Malabsorption

DR. SALMA BURAYZAT

PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

Q1. Mention six signes and symptoms of malabsorption

Q2. Name two screening tests for protein loosing enteropathy

Q3. Malabsorption of fat-soluble vitamins

- Vitamin A deficiency……
- Vitamin E deficiency leads to……
- Malabsorption of vitamin D leads to ……
- Malabsorption of vitamin K is associated with……

Q4. Most common causes of malabsorption in children (name 5)

Malabsorption

- The primary function of the small intestine is digestion and absorption of ingested nutrients. The term malabsorption refers to impairment in the absorption of one or more substances by the small intestine.

Malabsorption

Signs and Symptoms of Malabsorption

- Weight loss
- Failure to thrive
- Diarrhea
  - –Loose and watery due to carbohydrate, bile acids, or fatty acids malabsorption
  - –Bulky and foul-smelling due to fat malabsorption
- Abdominal pain
- Abdominal distention
- Anemia
- Increased flatulence
- Edema
- Osteomalacia
- Bleeding tendencies

Diagnostic Investigations

Initial Evaluation of Malabsorption

- Detailed history
- Complete physical examination
- Serial growth and anthropometric measurements
- Screening laboratory tests:
- Blood:
  - Complete blood count, complete metabolic panel, erythrocyte sedimentation rate, tissue transglutaminase immunoglobulin A (IgA) antibody, total IgA
- Stool:
  - Culture, ova and parasites, Clostridium difficile testing, occult blood, pH, reducing substances, fecal hydrolysis for detection of nonreducing carbohydrates, ***elastase***, alpha-1- antitrypsin, stain for fat globules
- Sweat chloride test

Diagnostic Investigations

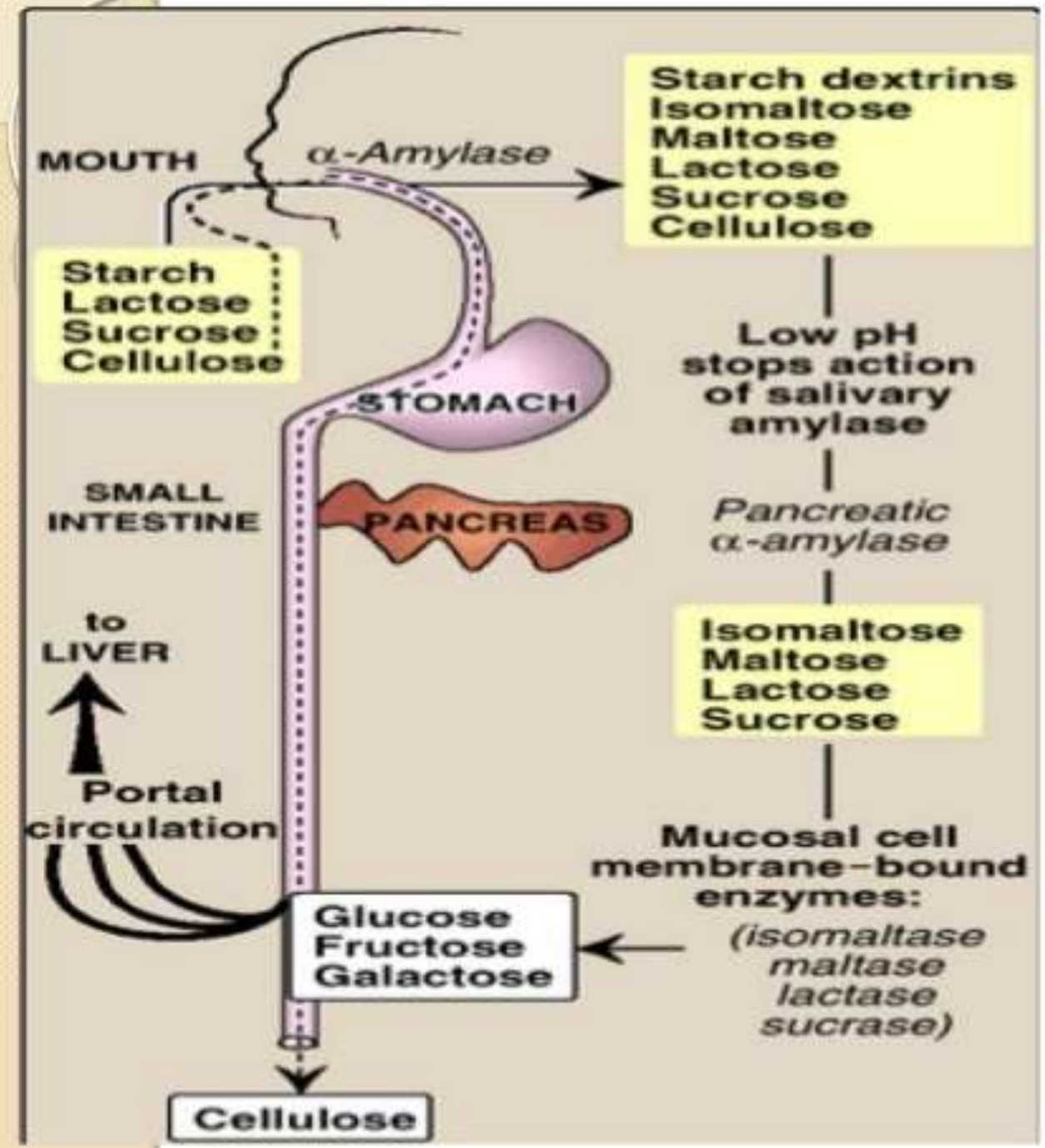
Second-phase Evaluation

- 72-hour quantitative fecal fat
- Breath hydrogen test
- Vitamins A, D, E, and B12; prothrombin time; folate, zinc, iron, ferritin
- Radiolabeled Tc albumin lymphatic scan
- Endoscopy with biopsy for histology and disaccharidase analysis
- Pancreatic enzyme analysis

Physiology and Pathophysiology of Digestion and Absorption

CARBOHYDRATES

Digestion of carbohydrate



Carbohydrates

In malabsorption, maldigested oligosaccharides and unabsorbed monosaccharides are emptied into the colon

