Obesity and Inflammatory Bowel Disease In Children

Dinesh Pashankar, MD, MRCP
Pediatric Gastroenterologist
Director- Yale Pediatric IBD Program
Yale University
New Haven, USA

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Yale New Haven Hospital





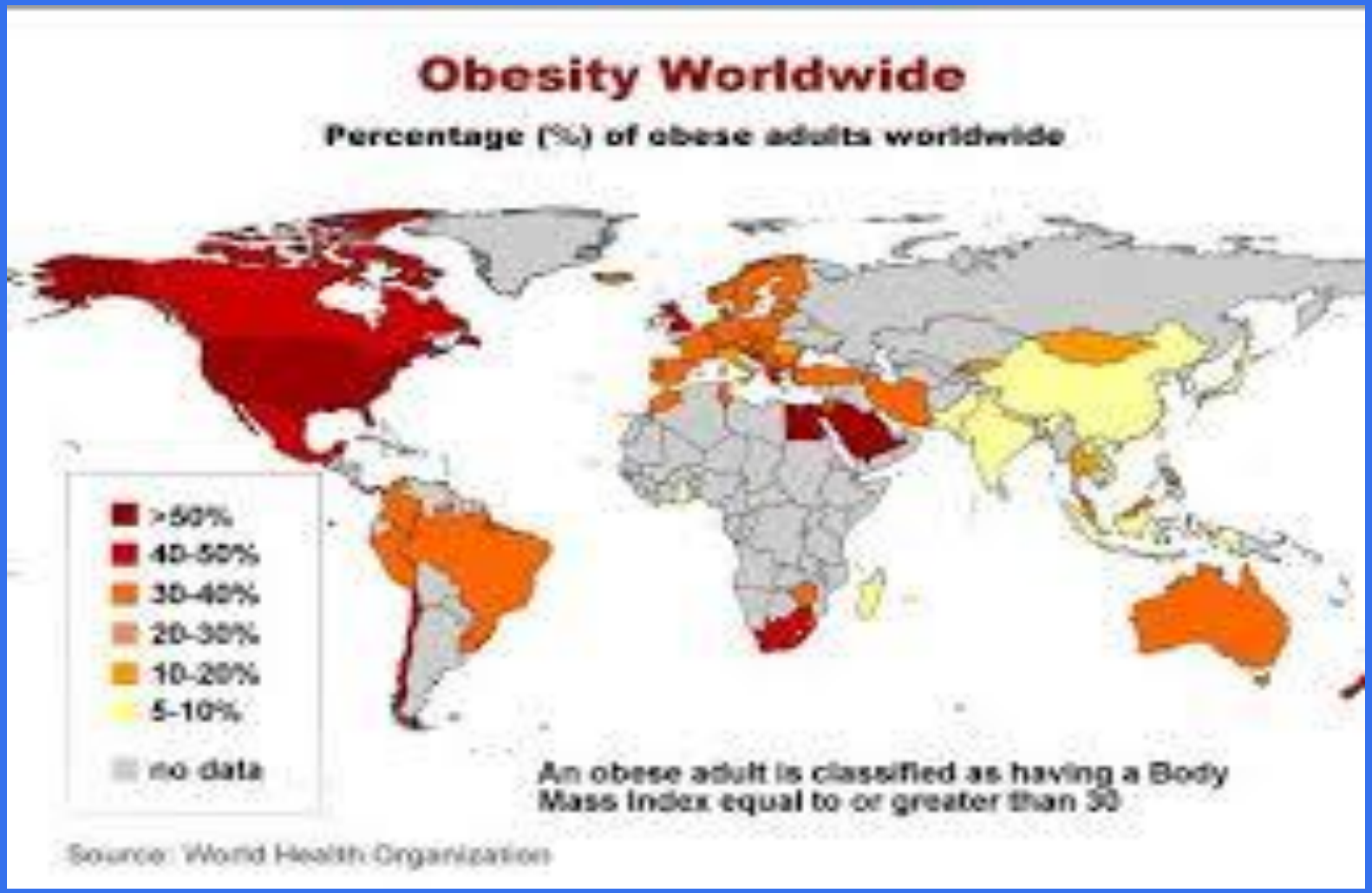
Objectives

- 1. Obesity prevalance and GI disorders
- 2. IBD diagnosis and therapy
- 3. Obesity and IBD – Prevalence
  - Mechanism
  - Clinical significance

Obesity

- CDC Definition for children
- Overweight = > 85th percentile BMI
- Obese = >95th percentile BMI

