UNIT 4
INVESTIGATION OF ESOPHAGUS, STOMACH, INTESTINE AND PANCREATIC DISORDERS

LEARNING OBJECTIVES

At the end of this chapter, students are expected to:
1. Ask for investigations needed to diagnose the main disorders of esophagus, stomach, and duodenum
2. Ask for tests of diagnosis and monitoring of Helicobacter pylori infection
3. Ask for tests useful in malabsorption syndromes
4. Ask for the investigations used for the early detection in colorectal cancer
5. Ask for enzymatic and secretory tests in diagnosing pancreatic disorders

I. INVESTIGATION OF ESOPHAGUS DISORDERS

Indications:
Patients that manifest:
- heartburn (acid reflux)
- non cardiac chest pain
- sore throat (pain during swallowing)
- dysphagia (difficult swallowing)
The main investigations for the diagnosis of esophagus disorders are:
1. Esophagoscopy
2. Barium swallow
3. Special tests: esophageal pH determination, manometry

1. Esophagoscopy

- Clinical value:
  - direct examination of esophageal lesions encountered in:
    - reflux esophagitis (brittle mucosa, with erosions and ulcerations)
    - benign (scar-like) or malignant (carcinoma) esophageal strictures
    - esophageal varices
    - achalasia
  - obtaining biopsy samples in order to diagnose Barrett’s esophagus and esophageal cancer

2. Barium swallowing

- Clinical value:
  - examination of the esophageal and mediastinal lining
  - evaluation of esophageal motility in disorders like:
    - achalasia
    - esophageal spasms
    - esophageal strictures
    - diagnosis of hiatal hernia if the examination is performed in Trendelenburg position

3. SPECIFIC examinations

a) ESOPHAGEAL pH measurement

- Principle: esophageal pH monitoring (5 cm above the inferior esophageal sphincter) during a 24 hour period of time, using a portable monitoring device
- Clinical value:
  - gold standard for the diagnosis of acid reflux:
    - a pH value less than 4, indicates the presence of acid reflux
    - a pH value above 8 indicates bile reflux

b) ESOPHAGEAL manometry

- Principle: measurement of the movement, coordination, and strength of esophageal peristalsis as well as the function of esophageal
- Normal values:
  - the normal values between meals variate between +2 and –2 cmH₂O.
  - during swallowing: between +40 și +80 cmH₂O
Clinical value:
- diagnosis of esophageal motility disorders
- gold standard for the diagnosis of achalasia:
  - hypertony of the inferior esophageal sphincter between meals
  - absence of peristaltic movement in the inferior esophagus
  - incomplete relaxation of the inferior esophageal sphincter during swallowing

II. INVESTIGATION OF STOMACH AND DUODENUM DISORDERS

Indications:
Patients that manifest:
- organic or functional dyspepsia (epigastric pain/heartburn, nausea, vomiting, fullness sensation, abdominal swelling or discomfort)
- upper gastrointestinal bleeding
- weight loss

The main investigations for the diagnosis of stomach and duodenum disorders are:
1. Gastroscopy
2. Barium meal
3. Identification of Helicobacter pylori infection
4. Identification of occult bleeding – in cases with possible upper gastrointestinal bleeding

1. Gastroscopy:

Clinical value:
- high sensibility and specificity in comparison to barium meal
- it also allows gastric biopsies during the examination

Indications (diagnosis and evaluation of):
- acute and chronic gastritis
- gastro-duodenal ulcers (where biopsies are mandatory in order to exclude a malignant gastric ulcer)
- upper gastrointestinal bleeding
- anemia with unknown origin
- post-gastrectomy syndrome (10 years after the surgery)
- pernicious anemia or Biermer’s anemia (every 6-12 months)

2. Barium meal

Indications (diagnostical):
- giant hypertrophic gastritis (Menetrier gastritis)
- peptic ulcers: direct modifications (ulcer craters) or indirect modifications (convergent mucosa folds or increased evacuation from the duodenal bulb)
- gastric cancer: infiltrating lesions, heterogenous malignant craters, malignant tumor formation
- hypertrophic pyloric stenosis: hypertonic dilation with increased gastric fluid and delayed gastric emptying

3. Diagnosis of Helicobacter pylori infection

Helicobacter pylori (HP) infection is the main cause for peptic ulcers, therefore the diagnosis of such an infection, thru direct or indirect methods is mandatory.

a) DIRECT methods (invasive) – an endoscopy together with gastric biopsies are necessary, in order to identify H. pylori infection:
- histology techniques (special stainings)
- rapid urease test (a pH indicator that modifies its colour in the presence of H. pylori that produces a high amount of urease)
- culture techniques

b) INDIRECT methods (non-invasive):

Serum H. pylori antibody measurement
- IS NOT VERY ACCURATE for the diagnosis because:
  - a positive result indicates either a current infection or an old infection
  - patients with early stage acute infection may present with undetectable levels of HP antibodies
  - THERE IS NO relation between antibody serum levels and the severity of HP infection
- the test cannot be used in order to verify treatment efficiency, because HP antibodies remain in the blood stream almost 3 years after the infection.