- Osmotic effect
- Gases
- Acids
- Unabsorbed reducing sugars

The hydrogen breath test

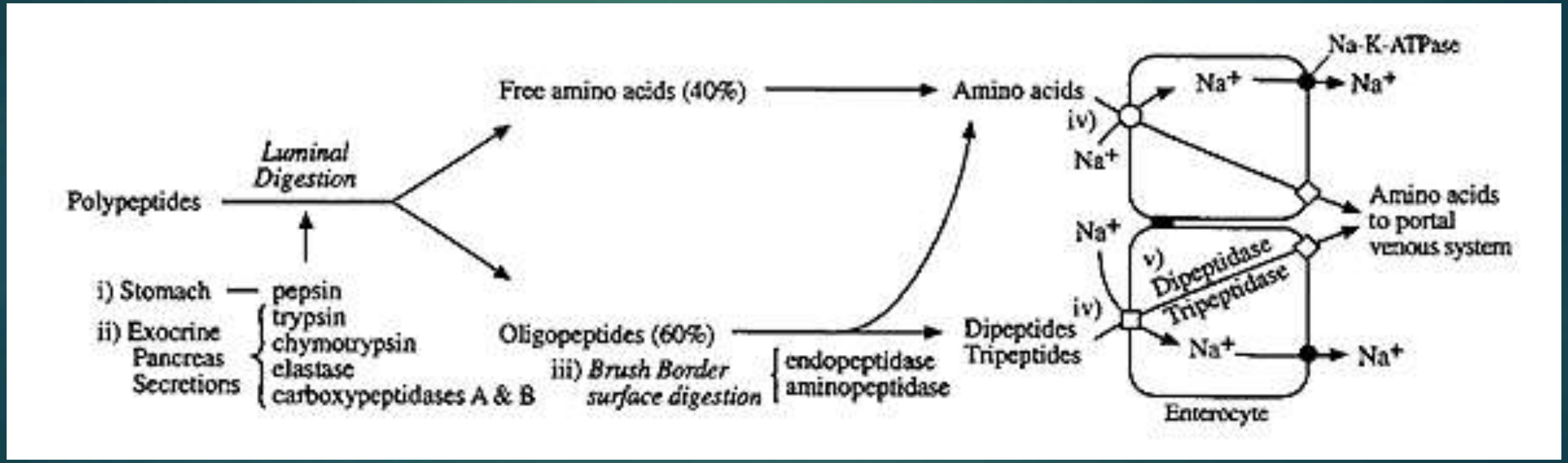
Carbohydrates

- **Carbohydrate malabsorption may be due to:**
  - Mucosal damage
    - Brush border enzyme deficiencies can follow injury to the small intestinal mucosa caused by disorders such as
      - infectious gastroenteritis
      - gluten-induced enteropathy
      - cow milk protein sensitivity
  - Short bowel syndrome
  - Congenital intestinal transport or enzyme deficiencies
  - Excessive ingestion of juices
  - "Adult-onset" lactase deficiency.
  - Sucrase-isomaltase deficiency
  - Glucose-galactose malabsorption

Physiology and Pathophysiology of Digestion and Absorption

PROTEINS

Proteins


Free amino acids (40%)
Amino acids
Na-K-ATPase
Na+
Na+
iv)
Na+
Luminal Digestion
Polypeptides
Amino acids to portal venous system
Na+
v)
Dipeptidase
Tripeptidase
iv)
i) Stomach — pepsin
ii) Exocrine Pancreas Secretions
trypsin
chymotrypsin
elastase
carboxypeptidases A & B
Oligopeptides (60%)
Dipeptides
Tripeptides
Na+
Na+
iii) Brush Border surface digestion
endopeptidase
aminopeptidase
Enterocyte

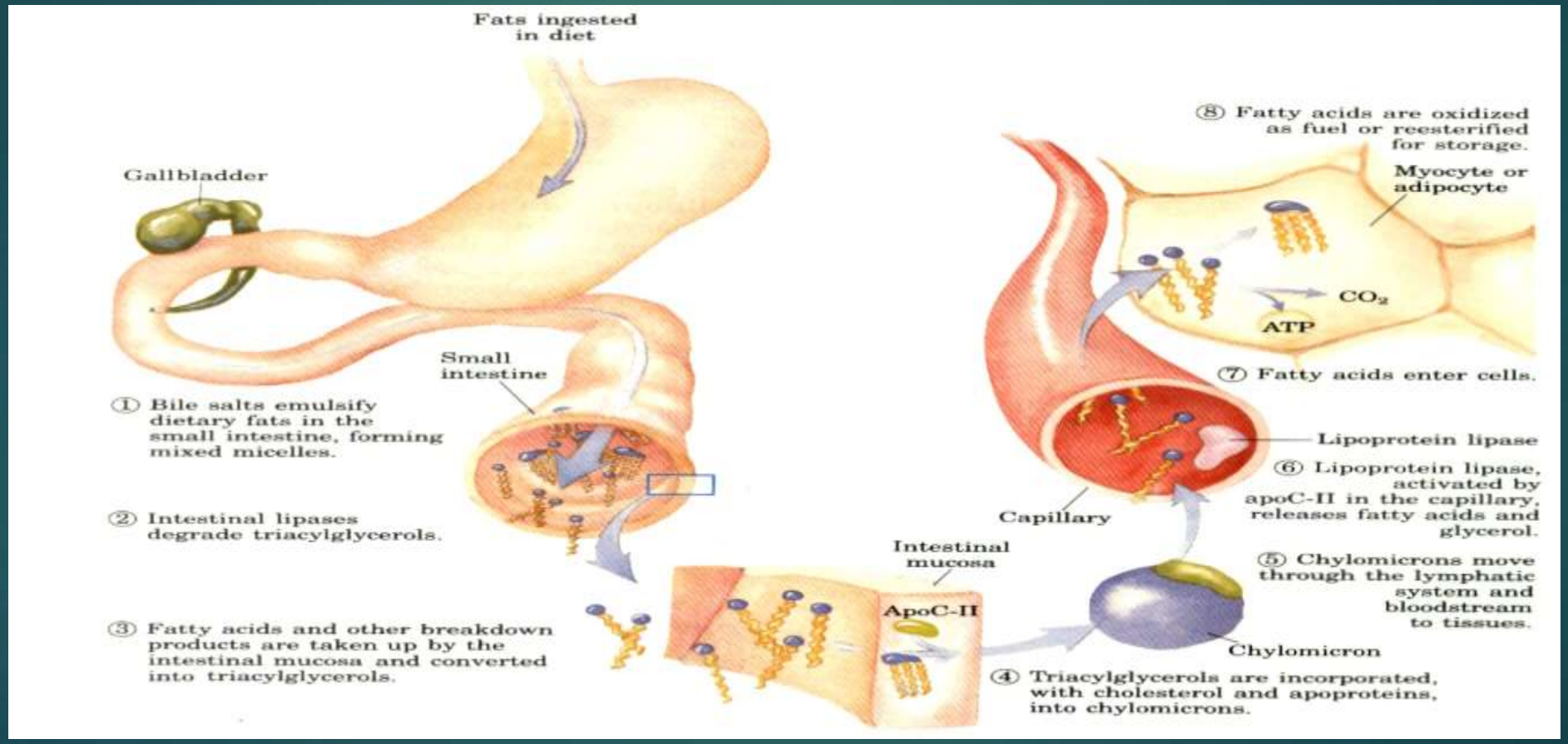
Proteins

- Protein malabsorption leads to failure to thrive, hypoproteinemia, and edema; and can be seen in:
  - Pancreatic insufficiency
  - enterocyte deficiency
  - impaired AA or peptide transport by the enterocyte.
- A fecal elastase test is a good screening test for……..
- Measuring fecal clearance of alpha-1-antitrypsin in…….
- Other features of protein deficiency include
  - recurrent or severe infections
  - muscle atrophy
  - Weakness
  - hair loss
  - irritability

Physiology and Pathophysiology of Digestion and Absorption

LIPIDS

Lipids


Fats ingested in diet
Gallbladder
Small intestine
① Bile salts emulsify dietary fats in the small intestine, forming mixed micelles.
② Intestinal lipases degrade triacylglycerols.
③ Fatty acids and other breakdown products are taken up by the intestinal mucosa and converted into triacylglycerols.
Intestinal mucosa
ApoC-II
④ Triacylglycerols are incorporated, with cholesterol and apoproteins, into chylomicrons.
⑤ Chylomicrons move through the lymphatic system and bloodstream to tissues.
Chylomicron
⑥ Lipoprotein lipase, activated by apoC-II in the capillary, releases fatty acids and glycerol.
Capillary
Lipoprotein lipase
⑦ Fatty acids enter cells.
⑧ Fatty acids are oxidized as fuel or reesterified for storage.
Myocyte or adipocyte
CO_2
ATP

Lipids

Fat maldigestion or malabsorption results in a variety of manifestations due not only to malassimilation but also to

- weight loss and malnutrition
- fat-soluble vitamin (A, D, E, and K) deficiency
- Diarrhea
- Steatorrhea
- Increase risk for oxaluria and calcium oxalate kidney stones.