Rising obesity prevalence



View from space



1970



2016

Obesity in children

- USA – 5 % in 1980 to 17% in 2012
- Rising prevalence in the world
- Co-morbidity

Diabetes Hypertension

Metabolic syndrome Fatty liver

Gastrointestinal disorders

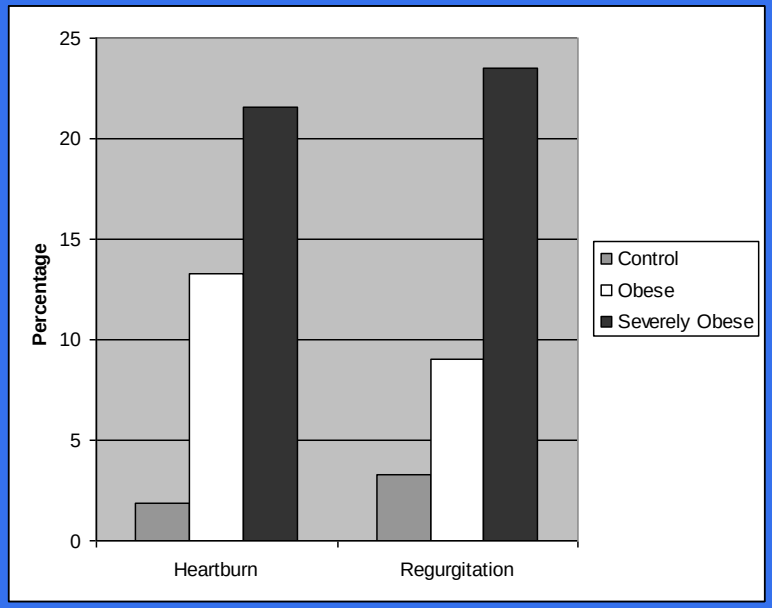


Obesity and GI disorders

- Gastroesophageal reflux GER
- Functional Gastrointestinal disorders (FGID)
  - Constipation
  - Irritable Bowel syndrome
- Organic GI disorders
  - Celiac disease
  - Inflammatory bowel disease