Fecal HP antigen measurement
- 90% accurate for the diagnosis and monitoring of treatment efficiency (it confirms the eradication of HP or its persistance after treatment)
- undetectable levels DO NOT exclude an active HP infection
**UREA breath test**
- a radioactive isotope (C\textsuperscript{14}) is used to mark an urea sample, which will be swollen by the patient
- by urease production, HP can generate carbon dioxide which contains the C\textsuperscript{14} isotope, absorbs and will then be measured in the breath of the patient
- **gold standard** for the diagnosis of HP infection

III. INVESTIGATION OF SMALL BOWEL DISORDERS

- **Indications:**
  In patients which manifest:
  - **acute or chronic diarrhea**
  - **malabsorption syndromes:** dyspepsia (abdominal swelling, belching, flatulence), abdominal cramps, chronic diarrhea and/or steatorrhea, appetite modifications, weight loss
  - **various deficiencies:** iron, B12 and folic acid, vitamins A,D,K, hydric and mineral (calcium, magnesium, potassium), weight loss (moderate to cachexia)

The MAIN CAUSES for malabsorption are:

- **DIGESTIVE disorders:**
  1. Alterations of intraluminal digestion:
     - pancreatic failure
  2. Alterations of intestinal absorption:
     - disorders of the intestinal mucosa (hereditary lactose intolerance, celiac disease)
- **METABOLIC and ENDOCRINE disorders:**
  - diabetes mellitus
  - hyperthyroidism
  - adrenal failure

Investigation of small bowel disorders and malabsorption syndromes can be realised thru:

A. **Static measurements:**
- evaluate nutritional modifications due to malabsorption and consist of:
  - Blood tests
  - Bone X-rays (osteoporosis, osteomalacia)
- allow the diagnosis of malabsorption syndromes:
  - Stool examination
  - Increased levels of inflammatory markers (VSH, leucocytosis, CRP) – *inflammatory bowel disorders*
  - Serum autoantibodies to gliadin and transglutaminase – for celiac disease diagnosis

B. **Dynamic measurements** – specific tests that differentiate the types of malabsorption syndromes, most frequently for carbohydrates (lactose tolerance test, D-xilose test), lipids (respiratory test with radioactive trioleine or oleic acid)

C. **Tests that evaluate intestinal bacterial proliferation**

D. **Barium meal** – in order to explore bowel motility

E. **Computed virtual endoscopy** is used to:
  - evaluate patients with small bowel disorders evaluarea pacienților cu boli ale intestinului subțire
  - diagnose gastro-intestinal bleeding of unknown origins

F. **Intestinal mucosa biopsy:**
  - is obtained thru upper GI tract endoscopy
  - is mandatory in order to certify the diagnosis and causes for a malabsorption syndrome

A. **STATIC MEASUREMENTS**

1. Blood tests
   - **Full blood count** – can show the presence of *microcytic or macrocytic anemia*
     - Serum ferritin, serum iron and total iron-binding capacity are then performed if the MCV is low.
     - Serum B\textsubscript{12}, serum folate, and red cell folate are performed if the MCV is high
   - **Serum ions** – indicate a decreased level of electrolytes in disorders characterised by chronic diarrhea:
     - hypocalcemia: the increase of alkaline phosphatase suggests the presence of osteomalacia
     - hypomagnesemia
     - hypokalemia
   - **Serum protein levels** – constitute an indicator for the nutrition state of the patient:
     - hypoproteinemia and hypoalbuminemia can manifest in advanced stages of any malabsorption syndrome
   - **Coagulation tests** – increased protrombin indicates a vitamin K deficiency encountered in lipid malabsorption
• Lipid profiles – can show hypolipidemia and hypocholesterolemia encountered in lipid malabsorption

