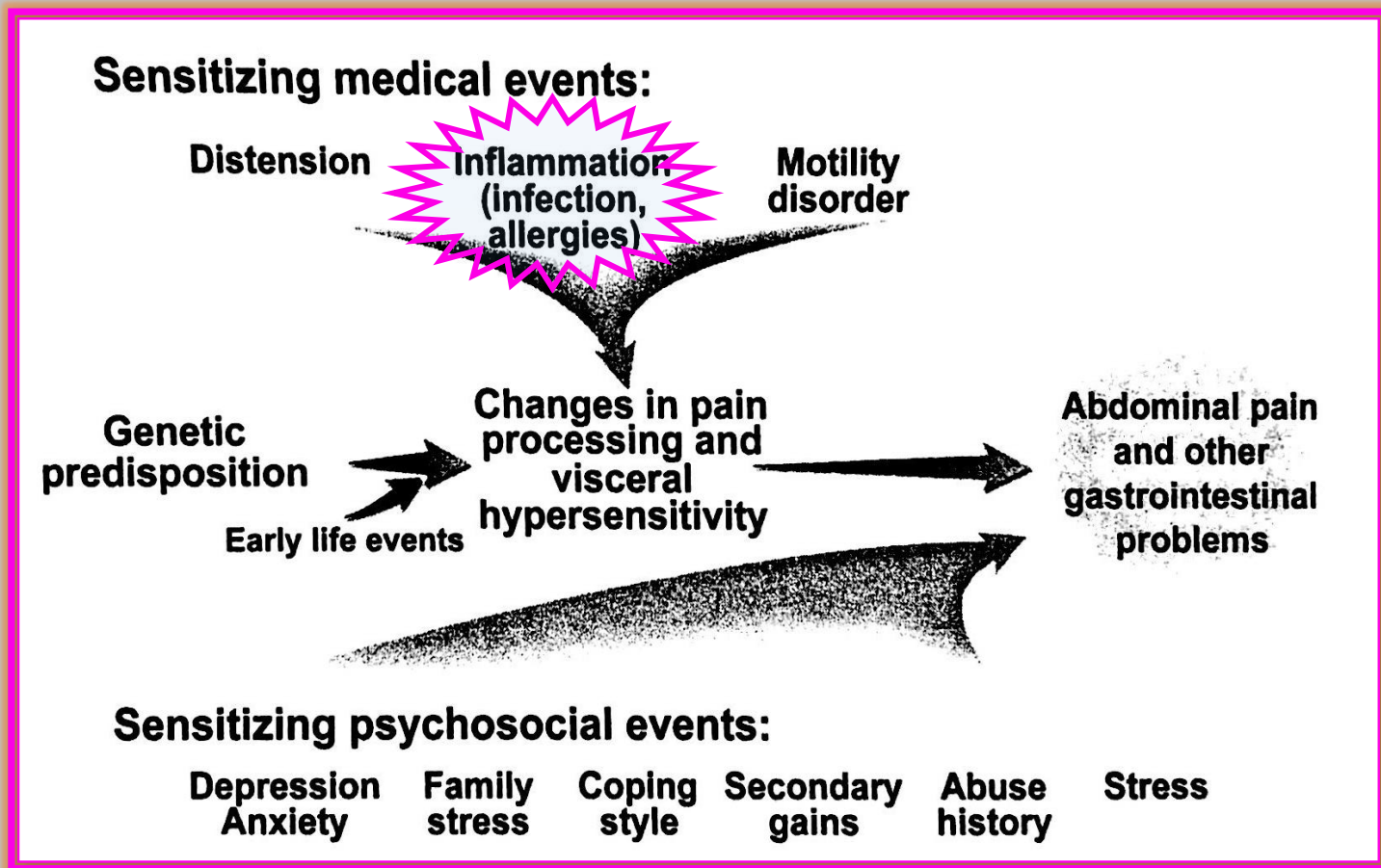
- Rome IV Functional GI Disorders

Age at Presentation

IBS Pathophysiology: Disorder of Brain-Gut Axis

Di Lorenzo C, Nurko S, et al. (eds). Rome IV Pediatric Functional GI Disorders: Disorders of Gut-Brain Interaction. 1st ed. Raleigh, NC: The Rome Foundation 2016: 122.