Fat malabsorption occurs in:

- Pancreatic insufficiency
  - Congenital, such as in cystic fibrosis and Shwachman-Diamond syndrome
  - Acquired, as in chronic pancreatitis.
- In diseases that impair bile production or excretion
- Abetalipoproteinemia……

Physiology and Pathophysiology of Digestion and Absorption

VITAMINS AND MINERALS

Vitamins and Minerals

- malabsorption of fat-soluble vitamins
  - Vitamin A deficiency……
  - Vitamin E deficiency leads to……..
  - Malabsorption of vitamin D leads to ……
  - Malabsorption of vitamin K is associated with ……
- vitamin B12 deficiency.
  - lack of intrinsic factor
  - Ileal resection or inflammation
  - pancreatic insufficiency

if severe, vit B12 deficiency can lead to……..

- Zinc malabsorption……..

Specific Disorders Leading to Malabsorption

PANCREATIC INSUFFICIENCY

Pancreatic Insufficiency

Pancreatic Causes of Malabsorption

- Cystic fibrosis
- Shwachman-Diamond syndrome
- Johanson-Blizzard syndrome
- Pearson syndrome
- Chronic pancreatitis
- Trypsinogen deficiency
- Amylase deficiency
- Lipase deficiency

Specific Disorders Leading to Malabsorption

DEFECTS IN BILE ACID MICELLAR SOLUBILIZATION

Defects in Bile Acid Micellar Solubilization

Moderate steatorrhea can occur in any hepatobiliary disorder leading to bile acid deficiency, which can result from impaired hepatic synthesis or impaired bile flow.

Conditions Leading to Bile Acid Deficiency

- Chronic cholestasis
- Bile acid pool depletion
- Ileal resection
- Bile acid deconjugation by bacteria

Specific Disorders Leading to Malabsorption

INTESTINAL BRUSH BORDER DISORDERS

Intestinal Brush Border Disorders

Brush Border Disorders

- Congenital Causes
- Microvillus inclusion disease
- Tufting disease
- Primary lactase deficiency
- Sucrase-isomaltase deficiency
- Glucose/galactose malabsorption

Reduced Mucosal Surface Area

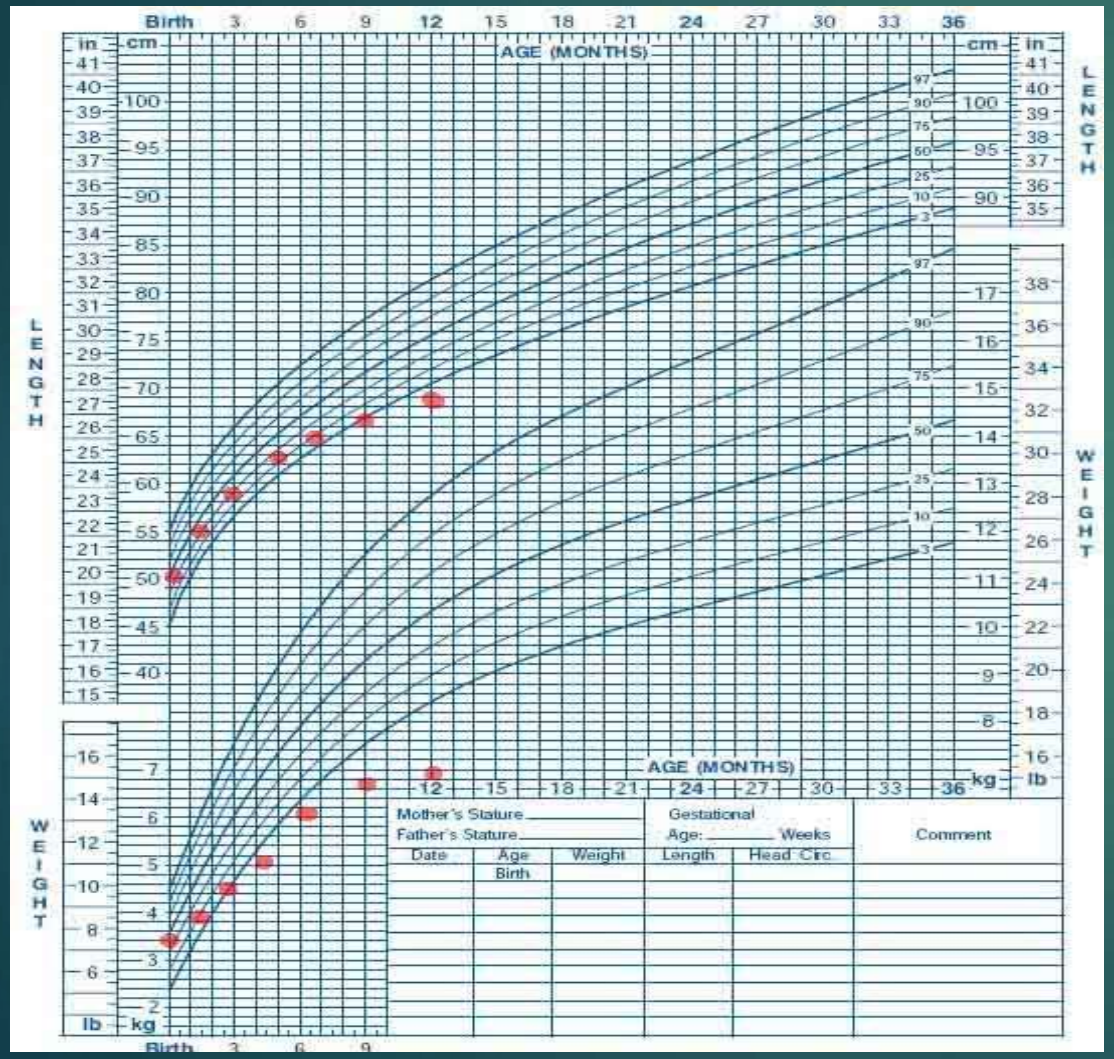
- Short bowel syndrome
- Ileal resection (such as necrotizing enterocolitis or Crohn disease)

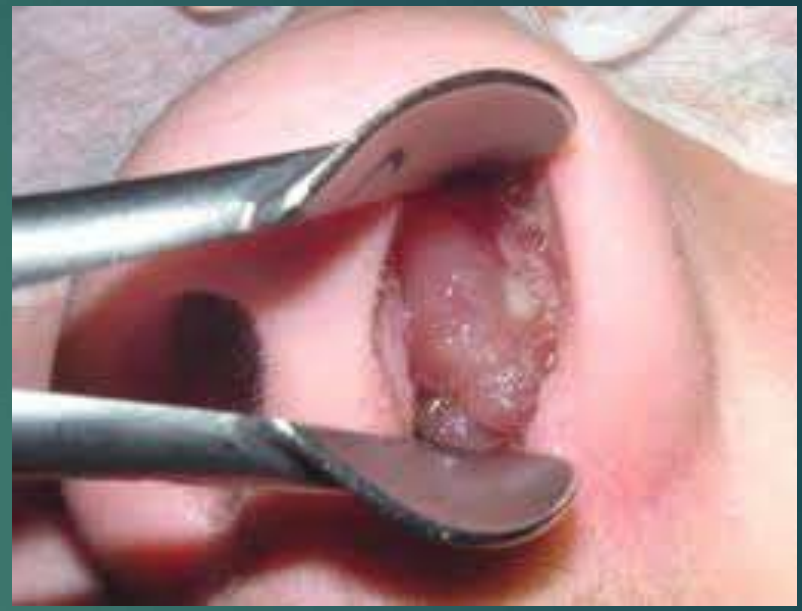
Inflammatory Causes

- Celiac disease
- Crohn disease
- Postinfectious diarrhea
- Allergic enteropathy
- Autoimmune enteropathy