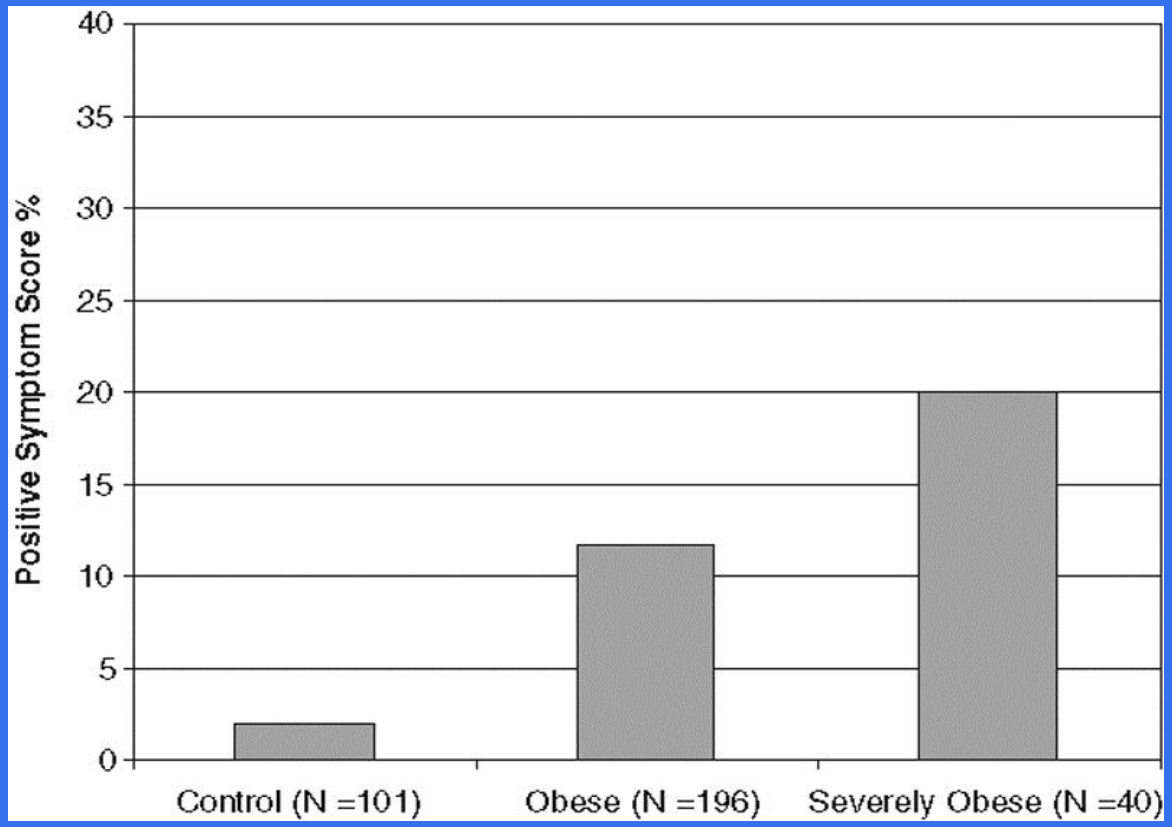
Obesity and GER in children

- Prospective study in CT, USA
- Prevalence of GER symptoms
- 236 obese children and 101 controls
- Obesity – BMI > 95th centile
- Heartburn and regurgitation
- Reflux score



Pashankar DS, et al. J Clin Gastroenterol 2009

Obesity and reflux score



Pashankar DS, et al. J Clin Gastroenterol 2009

Obesity and Functional Gastrointestinal Disorders

- Functional constipation

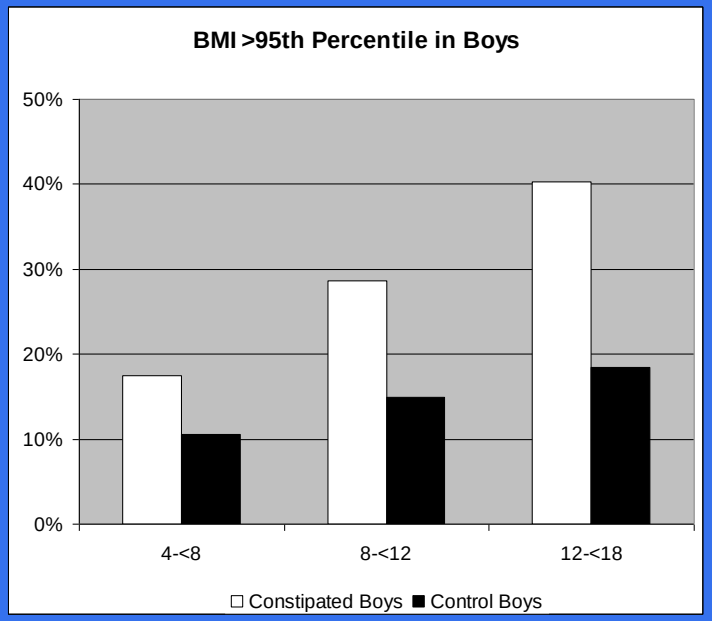
- Irritable bowel syndrome (IBS)

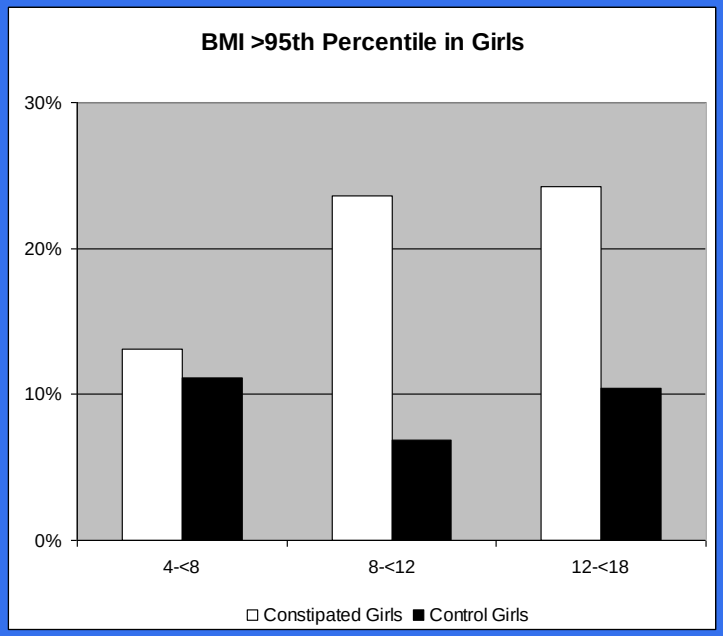
Constipation and Obesity

- Chart review - Iowa, USA
- 719 children with functional constipation
- 930 matched controls
- Obesity - BMI > 95th percentile
- Children with constipation - 22.4 % obese
- Control group – 11%