Pediatric IBS: Epidemiology

- Data from meta-analysis
  - Affects 8.8% (6–12%) of population worldwide

- Philippine data:
  - 2.7% of 779 subjects (Rome III criteria)
  - 5.6% of 2,146 subjects (Rome II criteria)

Korterink JJ, et al. PLOS ONE 2015; 10(5): e0126982.doi:10.1371.
Tan M. Pediatric Functional GI Disorders: A Filipino Translated Questionnaire Based on Rome III Criteria. 2011.
Gatcheco FN. Epidemiology of dyspepsia, IBS and FAP among Filipino children. J Pediatr Gastroenterol Nutr 2004; 39: P0838.

Post-infectious IBS (PI-IBS): Epidemiology

- Prevalence
  - 14.7% of pediatric patients with infectious enteritis (IE)*
  - 11.1% of adult patients with IE*

  *significant heterogeneity [I^2=79% (P) and I^2=98% (A)]

- Relative Risk of PI-IBS
  - 4.1 times higher compared to age- and sex-matched controls (pediatric cases)
    - 95% CI: 2.05,8.15; I^2=0
  - 3.8 times higher (overall) compared to age- and sex-matched controls

Klem F, et al. Gastroenterology 2017; 152: 1042–54.

PI-IBS: Risk Factors

- Infectious enteritis
  - Bacteria (C. jejuni, Salmonella enterica, Shigella sonnei, E. coli O157:H7)
  - Virus (norovirus)
  - Protozoa (G. lamblia)
- Age: younger
- Gender
- Bloody stools
- Prolonged diarrhea

Thabane M, et al. Am J Gastroenterol 2009; 104: 2267–74; Thabane M, et al. Aliment Pharmacol Ther 2007; 26: 535–44; Marshakk JK, Thabance M, et al. Gastroenterology 2006; 131: 445–50.

PI-IBS: Risk Factors

- Infectious enteritis (IE)
  - **Viral IE** rates
    - Within 12 mos of IE (Prevalence = **19.4**; 95% CI: 13.2–27.7)
    - > 12 mos of occurrence (Prevalence = **4.4**; 95% CI: 0.3–39.9)
  - **Protozoal/parasitic rates**
    - Stable over time
  - **Bacterial IE rates**
    - RR = **4.2** (within 12 mos) vs. 2.2 (> 12 mos); p=0.01)

- Gender
  - **Female**:
    - OR = 2.19; 95% CI: 1.57–3.07; I^2=72%

- **Abdominal pain**
  - OR = **3.26**; 95% CI: 1.3–8.14; I^2=86%

- **Prolonged diarrhea** (>7 days)
  - OR = **2.62**; 95% CI: 1.48–4.61; I^2=86%

- **Bloody diarrhea**
  - **O**R = **1.86**; 95% CI: 1.14–3.03; I^2=65%

- **Antibiotic intake**
  - OR = **1.69**; 95% CI: 1.20–2.37; I^2=32%

Klem F, et al. Gastroenterology 2017; 152: 1042–54.

IBS: Clinical Manifestations

- Abdominal pain at least <u>4 days per month</u> for at least <u>2 months</u> associated with erratic bowel habit or variable changes in stool form and frequency
    - Pain unresolved with resolution of constipation
    - Symptoms not fully explained by another medical condition