Clinical Cases

1.5 year old presented with





8 months old boy presented with

4 month presented with

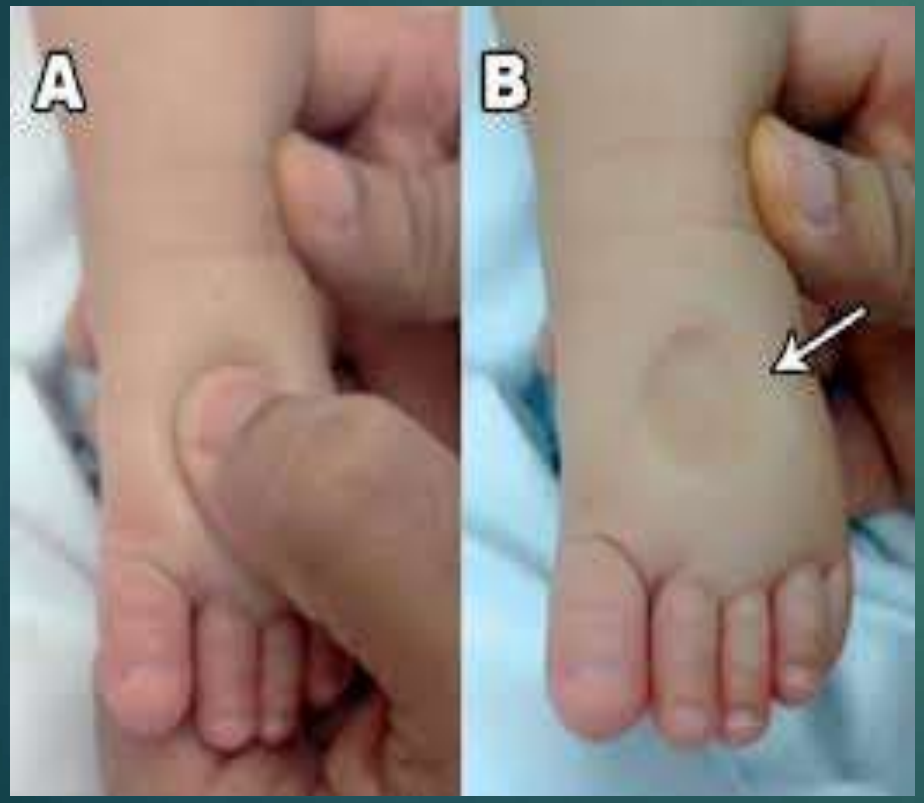
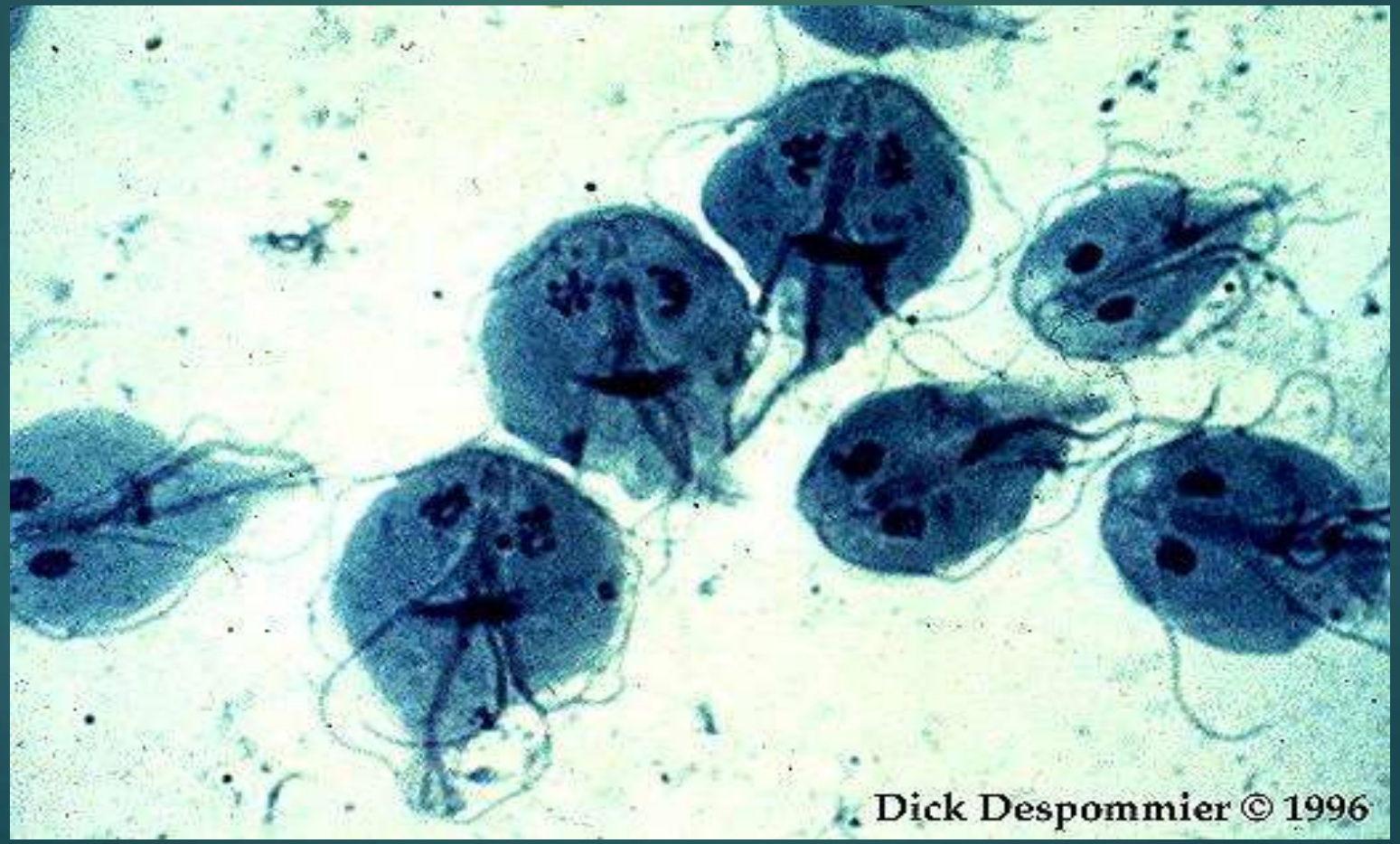


