

# Malabsorption syndromes in children

Oxana TURCU  
PhD, Associate Professor  
Department of Pediatrics

- Malabsorption syndromes include a number of different clinical manifestations that result in chronic diarrhea, abdominal distention, and failure to thrive.
- Malabsorption syndromes are caused by a disorder in the intestinal processes:
  - digestion
  - transport
  - or both of these nutrients across the intestinal mucosa into the systemic circulation
- The major site of absorption is the small intestine
- Causes of malabsorption
  - congenital
  - acquired

## Pathophysiology

- Carbohydrate, fat, or protein malabsorption is caused by a disorder in the intestinal processes of digestion, transport, or both of these nutrients across the intestinal mucosa into the systemic circulation.
- A congenital abnormality in the digestive or absorptive processes or, more commonly, a secondarily acquired disorder of such processes may result in malabsorption.

## Digestion and absorption

- **Luminal phase:** dietary fats, proteins and carbohydrates – solubilized by digestive enzymes and bile
  - Deficiency in lipase and proteases leads to lipid and protein malabsorption
- **Mucosal phase:** brush-border hydrolase activity
  - Primary or secondary lactase deficiency
- **Postabsorptive phase:** hydrolyzed nutrients are transported via lymphatic and portal circulation
  - Impairs of chylomicrons and lipoproteins may cause fat malabsorption or protein-losing enteropathy

## Absorption of carbohydrates

- Of the carbohydrates most commonly present in the diet (starches, sucrose, lactose), only **starches require preliminary luminal digestion by salivary and, more importantly, pancreatic amylases.**
- Despite the slow development of pancreatic amylase, whose secretion reaches adult levels only at 1 year of life, **cooked starch malabsorption is rare in infants** because of the activity of the **brush-border glucoamylase** that develops early in life.
- The **final hydrolysis of disaccharides and oligosaccharides** occurs at the brush border of the enterocytes, where sucrase-isomaltase breaks down maltose, isomaltose (to glucose), and sucrose (to glucose and fructose)
- The entry of the final **monosaccharides (glucose, galactose, fructose)** into the enterocytes through the brush border occurs via **carrier molecules**

## Malabsorption of carbohydrate

Disorders of these processes of carbohydrate absorption

- **congenital**
  - cystic fibrosis
  - Shwachman-Diamond syndrome
  - congenital lactase deficiency (extremely rare)
  - glucose-galactose malabsorption
  - sucrase-isomaltase deficiency

- adult-type hypolactasia
- **acquired**
  - lactose intolerance, typically secondary to a damage of the mucosa, such as a viral enteritis or conditions that cause mucosal atrophy, such as celiac disease

#### **Absorption of proteins**

- Proteins are **first digested in the stomach**, where pepsinogen is activated to pepsins by a pH of less than 4, hydrolyze them in large molecular weight peptides.
- Upon entering the duodenum, the **pancreatic proteases** (activated by trypsin,) split large peptides into low molecular weight peptides (2-6 amino acid residues) for 70% and of free amino acids for 30%
- Free amino acids are taken up by enterocytes through **specific Na-linked carrier systems**

#### **Disorders of protein digestion**

- ***Congenital disorders*** of protein digestion (cystic fibrosis, Shwachman-Diamond syndrome, and enterokinase deficiency) cause inadequate intraluminal digestion.
  - No congenital defects have been described in any of the brush border-bound peptidases or in the peptide carrier.
- ***Acquired disorders*** of protein digestion and/or absorption are nonspecific (they also affect the absorption of carbohydrates and lipids)
  - damage of absorptive intestinal surface, such as extensive viral enteritis, milk protein allergy enteropathy, and celiac disease.

#### **Absorption of fat**

- A **lingual lipase** is responsible for the **first partial hydrolysis of triglycerides**; this enzyme becomes active in persons with low gastric pH levels and is active even in premature infants.
- The largest part of triglyceride digestion is accomplished in the duodeno-jejunal lumen because of a complex of pancreatic enzymes – **lipase-colipase complex**.
  - Like amylase, these enzymes also develop slowly, and this low capacity of babies to absorb lipids, termed physiological steatorrhea of the newborn.
- Additionally, adequate concentrations of intraluminal conjugated bile salts are needed to form micelles, and the secretion of bile acids may also be partially inadequate in very young patients.

#### **Malabsorption of fats**

##### **Disorders of lipids absorption**

- ***congenital*** (cystic fibrosis and Shwachman-Diamond syndrome), which cause lipase and colipase deficiency;
  - The extremely rare congenital primary bile acid malabsorption, which results in low bile acids concentrations)
- ***acquired***
  - Secondary to disorders of the liver and the biliary tract or to chronic pancreatitis.
  - Any condition that results in the loss of small intestinal absorptive surface also causes steatorrhea

#### **Epidemiology**

##### **Genetically determined syndromes**

- **Celiac disease** is considered the most common inherited malabsorption syndrome because the documented prevalence is close to 1%.
- **Cystic fibrosis** is the second most common malabsorption syndrome.
- Other congenital disorders are rare, with the exception of adult-type hypolactasia, which has a prevalence that varies greatly among different ethnic groups.