Pashankar DS, et al. Pediatrics 2005

Obesity and constipation





Pashankar DS, et al. Pediatrics 2005

Obesity and FGID

- Interview study – Connecticut, USA
- 450 healthy children for routine visit
- Rome III criteria for constipation
- Constipation more common in obese children (23%) than normal weight children (14%)
- IBS more common in obese children (16 %) than normal weight children (7%)

Phatak UP and Pashankar DS. Int J Obes 2014

Obesity and Organic GI disorders

- Celiac disease

  Gluten allergy Duodenitis

- Inflammatory Bowel Disease (IBD)

  Crohn's disease

  Ulcerative colitis

- Usually associated with malabsorption, weight loss and growth failure

Obesity and celiac disease

References	Sample size	Underweight at presentation	Overweight/obese at presentation	Effect of gluten-free diet
Norsa et al Italy	114	9.6%	14.1%	Increase in BMI. Increase in obesity to 19.4%
Reilly et al USA	142	7%	19%	Decrease in BMI z-score in 75%
Valletta et al Italy	149	5%	14%	Increase in BMI Increase in obese to 25%
Brambilla et al Italy	150	16%	12 %	Decrease in overweight/obese to 9.4%
Venkatasubramani USA	143	Not known	5%	Decrease in overweight/obesity to 3%

Phatak UP and Pashankar DS. J Pediatr Gastroenterol Nutr 2015

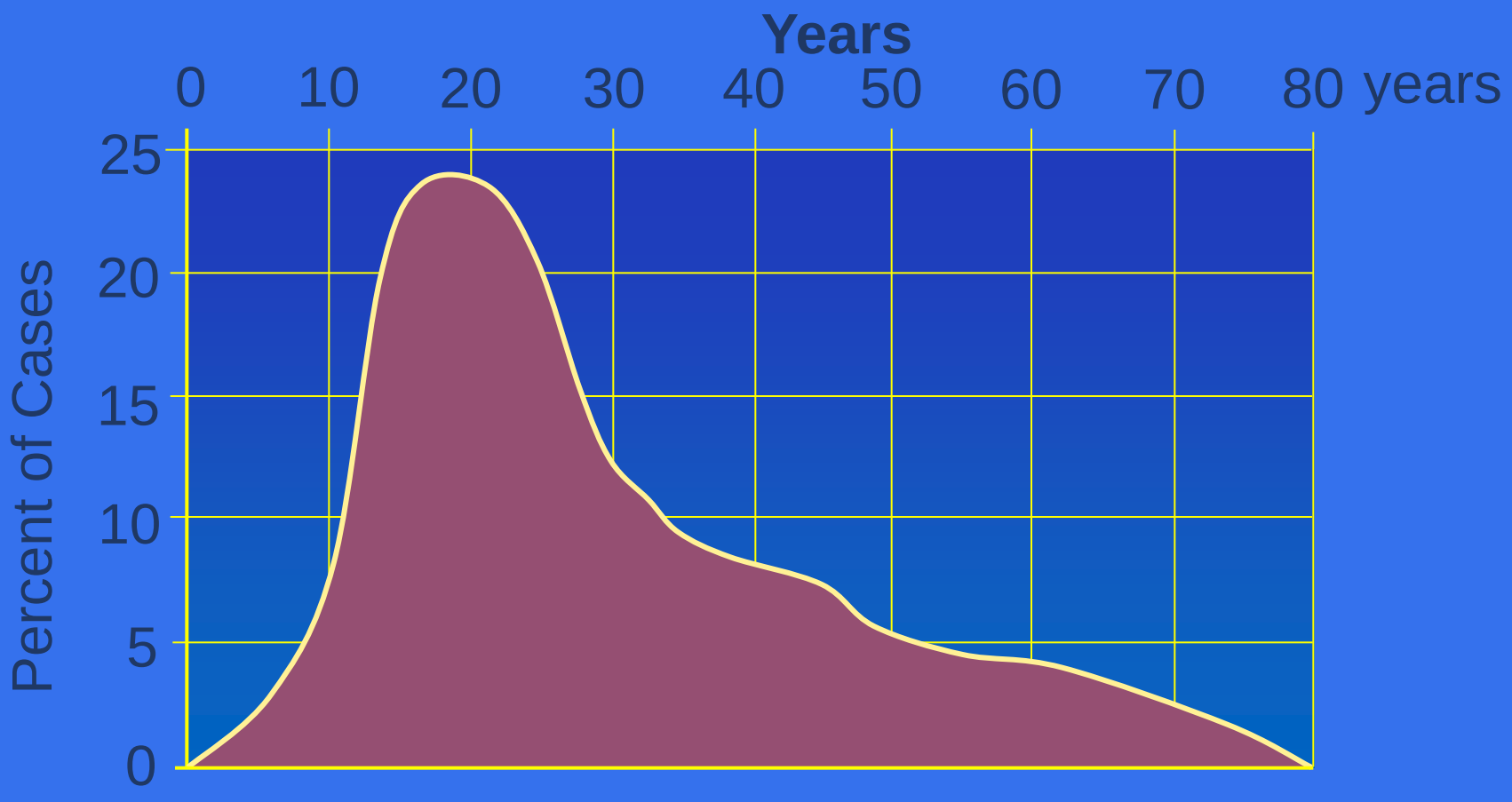
Obesity and Inflammatory Bowel Diseases (IBD)