Chey WD, et al. JAMA 2015; 313: 949–58.
Di Lorenzo C, Nurko S, et al. (eds). Rome IV Pediatric Functional GI Disorders: Disorders of Gut-Brain Interaction. 1st ed. Raleigh, NC: The Rome Foundation. 2016.
Spiller R. *F1000* Research 2016; 5(F1000 Faculty Rev); 780.
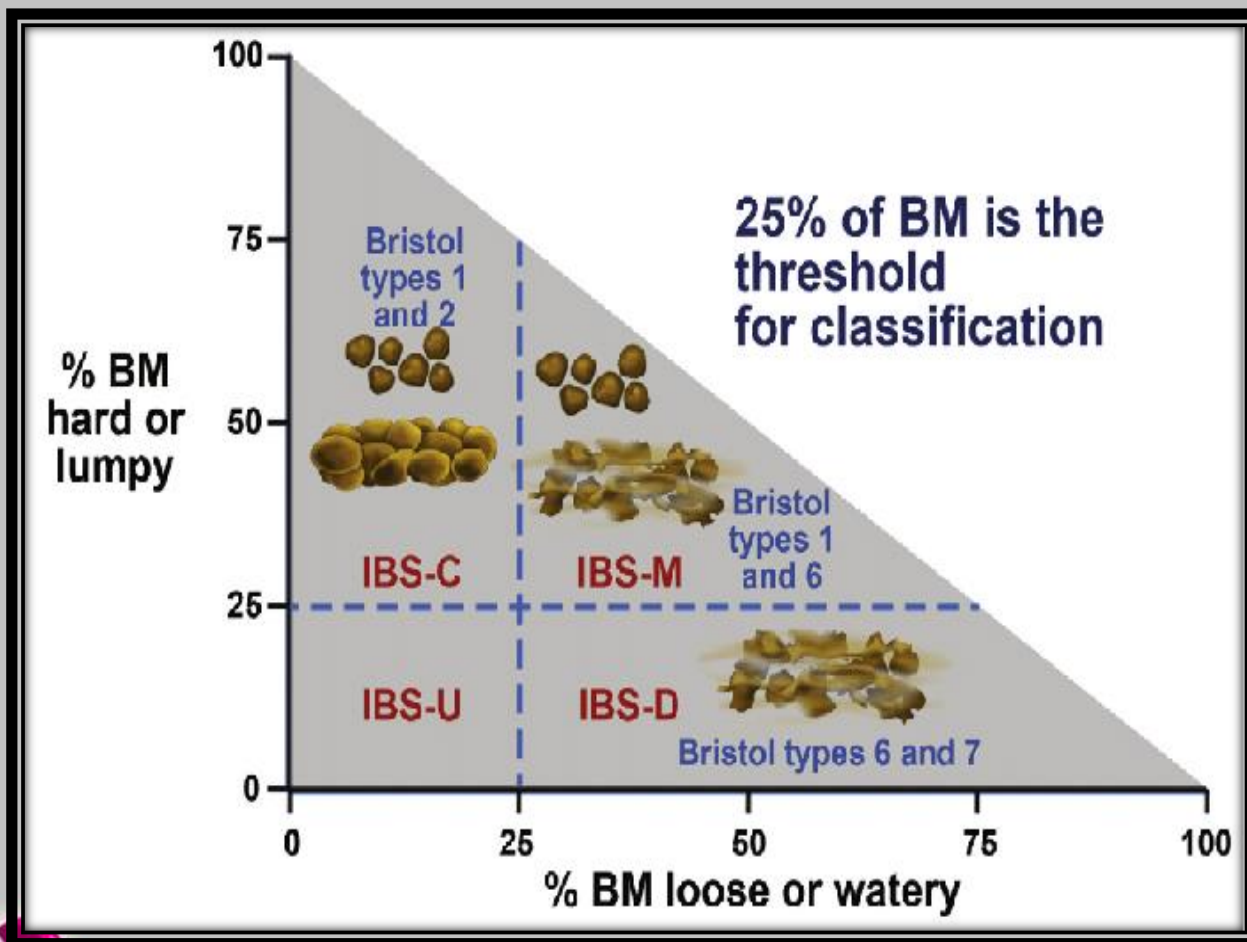
IBS Subtypes (by Stool Form)