##### **Acquired syndromes**

- Among acquired conditions, **cow's (and soy) milk protein allergic enteropathy** is very common.
- The prevalence of milk protein allergy, of which enteropathy is one of the presenting clinical symptoms, is estimated to be around 3%.

- A transient and common form of malabsorption in infants results from acute-onset enteritis (mostly viral, specifically rotaviral), which causes transient lactose intolerance

### **GI tract symptoms**

- Abdominal distention and watery diarrhea, with or without mild abdominal pain, associated with skin irritation in the perianal area due to acidic stools *are characteristic of carbohydrate malabsorption syndromes*.
- Periodic nausea, abdominal distention and pain, and diarrhea are common in patients with chronic *Giardia infections*.
- Vomiting, with moderate-to-severe abdominal pain and bloody stools, is characteristic of *protein sensitivity syndromes* or other causes of intestinal injury (eg, *inflammatory bowel disease*).
- Poor appetite is common in *food sensitivity syndromes*. The child becomes conditioned to refuse foods that cause inflammatory reactions of the intestine (this is typical in *celiac disease*).
- Malabsorption syndromes not associated with inflammatory reactions typically cause an increase in appetite (eg, *cystic fibrosis*)

### **Physical examination**

#### **Clinical signs of malnutrition**

- failure to thrive, malnutrition
- poor weight gain
- delayed puberty
- reduced muscle and fat mass
- atrophic tongue changes
- enlarged liver or spleen
- eczematous rash (protein sensitivity)

### **Celiac disease**

- Immune-mediated enteropathy caused by a **permanent** sensitivity to gluten in genetically susceptible individuals:
  - DQ2 and/or DQ8 positive HLA haplotype is necessary but not sufficient
- Occurs in symptomatic subjects with gastrointestinal and non-gastrointestinal symptoms, and in some asymptomatic individuals, including those affected by:
  - Type 1 diabetes
  - Down syndrome
  - Selective IgA deficiency
  - Williams syndrome
  - Turner syndrome
  - First degree relatives of individuals with celiac disease

### **Classification**

- Gastrointestinal (*“classical”*)
- Non-gastrointestinal (*“atypical”*)
- Asymptomatic
- may be associated with other conditions including:
  - Autoimmune disorders
  - Genetic syndromes

### **Gastrointestinal Manifestations (“Classic”)**

Most common age of presentation: 6-24 months

- Chronic or recurrent diarrhea
- Abdominal distension
- Anorexia
- Failure to thrive or weight loss
- Abdominal pain

- Vomiting
- Constipation
- Irritability

### **Non Gastrointestinal Manifestations**

Most common age of presentation: older child to adult

- Dermatitis Herpetiformis
  - Erythematous macule > urticarial papule > tense vesicles
  - Severe pruritus
  - Symmetric distribution
- Dental enamel hypoplasia of permanent teeth
- Osteopenia/Osteoporosis, Dental Enamel Defects
- Short Stature
- Delayed Puberty
- Iron-deficient anemia resistant to oral Fe
- Hepatitis
- Arthritis
- Epilepsy with occipital calcifications

### **Asymptomatic**

- Silent: no or minimal symptoms, “damaged” mucosa and positive serology
  - Identified by screening asymptomatic individuals from groups at risk such:
    - ✓ First degree relatives
    - ✓ Down syndrome patients
    - ✓ Type 1 diabetes patients, etc.
- Latent: no symptoms, normal mucosa
  - May show positive serology
  - Identified by following in time asymptomatic individuals previously identified at screening from risk groups
  - These individuals, given the “right” circumstances, will develop at some point in time mucosal changes ( $\pm$  symptoms)

### **Diagnosis**

- Antigliadin antibodies
- Endomysial antibodies
- Tissue transglutaminase antibodies
- Endoscopic Findings + Histological Features

### **Treatment**

- Only treatment for celiac disease is a gluten-free diet (GFD)
  - Strict, lifelong diet
  - Avoid:
    - ✓ Wheat
    - ✓ Rye
    - ✓ Barley

### **Potential Nutritional Complications in Untreated Celiac Disease**

- Low Iron
- Low Folate
- Low Vitamin B-12
- Low Vitamins ADEK
- Low Thiamine
- Low Niacin
- Low B6 (rare)
- Low Beta-carotene
- Low Zinc
- Essential Fatty Acid Deficiency

## Cystic fibrosis

- Cystic fibrosis – a multisystem disease, autosomal recessive inheritance
- Most common lethal genetic disease in Caucasians
- Cause: mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) – chromosome 7
  - Over 1900 genotypes identified, most common F508del
- Abnormality in CFTR blocks chloride transport, inadequate hydration results in thick secretion of exocrine glands and organ affection

### Chronic Sino-Pulmonary Disease

- Chronic infection with CF pathogens (*Ps.aeruginosa*)
- Bronchial disease
  - Cough/sputum production
  - Air obstruction – wheezing; evidence of obstruction on PFTs
  - Chest x-ray anomalies
  - Digital Clubbing
- Sinus disease
  - Nasal Polyps
  - CT or x-ray findings of sinus disease