2. STOOL examination

a) MACROSCOPIC examination – can show:
   - modifications is appearance, colour and smell
   - pathological elements such as: mucus, pus, blood, undigested residue, intestinal parasites

b) MICROSCOPIC examination – can show:
   1. Muscle fibres (creatorrhoea):
      - a large quantity of undigested muscle fibres is called creatorrhoea and demonstrates a pancreatic failure or accelerated peristaltic movement of the bowels
   2. Lipids (steatorrhoea):
      - are normally present in a low quantity or absent in the normal stool (2-6 g per day for a 100 grams lipid intake)
      - can be present in the stool as neutral lipids (orange-red due to Sudan III stain) or as fatty acids (dark blue due to Nile blue stain)
      - an increase in lipid excretion in the stool greater than 7 g/day is called steatorrhoea and can be a consequence of:
         o hepatic disorders (low synthesis of biliar salts)
         o jaundice (due to the absence of biliar salts in the intestine)
         o pancreatic disorders (decreased secretion of pancreatic lipase)
         o intestinal disorders (decreased lipid absorption due to increased bacterial proliferation, intestinal resection, lesions of the intestinal mucosa)
   3. Starch:
      - its presence can be shown using Lugol solution (undigested starch appears blue, whilst partially digested starch gains a dark violet colour)
      - it is not unusual for small quantities to exist in the normal stool
      - a large amount of undigested starch usually indicates pancreatic failure
   4. Cellulose:
      - can be found in the stool as digested (completely digested in the colon) and undigested (that escapes the intestinal bacteria’s action)

   - the presence of digestible cellulose in the stool indicates a deficit of mastication or increased peristaltic movements

   5. Cells:
      - erythrocytes: digested in upper gastrointestinal bleeding, undigested in hematochasia
      - leukocytes: indicate an inflammatory phenomenon in the bowel and compel to do a stool culture
      - parasite eggs: compel the clinician to do a complete parasite investigation of the stool (normally, 3 samples are analysed at a 2-3 days interval)

c) CHEMICAL examination – enfers to:
   1. pH measurement:
      - normally the stool must have a neutral or slightly alkaline pH
      - an acid reaction results from increased fermentation processes
      - an alkaline reaction results from increased putrid processes
   2. OCCULT BLEEDING tests:
      - The Hemocult test
         - is based upon hemoglobin’s property to decompose hydrogen peroxide, resulting in a colour reaction which is indicative of a blood loss
         - in order to perform such a test the patient requires a 2-3 day preparation:
            o no red meat intake or vegetables
            o no intake of aspirin/non-steroidal antiinflammatory drugs, iron or vitamin C suplements (false positive results)
            o the test will not be performed during menstruation or in patients with active bleeding due to hemorrhoids

      - The IMUNO Hemocult test:
         - is based upon the identification of hemoglobin by using anti-hemoglobin antibodies
         - no restriction in meat intake

B. DYNAMIC tests

The LACTOSE tolerance test
   - Principle:
      - measurement of glucose levels in the morning, after which 50 g of glucose dissolved in 400 mL of water are
administered orally together with barium sulphate
- glucose levels will be determined after 60 and 120 minutes
- after 60 minutes an abdominal x-ray is performed

• The test is positive for lactose intolerance if three types of manifestations are present:
  - clinical: diarrhea (hyperacidic stools), abdominal pain, flatulence (minutes after the administration)
  - biological: an increase less than 25% in glucose levels
  - radiological: barium sulphate dilution (due to hipersecretion), air accumulation with bowel distention and extremely accelerated peristaltic movements with barium in the colon in maximum 60 minutes after the administration.

C. INVESTIGATION of INTESTINAL BACTERIAL PROLIFERATION

1. The hydrogen breath test
   • Principle:
     - administration of 50 g lactulose orally, that will be decomposed by bacteria, with hydrogen release
     - an early increase of hydrogen levels in the exhaled air can indicate:
       o rapid degradation of lactulose in the proximal small bowel due to bacterial activity or
       o increased peristaltic activity in the colon

2. Radioactive Glycocolic acid breath test
   • Principle:
     - administration of radioactive marked biliar salts orally
     - due to bacterial activity, the biliar salts will be decomposed with radioactive glycine release
     - radioactive glycine will be metabolised with radioactive marked carbon dioxide release in the exhaled air
     - an early increase respiratory radioactivity can indicate:
       o increased bacterial proliferation in the proximal small bowel or
       o accelerated peristaltic activity in the colon

D. BARIUM MEAL

• Clinical value:
  - indirect evaluation of small bowel motility
  - diagnosis of jejunal or ileum lesions or obstructions due to an inflammatory or proliferative phenomenon

IV. INVESTIGATION OF LARGE BOWEL DISORDERS

Indications:
Patients that manifest:
- abdominal pain
- constipation, diarrhea
- occult hemorrhages
- hematochesia (fresh, red blood in the fecal matters)