Table 1: Complete blood count (CBC) before treatment

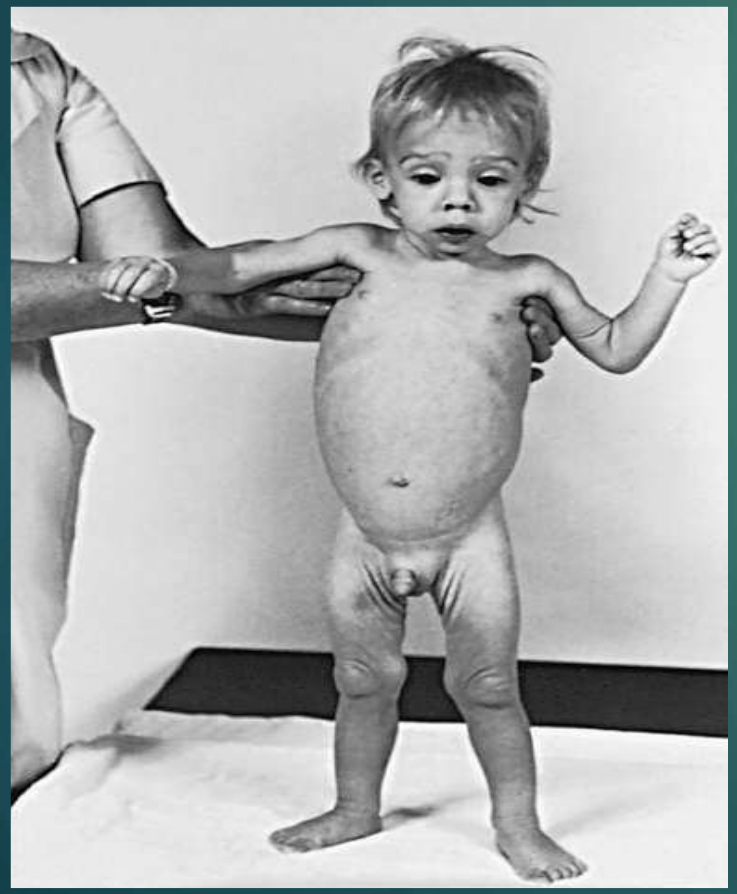
CBC Report

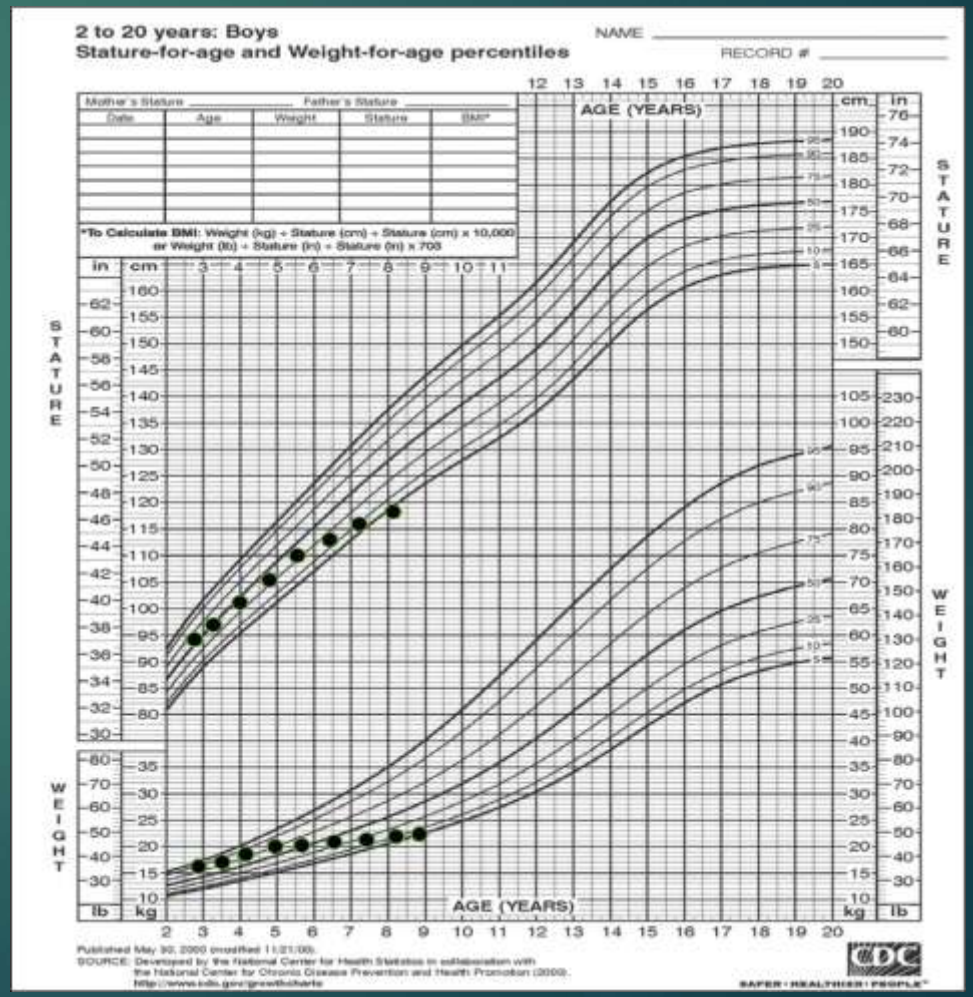
Parameters	Results	Reference values
Red blood cells count (10^{12}/l)	12.2	8–18
Packed cell volume %	29	22–38
Hemoglobin Conc. (g/dl)	12.5	8–12
Mean corpuscular volume (fl)	21.3	16–25
Mean corpuscular hemoglobin (pg)	10.9	5.2–8
Mean corpuscular hemoglobin concentration (g/dl)	39	30–36
White blood cells (10^{9}/l)	10.5	4–13
Neutrophils %	66	30–48
Lymphocytes %	29	50–70
Monocytes %	03	0–4
Eosinophilia %	02	1–8
Basophils %	Nil	0–1

A 4 year old girl presented with diarrhea for 20 days; stool cx showed this parasite that lives in swimming pools



48 months old child with failure to thrive, chronic diarrhea, severe rickets and iron deficiency anemia





Celiac disease

- Celiac disease is an immune-mediated enteropathy caused by permanent sensitivity to gluten in genetically susceptible individuals.
- Its prevalence is estimated to be 1 in 300 to 1 in 80 children.
- Gluten protein is derived from a group of cereal grains that includes wheat, rye, and barley. Pure oats are not considered an offending agent.

Risk groups of CD

- First-degree relatives
- Dermatitis herpetiformis
- Unexplained iron-deficiency anemia
- Autoimmune thyroiditis
- Type 1 diabetes
- Dental enamel hypoplasia
- Autoimmune liver disease
- Short stature
- Delayed puberty
- Down, Williams, and Turner syndromes
- Irritable bowel syndrome
- Sjögren syndrome
- Epilepsy (poorly controlled) with occipital calcifications
- Selective immunoglobulin A deficiency
- Autoimmune endocrinopathies
- Addison disease
- Aphthous stomatitis
- Ataxia
- Alopecia
- Polyneuropathy

Clinical manifestations in C.D

- Gastrointestinal tract (Atrophy of the small bowel mucosa /Malabsorption)
  - Diarrhea
  - Distended abdomen
  - Vomiting
  - Anorexia
  - Weight loss
  - Failure to thrive
  - Rectal prolapse
  - Aphthous stomatitis
  - Intussusception
- Endocrinologic (Malnutrition, Calcium/vitamin D malabsorption)
  - Short stature
  - Pubertas tarda
  - Secondary hyperparathyroidism
- Dermatologic (Autoimmunity)
  - Dermatitis herpetiformis
  - Alopecia areata
  - Erythema nodosum