IBD

- Crohn's disease
- Ulcerative Colitis

IBD Epidemiology

Age of Onset of IBD



Loftus, *Gastroenterology* 2003; 124:abstract 278

How Common is IBD in Children?

- Impact in children:
  - Pediatric IBD : getting younger !
  - 25% of IBD diagnosed at pediatric age
- Incidence and prevalence:
  - An estimated million people (all ages) in the United States currently have IBD
  - 7-10 children out of 100,000 develop IBD in any given year in the United States

IBD Diagnosis

Crohn's disease – Presentation

Acute or chronic time course

- Abdominal pain
- Diarrhea
- Bloody stools
- Weight loss
- Mouth ulcers
- Perianal lesions

Ulcerative colitis – Presentation

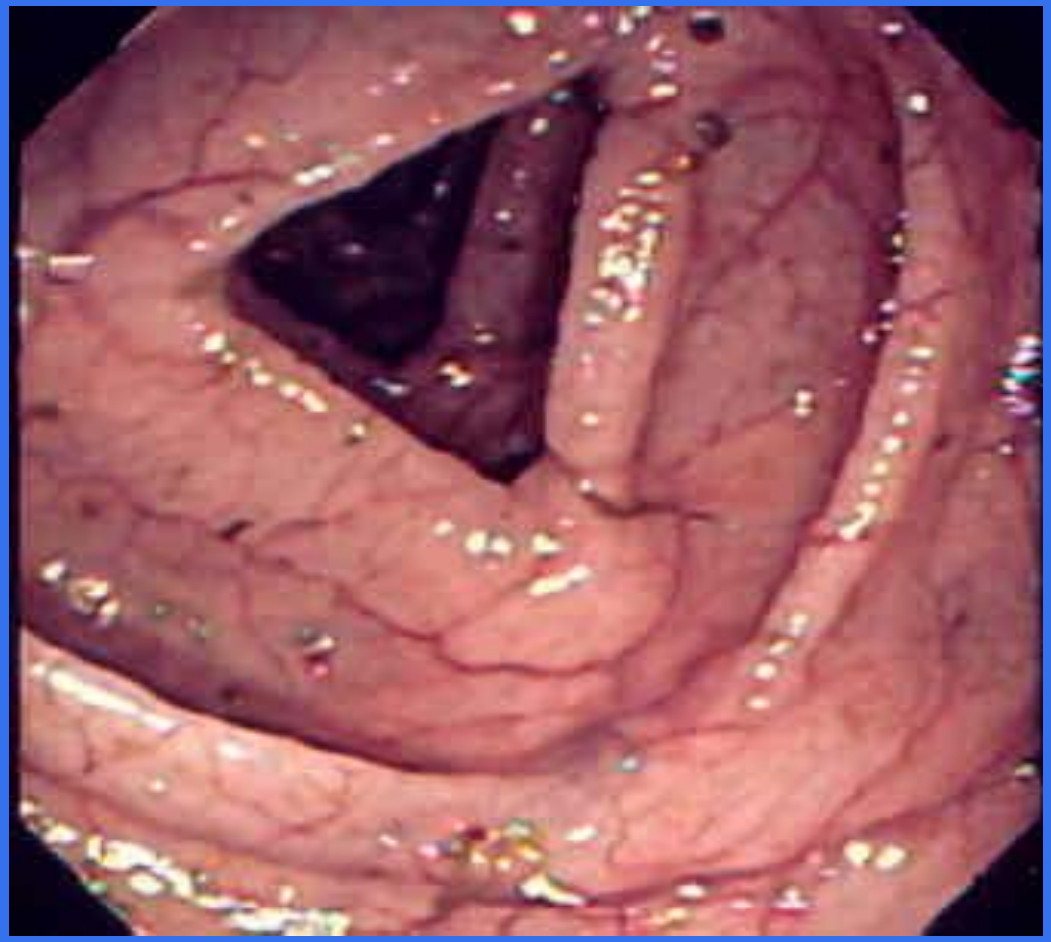
Usually acute

- Diarrhea
- Abdominal pain
- Rectal bleeding