Di Lorenzo C, Nurko S, et al. (eds). Rome IV Pediatric Functional GI Disorders: Disorders of Gut-Brain Interaction. 1st ed. Raleigh, NC: The Rome Foundation 2016: 13.
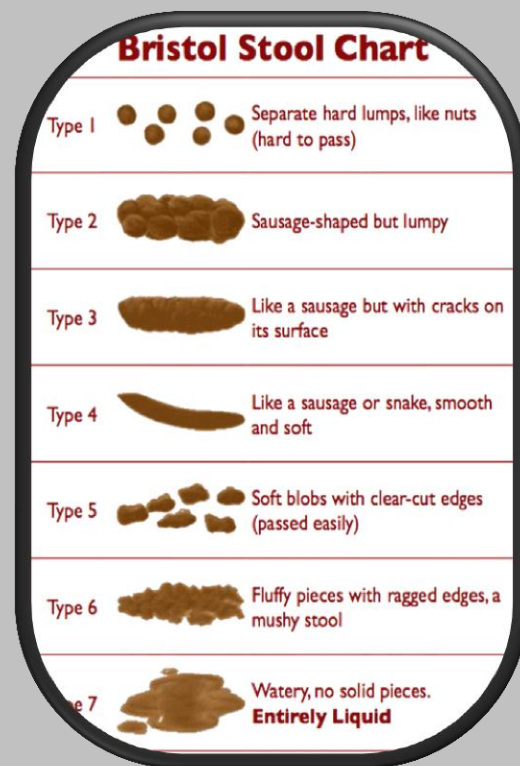
Post-infectious IBS: Prevalence of Subtypes

- IBS-M (most common)
  - **46%**; 95% CI: 31–62%
- IBS-D
  - **40%**; 95% CI: 25–57%
- IBS-C
  - **15%**; 95% CI: 10–21%

Klem F, et al. Gastroenterology 2017; 152: 1042–54.

Diagnostic Approach in IBS

- History
  - Dietary, family, social, educational history
  - Other historical cues
    - Endemicity of infections/parasitic infestations
    - Malabsorption syndromes (CHO)
- Physical examination
  - Based on the Rome IV criteria and subtype classification using Bristol Stool Form Scale
  - Focus on growth and development
  - Look for alarm signals

Alarm Signals in Pediatric Chronic Abdominal Pain

- Unexplained fever

- Persistent vomiting

- Dysphagia, odynophagia

- Persistent RUQ or RLQ pain

- GI bleeding

- Nocturnal diarrhea

- Poor growth and development
  o Involuntary weight loss
  o Deceleration of linear growth
  o Delayed puberty

- Family history of IBD and peptic ulcer disease

- Arthritis

Di Lorenzo C, Nurko S, et al. (eds). Rome IV Pediatric Functional GI Disorders: Disorders of Gut-Brain Interaction. 1st ed. Raleigh, NC: The Rome Foundation 2016: 13.

Diagnostic Approach in IBS

- Basic diagnostics
  - CBC, liver and renal function test
  - Inflammatory markers
  - Amylase, lipase (as indicated)
  - Stool culture and reducing sugars (diarrhea)

- Special investigations
  - Abdominal ultrasound
  - GI endoscopy
  - MRI abdomen
  - Fecal calprotectin
    - May help differentiate IBS from IBD
    - Values < 50 mg/g stool less likely to be IBD