Clinical manifestations in C.D

- Hematologic (Iron malabsorption)
  - Anemia
- Skeletal (Calcium/vitamin D malabsorption)
  - Rickets
  - Osteoporosis
  - Enamel hypoplasia of the teeth
- Respiratory
  - Idiopathic pulmonary hemosiderosis
- Muscular (Malnutrition)
  - Atrophy
- Neurologic (Thiamine/vitamin B12 deficiency)
  - Peripheral neuropathy
  - Epilepsy
  - Irritability
  - Cerebral calcifications
  - Cerebellar ataxia

Clinical spectrum of CD

- SYMPTOMATIC
  - With symptoms mentioned above.
- SILENT
  - No apparent symptoms in spite of histologic evidence of villous atrophy
    In most cases identified by serologic screening in at-risk groups
- LATENT
  - Subjects who have a normal histology, but at some other time, before or after, have shown a gluten-dependent enteropathy
- POTENTIAL
  - Subjects with positive celiac disease serology but without evidence of altered jejunal histology It might or might not be symptomatic

Diagnosis of CD

- The diagnosis of celiac disease is based on a combination of symptoms, antibodies, HLA, and duodenal histology.
- The initial approach to symptomatic patients is to test for anti-TG2 IgA antibodies and in addition for total IgA in serum to exclude IgA deficiency.
- If IgA anti-TG2 antibodies are negative and serum total IgA is normal for age celiac disease is unlikely to be the cause of the symptoms.
  - Patients with positive anti-TG2 antibody levels <10 × upper limits of normal should undergo upper endoscopy with multiple biopsies.
  - In patients with positive anti-TG2 antibody levels at or >10 × upper limits of normal, blood should be drawn for HLA and EMA testing. If the patient is positive for EMA antibodies and positive for DQ2 or DQ8 HLA testing, the diagnosis of celiac disease is confirmed

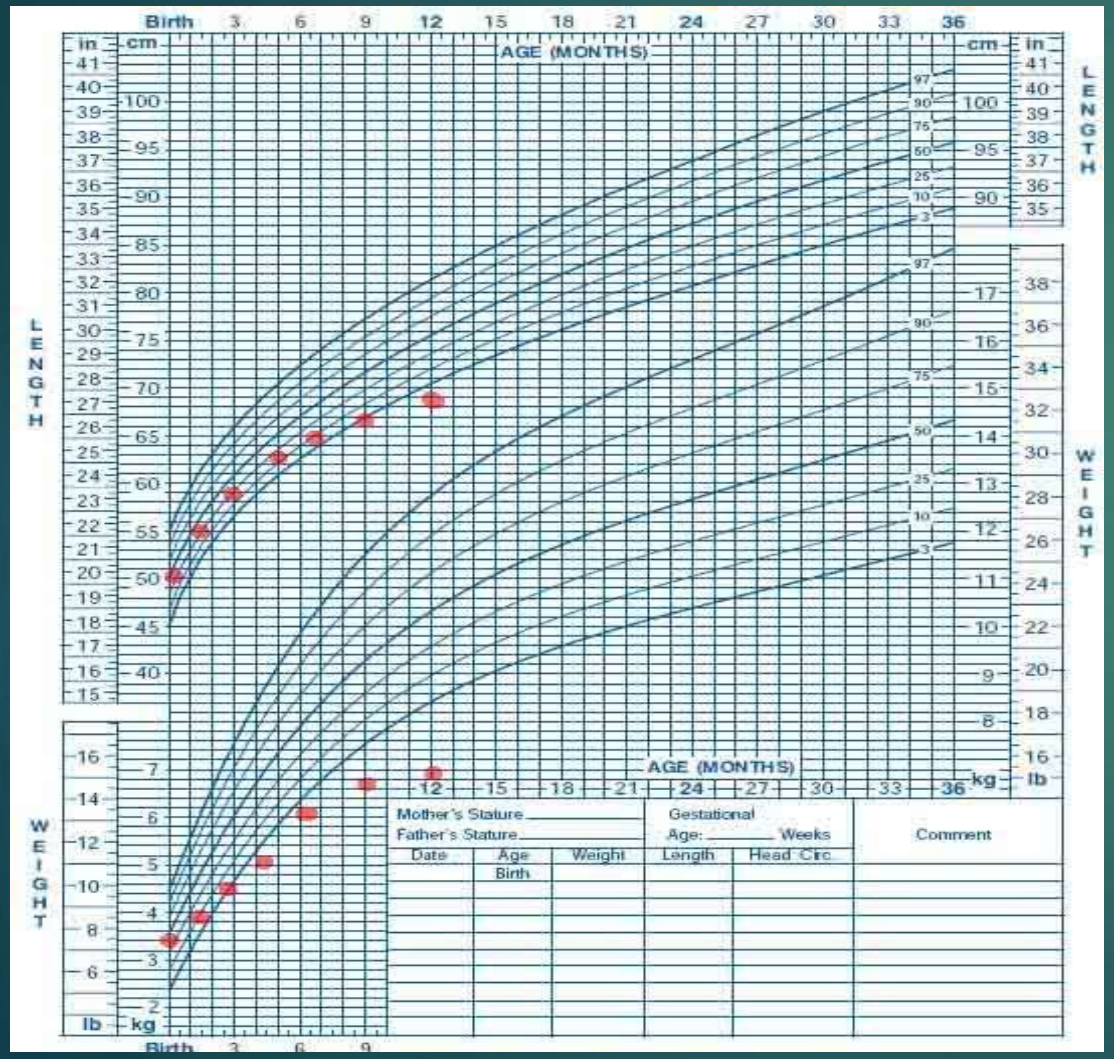
Other causes of flat mucosa

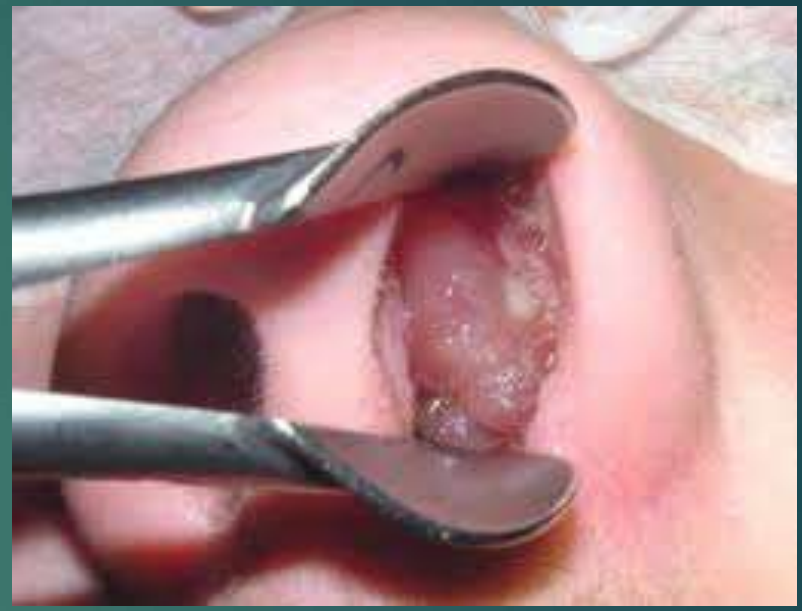
- Autoimmune enteropathy
- Tropical sprue
- Giardiasis
- HIV enteropathy
- Bacterial overgrowth
- Crohn disease
- Eosinophilic gastroenteritis
- Cow's milk enteropathy
- Soy protein enteropathy
- Primary immunodeficiency
- Graft-versus-host disease
- Chemotherapy and radiation
- Protein energy malnutrition
- Tuberculosis
- Lymphoma
- Nongluten food intolerances

Management

- The only treatment for celiac disease is lifelong strict adherence to a gluten-free diet. This requires a wheat-, barley-, and rye-free diet.
- It is recommended that children with celiac disease be monitored with periodic visits for assessment of symptoms, growth, physical examination, and adherence to the gluten-free diet.
- Periodic measurements of TG2 antibody levels to document reductionin antibody titers can be helpful as indirect evidence of adherence to a gluten-free diet

1.5 year old presented with





Cystic Fibrosis CF

- Cystic fibrosis (CF) is a major cause of pancreatic exocrine failure in children.
- Autosomal recessive disorder caused by a mutation in the CFTR gene on chromosome 7.
- Commonest mutation is Delta F508
- Up to 90% of patients with CF have loss of exocrine pancreatic function as well as inadequate digestion and absorption of fats and proteins.