- Nocturnal diarrhea

IBD Diagnosis

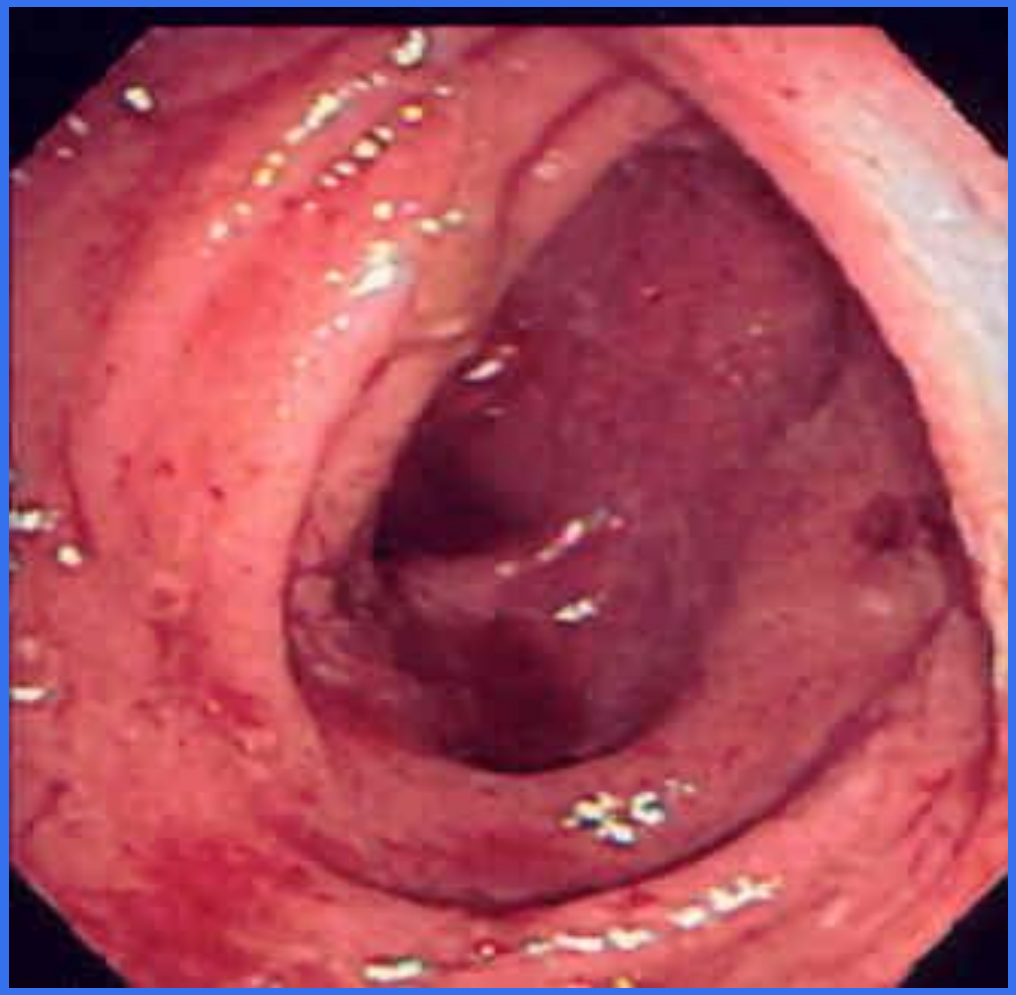
- Stool test – to rule out infection
- Labs – anemia, raised inflammatory markers
- Endoscopy - determine disease location
  - Upper endoscopy, colonoscopy,
  - MR enterography
  - Classify disease as CD or UC

Normal Colon



- Smooth and shiny
- Normal vascularity
- Tortuous
- Normal folds

Ulcerative Colitis



- Loss of vascular pattern
- Granularity
- Exudates
- Diffuse continuous disease
- No ileal involvement

Crohn's Colitis



- Deep fissures
- Cobblestoning
- Segmental distribution
- Rectal sparing
- Ileal involvement
- Granulomas on biopsy

IBD therapy

Nutrition

Medication

- Mesalamine
- Immunosuppressant – 6MP, Methotrexate
- Biologics – Infliximab, Adalimumab