### Nutritional deficiency

- Pancreatic insufficiency
  - Pancreatic enzymes stay in ducts and are activated intraductally
    - ✓ Autolysis of pancreas
    - ✓ Inflammation, calcification, plugging of ducts, fibrosis
  - Malabsorption
    - ✓ Failure to thrive
    - ✓ Fat soluble vitamin deficiency

### GI disease

- Intestinal abnormality
  - Meconium ileus (15% newborns with CF)
  - Distal intestinal obstruction syndrome (DIOS)
  - Rectal prolapse
- Hypoproteic edema
- Pancreatic endocrine dysfunction
  - Cystic fibrosis related diabetes (children older than 10 years)

### Cystic fibrosis related liver disease

- Focal inspissation of bile
  - obstructs biliary ducts
- Prevalence 9-37%
- Second leading cause of death in CF

### Clinical diagnosis

- Symptoms may include
  - Meconium ileus
  - Salty-tasting skin
  - Steatorrhea (greasy, bulky and foul smelling)
  - Poor growth/weight gain in spite of good appetite
  - Chronic coughing, at times with phlegm
  - Frequent lung infections

### Diagnosis

#### Sweat chloride test

- Positive Sweat chloride: > 60 mmol/L
- Borderline sweat chloride: 40-60 mmol/L

- Normal sweat chloride: 0-40 mmol/L

### **Genetic testing**

- Varies from screening for most common mutations to sequencing entire CFTR gene

### **Newborn Screening for CF**

- Goal: diagnose early – evidence that early diagnosis may be associated with better nutritional outcome and chest radiographic scores
- Several different protocols

### **Cystic fibrosis care**

#### **Multidisciplinary**

- Airway Clearance
- Infection control
- Nutrition
- Gastrointestinal
- Inflammation
- Infertility
- Social Issues

#### **Treatment**

- Treatment and control of chronic lung infection
- Nutrition correction
  - Follow growth parameters closely
  - Pancreatic enzymes
  - Vitamin supplementation
  - Other nutritional supplementation
  - Tube feedings
  - High calorie supplemental shakes, formulas

## **Lactose intolerance**

- Lactose intolerance is most common of all the syndromes of carbohydrate malabsorption
- Types of Lactose intolerance
  - Congenital – very rare
  - Primary – develops after 2 years of age
  - Secondary – usually resolves in 1-2 weeks
  - Developmental lactase deficiency
- **Lactose intolerance** is a clinical syndrome of 1 or more of the following: abdominal pain, diarrhea, nausea, flatulence, and/or bloating after the ingestion of lactose or lactose-containing food substances.
  - The amount of lactose that will cause symptoms varies from individual to individual, depending on the amount of lactose consumed, the degree of lactase deficiency, and the form of food substance in which the lactose is ingested.
- **Lactose malabsorption** is the physiologic problem that manifests as lactose intolerance and is attributable to an imbalance between the amount of ingested lactose and the capacity for lactase to hydrolyze the disaccharide.

#### **Clinical presentation**

- Symptoms of lactose intolerance, are independent of the cause of lactose malabsorption and are directly related to the quantity of ingested lactose
  - abdominal distention, flatulence
  - abdominal cramping
  - diarrhea
- These symptoms are not necessarily correlated with the degree of intestinal lactase deficiency.

- Malabsorbed lactose generates an osmotic load that draws fluid and electrolytes into the intestinal lumen, leading to loose stool.
  - The onset of diarrhea and other symptoms is related to the amount of lactose that is not absorbed.

#### **Diagnosis of lactose intolerance**

- A good clinical history often reveals a relationship between lactose ingestion and symptoms.
- When lactose intolerance is suspected, a lactose-free diet can be tried
  - During a diagnostic lactose-free diet, it is important that all sources of lactose be eliminated, requiring the reading of food labels to identify “hidden” sources of lactose.
  - Generally, a 2-week trial of a strict lactose-free diet with resolution of symptoms and subsequent reintroduction of dairy foods with recurrence of symptoms can be diagnostic.
- In more-subtle cases, the hydrogen breath test is the least invasive and most helpful test to diagnose lactose malabsorption.

#### **Treatment of lactase deficiency**

- Lactose-free and lactose-reduced milks (and lactose-free whole milk for children younger than 2 years): Lacto-free, NAN lactose-free.
- In older children elimination of milk and other dairy products is not usually necessary given newer approaches to lactose intolerance, including the use of partially digested products (such as yogurts, cheeses, products containing *Lactobacillus acidophilus*).
- Evidence that avoidance of dairy products may lead to inadequate calcium intake and consequent suboptimal bone mineralization makes these important as alternatives to milk.
- Mineral (calcium, iron, zinc) and vitamin (A,B E,D) supplementation
- Dairy products remain principle sources of protein and other nutrients that are essential for growth in children.
- Lactase enzymes medication may used.