CF

- Even though pulmonary disease is the major cause of morbidity and mortality, most patients (85%) have pancreatic insufficiency
- Clinical signs of pancreatic insufficiency develop when less than 10% of normal pancreatic enzyme activity is present in the duodenum.
- Patients usually present before 6 months of age with
  - failure to thrive.
  - hypoalbuminemia,
  - edema
  - anemia.

Complications of CF

- GASTROINTESTINAL
  - Meconium ileus, meconium plug (neonate)
  - Meconium peritonitis (neonate)
  - Distal intestinal obstruction syndrome (non-neonatal obstruction)
  - Rectal prolapse
  - Intussusception
  - Volvulus
  - Fibrosing colonopathy (strictures)
  - Appendicitis
  - Intestinal atresia
- Pancreatitis
- Biliary cirrhosis (portal hypertension: esophageal varices, hypersplenism)
- Hepatic steatosis
- Gastroesophageal reflux
- Cholelithiasis
- Inguinal hernia
- Growth failure (malabsorption)
- Vitamin deficiency states (vitamins A, K, E, D)
- Insulin deficiency, symptomatic hyperglycemia, diabetes
- Malignancy (rare)

Complications of CF

- RESPIRATORY
  - Bronchiectasis, bronchitis, bronchiolitis, pneumonia
  - Atelectasis
  - Hemoptysis
  - Pneumothorax
  - Nasal polyps
  - Sinusitis
  - Reactive airway disease
  - Cor pulmonale
  - Respiratory failure
  - Mucoid impaction of the bronchi
  - Allergic bronchopulmonary aspergillosis
- OTHER
  - Infertility
  - Hypochloremic hypokalemic metabolic alkalosis
  - Delayed puberty
  - Edema-hypoproteinemia
  - Dehydration–heat exhaustion
  - Hypertrophic osteoarthropathy-arthritis
  - Clubbing
  - Amyloidosis
  - Diabetes mellitus
  - Aquagenic palmoplantar keratoderma (skin wrinkling)

Diagnosis of CF

- Presence of typical clinical features (respiratory, gastrointestinal, or genitourinary)

or

- A history of CF in a sibling

or

- A positive newborn screening test

plus

- Laboratory evidence for CFTR dysfunction:
  - Two elevated sweat chloride concentrations obtained on separate days

or

  - Identification of two CF mutations

or

  - An abnormal nasal potential difference measurement

Maagement

- High caloric diet
- Pancratic enzymes replacement (Creon)
- Daily supplements of the fat-soluble vitamins.

Pancreatic Insufficiency

Shwachman-Diamond syndrome

- autosomal recessive disorder
- exocrine pancreatic failure due to fatty deposition
- skeletal abnormalities, and
- bone marrow dysfunction, primarily cyclic neutropenia.

Johanson-Blizzard syndrome is characterized by

- hypoplasia of the alae nasi
- deafness,
- imperforate anus or urogenital malformations
- dental anomalies.
- exocrine pancreatic failure due to fatty deposition

Pearson syndrome,

- deletions in mitochondrial DNA. Patients have
- pancreatic insufficiency and
- refractory sideroblastic anemia.

8 months old boy presented with

Cow's protein milk allergy

- The prevalence of CMA in children living in the developed world is approximately 2 to 3 %, making it the most common cause of food allergy in the pediatric population.
- There is some cross-reactivity with soy protein, particularly in non-IgE mediated allergy.
- CMA is mostly a disease of infancy and early childhood. Affected infants present usually within the first 6 months of life, and one review reported that the majority of infants develop symptoms before 1month of age, often within 1 week after the introduction of cow's milk proteins to their diet.

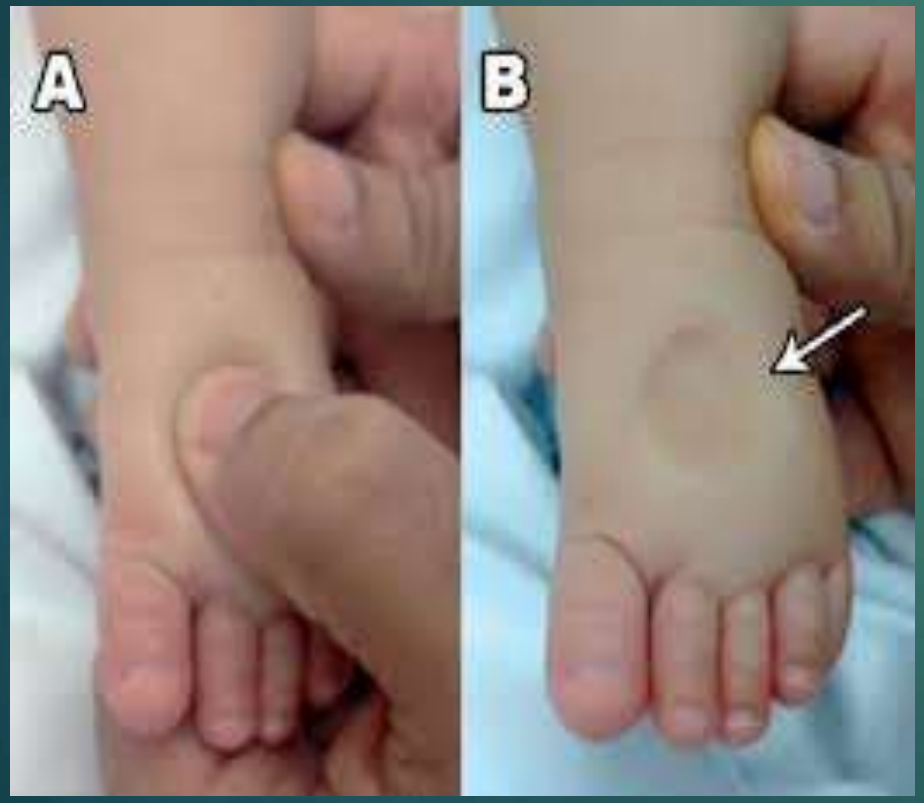
Cow's protein milk allergy

- However, breastfed infants can also be affected by dairy products ingested by the mother and eliminated in her breast milk.
- The majority of affected children have one or more symptoms involving one or more organ systems, mainly the gastrointestinal tract and/or skin
- In addition to the detailed medical history and physical examination, diagnostic elimination diets, skin prick tests (SPTs), specific IgE (sIgE) measurements, and oral food challenges are part of the routine work-up

Cow's protein milk allergy

- Avoidance of cow's milk protein in any form is the only available treatment.
- In the case of breastfed infants,
- Calcium supplements should be added to the mother's diet to replace milk intake .
- For infants 6 months old or younger, the recommended formulas for treatment of CMA are extensively hydrolyzed protein or amino acid-based formula

4 month presented with



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Protein loosing enteropathy

- Protein-losing enteropathy (PLE) is a rare condition characterized by protein loss through the gastrointestinal tract, leading to reduced serum protein levels, mainly albumin.
- Main laboratory findings are reduced serum concentration of albumin, gammaglobulins, and ceruloplasmin. Diminished oncotic pressure due to hypoalbuminemia may lead not only to edema, but also to ascites and pleural or pericardial effusions. PLE can also be associated with fat malabsorption and deficiencies of fat-soluble vitamins due to small bowel involvement

TABLE.