IBD Therapy

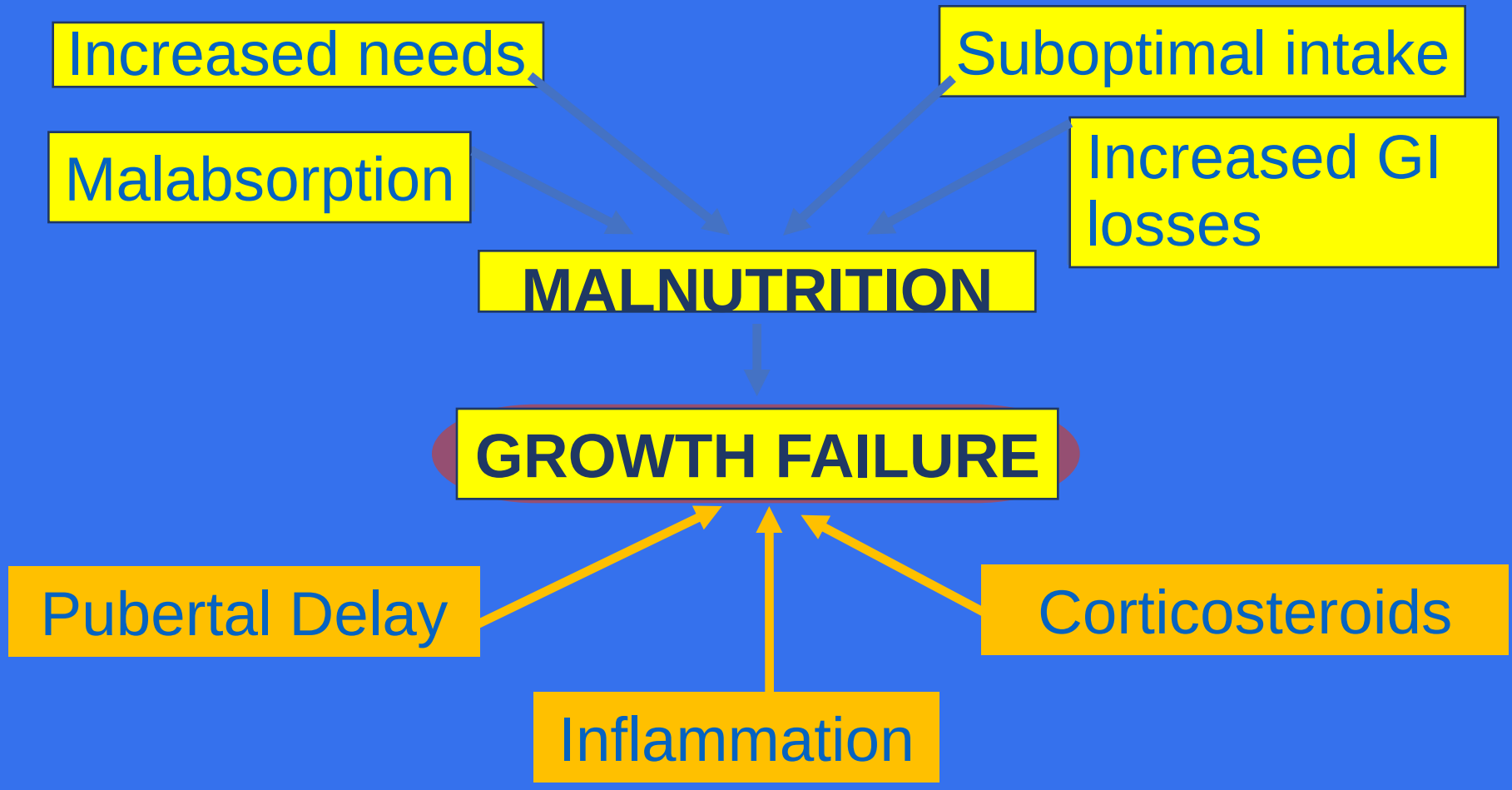
- Surgery

- Colectomy for UC is curative

- Surgery for Crohn's disease
- To cut is not to cure
- Limited indications

IBD and Growth Failure

Growth Failure in Crohn's disease



Impaired Linear Growth

Patients	% Occurrence
Pediatric IBD	35
Prepubertal CD	60–85
Children with UC	6–12

Obesity and IBD

Prevalence

Mechanism

Clinical significance

Obesity and IBD in adults

- Research study review
- 40 studies from 1991 to 2008
- 10,282 adults with IBD
- A significant increase in weight and BMI over time
- Crohn's disease activity also increased
- ? Adiposity increasing intestinal inflammation

Moran et al, IBD 2013

Obesity and IBD in adults

- European Prospective Nutrition study
- 300,750 patients recruited
- Weight, height, BMI measured and followup
- 177 patients developed UC and 75 Crohn's disease
- Case – control match
- No association of higher BMI with development of IBD