Management in Pediatric IBS

- Few double-blind, randomized trials
- No universally proven therapy

Management Strategies

- Dietary interventions
  - Fiber supplements
  - Lactose-free diet
  - Low fermentable oligo-, di-, monosaccharides and polyols (FODMAP) diet
  - Partially hydrolyzed guar gum
  - Probiotics (LGG, multi-strain VSL#3)
    - Inhibition of pathogen binding; modulation of gut inflammation; reduction in visceral hypersensitivity)
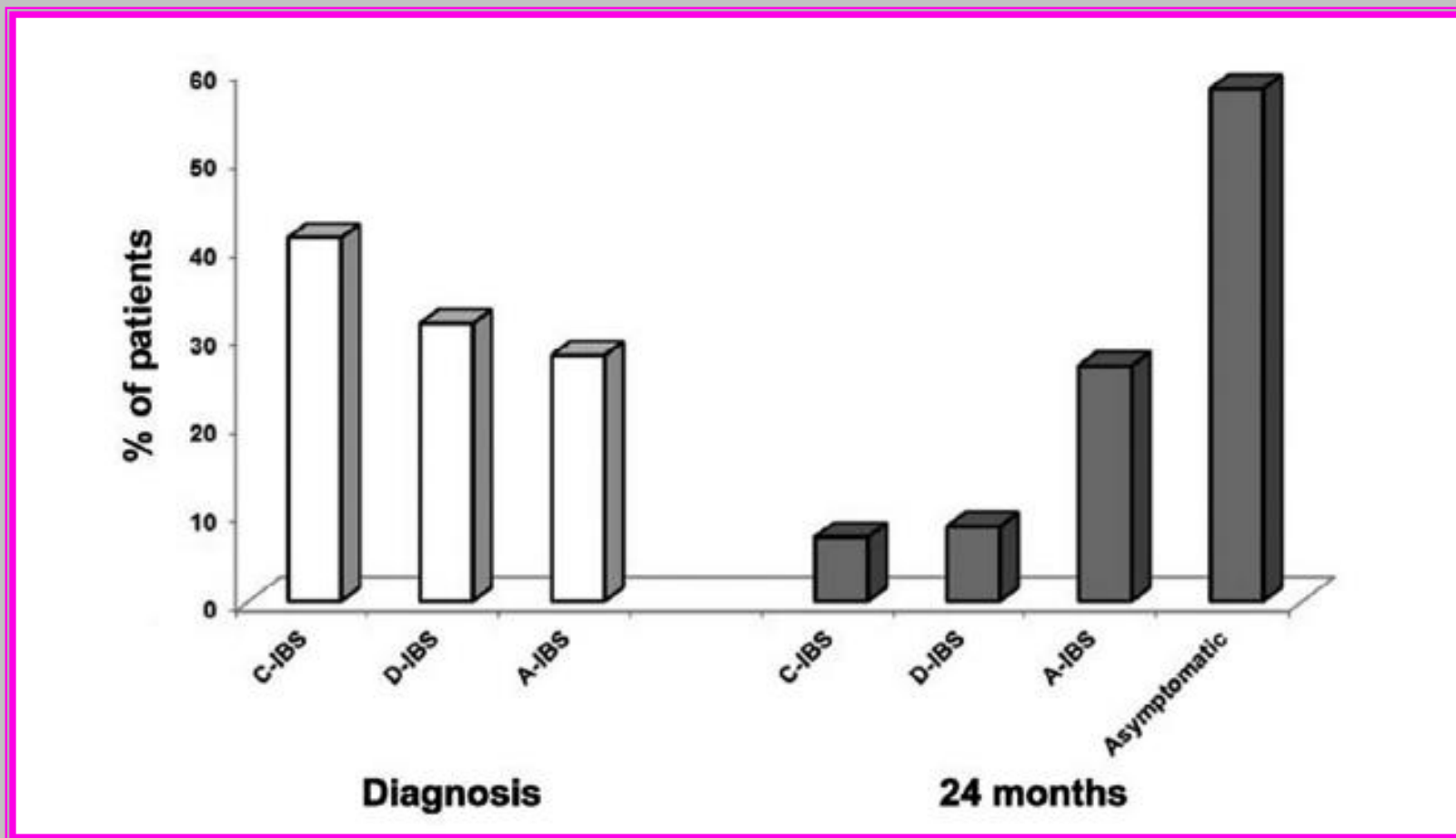
Management Strategies

- Pharmacologic treatment
  - Peppermint oil (antispasmodic, anti-flatulent)
  - Antispasmodics
  - Antibiotics

- Biopsychotherapy
  - Cognitive behavioral therapy
  - Hypnotherapy, yoga, acupuncture

Do Children Grow Out of IBS?

Distribution of IBS subtypes at diagnosis and after 24 months of follow-up
(83 children, aged 4–16.6 yrs, Naples, Italy)

Giannetti E, Staiano A, et al. J Pediatr 2017; 183: 122–6.

Summary Points: PI-IBS

- Recognition of infectious enteritis as a cause of Functional GI Disorder (IBS)
  - Usually presenting as abdominal pain and erratic bowel frequency and consistency
- Risk factors for IBS
  - Related to the etiologic agent, gender, clinical presentation (abdominal pain, prolonged and bloody diarrhea)
  - Increased with antibiotic intake
- Treatment
  - Mainly supportive