Causes of protein-losing enteropathy in children

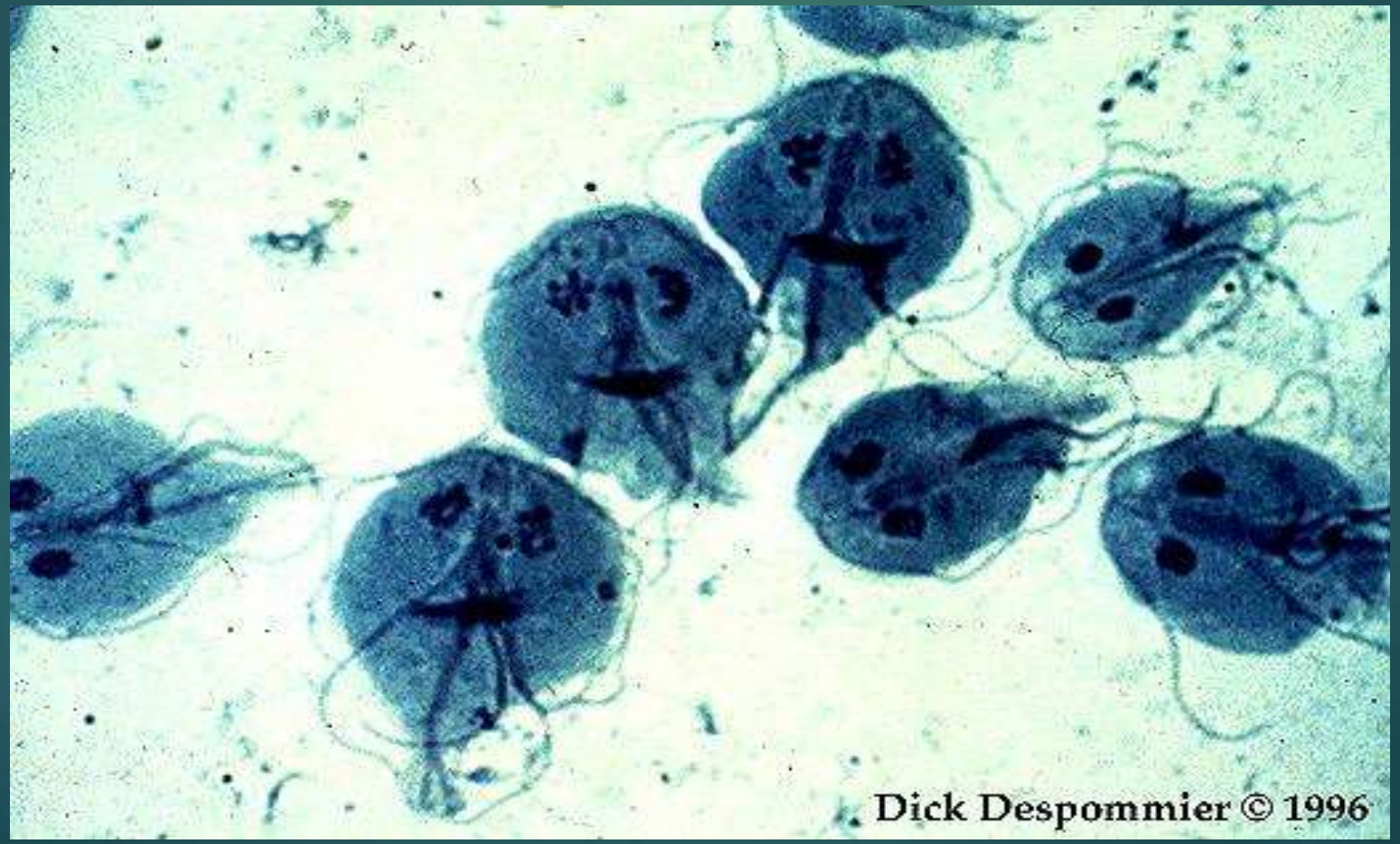
Infectious	CMV, *Helicobacter pylori*, *Clostridium difficile*, *Giardia lamblia*, measles, bacterial overgrowth
Noninfectious	Inflammatory bowel disease, celiac disease, Ménétrier's disease, allergic gastroenteropathy, eosinophilic gastroenteritis, Henoch-Schonlein purpura, system lupus erythematosus
Metabolic	Congenital enterocyte heparin sulphate deficiency, congenital disorders of glycosylation
Lymphatic obstruction	Thoracic duct damage, intestinal lymphangiectasia
Cardiac	Heart failure, pericarditis, post-Fontan procedure
Others	Post-chemotherapy, graft-versus-host disease

Source: Mohanty PH, Karjoo M, Beg M. Reprinted with permission.

Intestinal lymphangiectasia

- Intestinal lymphangiectasia is an uncommon disorder andan important cause of protein-losing enteropathy.
- The major symptoms were edema and hypoproteinemia, low serum albumin and gammaglobulin levels.
- Biopsies of the small intestine showed variable degrees of dilatation of lymph vessels in the mucosa and submucosa
- Treatment of PIL consists of lifelong dietary modification with high protein and low fat substituted with MCT

A 4 year old girl presented with diarrhea for 20 days; stool cx showed this parasite that lives in swimming pools



Giardia lamblia

- Giardia lamblia is a flagellated protozoan that is a major cause of diarrhea, especially in patients who travel to endemic areas.
- The life cycle consists of 2 stages: the trophozoite (motile form), and the cyst.
- IgA deficiency and hypogammaglobulinemia predispose patients to symptomatic infection.
- The clinical manifestations are foul-smelling diarrhea, with nausea, anorexia, abdominal cramps, bloating, belching, flatulence, and weight loss. Abdominal distention and cramps can last for weeks to months.
- The illness is usually self-limited, lasting 2 to 6 weeks, but may become chronic.

Giardia lamblia

- Chronic symptoms can include fatigue, nervousness, weight loss, steatorrhea, lactose intolerance, and growth retardation.
- The easiest way to diagnose Giardia is by identifying cysts in a stool specimen. However, these specimens are frequently falsely negative. The diagnosis can also be made by antigen detection tests, endoscopic examination of the upper small intestine, by mucosal biopsy or by collection of jejunal contents.
- The treatment of choice for both symptomatic and asymptomatic patients is furazolidone or metronidazole. An alternative drug is quinacrine

Glucose-Galactose malabsorption

- Autosomal recessive
- Neonatal presentation
- Diarrhea persistes on breast feeding as well as on lactose free infant formula, he was admitted so far 3 times with
- Hyper-natremic dehydration is often present
- Glucose/galactose free diet, fructose is well absorped (fructose based formula)
- Intestinal adaptation to glucose and galactose with age