Chan SM, AJG 2013

Obesity and IBD in adults

- US nurses Health study 1989
- 111,498 women studied
- Baseline weight, BMI
- 153 Crohn's disease and 229 UC diagnosed over 18 years , compared to controls
- Hazard ratio for Crohn's 2.23 in obese
- UC no significant relation

Khalili H, IBD 2015

Obesity and IBD in children

- Multicenter study from North America
- 783 newly diagnosed children with IBD

10% of Crohn's disease and 30% UC children were obese or overweight

- Low BMI in 24 % Crohn's and 9% UC children

Kugathasan, et al. J Pediatrics

Obesity and IBD in children

- Multicenter data from Improvecarenow
- 1598 children with new IBD diagnosis

- 20% of Crohn's disease and 30% UC were obese
- AA children more likely to be obese
- Obesity associated with need for surgery

Long MD et al, IBD 2011

Obesity and IBD

Mechanism

Obesity and IBD Mechanism

- Rising prevalence of obesity in IBD is due to high prevalence of obesity in general population

- Other mechanisms

Microbiome

Cytokines

Steroids

Obesity and IBD Mechanism

- Microbiome
- Preliminary studies suggest association
- IBD has a fairly distinct microbiome signature
- Obesity has less specific signature

Greenblum , et al. PNAS 2012

Obesity and IBD Mechanism

Cytokines

- Obesity associated with adipocytes
- Intestinal creeping fat is commonly seen in Crohn's
- Adipocytes secrete pro-inflammatory cytokines
- These can increase intestinal inflammation
- Can also increase intestinal permeability

Khalili et al. Inflamm bowel dis 2015

Obesity and IBD

Clinical Significance

Obesity and IBD - Significance

- Effect of obesity on IBD
- Studies in adults and children
- Comparison of obese vs normal weight patients
- Parameters assessed … complications, need for therapy, surgery
- Conflicting results

Obesity and effect on IBD

- Large retrospective study from Paris
- 2065 patients with Crohn's disease
- 62 obese patients compared to other controls
- Complications and treatment over time
- More perianal disease in obese
- More need for hospitalization in obese

Blain et al, Clin Nutr 2012

Obesity and effect on IBD

- Large retrospective study from Chicago
- 626 IBD patients undergoing laparoscopic surgery
- Obesity complicates surgery

	Overweight/obesity	Normal wt
Blood loss	+++	- -
Op time	+++	--
Conversion rate	++	--
Hernia	+	--

Krane MK, et al. J Am Coll Surg 2013

Obesity and Effect on IBD

- Study in Seattle
- 124 adults with IBD
- Starting infliximab therapy for Crohn's and UC
- Obese patients more likely to have flare than nonobese patients ($P < 0.001$)
- Obese patients more likely to have loss of response to infliximab than nonobese patients

Harper, et al. IBD 2013

Obesity and effect on IBD

- Retrospective study of 391 surgeries over 14 years
- Groups – obese, overweight, normal, underweight
- Operative time, blood loss, intra-operative and 30 day postop complications not higher in obese patients
- Obesity not a risk factor for surgery

Guardado et al, J Gastrointestinal Surg 2016

Obesity and effect on IBD

- Medical records of Dallas VA hospital
- 581 patients – 33 % obese, 67 % nonobese
- Obese patients – less likely to need biologic therapy, hospitalization or surgery
- Obesity – less severe disease ?

Flores et al , Dig Dis Sci 2015

Obesity and effect on IBD

- Retrospective data on 1494 patients with IBD
- 31 % obese patients
- Obesity not associated with IBD related ER visits, hospitalization , surgeries
- Obesity associated with diabetes, hypertension, hyperlipidemia

Seminerio, et al . IBD 2015

Obesity & effect on IBD in children

- 2009 Kids inpatient database for IBD related hospitalization
- 164 children were obese (1.9%)
- Obesity not related to incidence of hemorrhage, perforation, fistula or need for surgery
- Associated with central line complications

Zwintscher, et al . J Pediatr Surg 2014

Obesity and IBD in children

TREATMENT

- Monitoring of other obesity related complications
- Nutritional counseling
- Limiting calorie intake
- Healthy nutritious diet
- Vitamins, iron supplement
- Physical activity

Summary

- Obesity is associated with gastrointestinal disorders in children
- Obesity is present at diagnosis of IBD
- Effect of obesity on IBD is unclear at present.
- Nutritional counseling and weight management are important parts of therapy

Thanks