Investigation of large bowel disorders entails:
1. Abdominal X-rays
2. Colonoscopy
3. Air contrast barium enema

1. The abdominal X-ray
   • Indicates:
     - an excessive quantity of air in the colon
     - gas fluid levels in bowel obstructions
     - radioopaque foreign bodies: calculi, swollen objects or objects manually introduced in the rectum
     - Chilaiditi syndrome

2. Colonoscopy
   Two main types:
   - complete: all the way to the cecal valve, it can visualise the entire colon using the endoscope
   - rectosigmoidoscopy: limited only to the rectum and sigma, using a flexible sigmoidoscope

   • Clinical value:
     - it combines diagnosis together with treatment, because it allows biopsiei, polypectomies, hemostasis for lesions with active bleeding, stenosis dilations, stent insertion in critical bowel obstructions
     - gold standard in early detection of colon cancer in patients with fecal occult bleeding

Fecal occult bleeding determination is used as a screening test in patients which require a colonoscopy and must be analysed annually in patients over 45-50 years old.

3. Barium enema:
• Clinical value:
  - diagnosis of tumoral lesions (benign polyps or malignant tumors), ulcers, stenoses
  - it is less sensitive than colonoscopy regarding diagnosis of lesions smaller than 1 cm
  - air contrast barium enema (irigografia în dublu contrast) it is used to examine the lining of the colon’s mucosa

Both methods, colonoscopy and barium enema, require a thorough preparation of the patient in order for the procedures to succeed.

V. INVESTIGATION OF EXOCRINE DISORDERS OF THE PANCREAS

Indications:
In patients with acute and chronic disorders:
A. Serum and urine pancreatic enzyme determination:
  - for the diagnosis of acute pancreatitis
  - limited and inconclusive in chronic pancreatitis, except acute exacerbations
  - a correlation with imaging techniques must be done (ultrasound, CT) in order to have a rapid non-invasive diagnosis

B. Secretion tests – evaluate the pancreatic function in patients with pancreatic failure

C. Stool examination – useful in order to identify pancreatic failure in patients with chronic pancreatitis

A. Enzyme determinations in pancreatic disorders

1. Serum Amylase

• Normal value= 30 – 220 U/L
• Increased values – can be found in:
  ⊗ Pancreatic disorders: acute pancreatitis or exacerbations of chronic pancreatitis:
    - major modifications (5-12 times the normal values) in the first 24 hours, but also transitory, reaching a normal level after 3 days
    - serum amylase DOES NOT show the severity of the pancreatitis, but its persistence can show an active process
  ⊗ Extrapancreatic disorders:
    - salivary glands disorders (parotiditis, salivary calculi)
    - digestive tract disorders (perforated ulcer with peritonitis, bowel obstruction, mesenteric infarction, any kind of gall bladder disorder)
    - pancreatic failure
    - severe hepatic disorders

2. Urine amylase:

• Normal values (24 h) = 6,5 – 48 U/h
• Increased values:
  - in acute pancreatitis its values increase rather late (after serum levels regain normal values), but persistent (7-10 days), due to a temporary renal impairment that inhibits tubular reabsorption of amylase

3. Serum lipase

• Normal values = 10 - 160 U/l
• Increased values:
  - appear much slower that modifications in amylase levels, but their persistence is greater (3-8 days of evolution)
  - much more specific for the pancreas than serum amylase
  - simultaneous positivity of lipase and amylase serum levels increases diagnosis accuracy in acute pancreatitis and excludes salivary disorders

B. Pancreatic secretion tests

1. Secretin test

• Principle:
  - intravenous administration of 4U/kg secretin in order to stimulate pancreatic secretion
  - duodenal tubeage to obtain pancreatic juice
  - measurement of
    - full volume of pancreatic juice (normal value >3 mL/kg)
    - sodium bicarbonate levels (normal value > 80 mEq/L)
• Clinical value:
  - a decrease in pancreatic juice volume and sodium bicarbonate concentrations defines exocrine pancreatic failure (encountered in cystic fibrosis, chronic pancreatitis, pancreatic cancer).

2. Fecal elastase test

• Principle:
  - elastase-1 (E1) is a stable pancreatic enzyme that passes thru the small intestine without degradation, and eliminates thru the feces 5-6 times (normal value > 200 μg/g of fecal matter)
- elastase secretion is extremely low in pancreatic failure, and therefore in the stool (< 100 μg/g fecal matter in severe forms and 100-200 μg/g of fecal matter in moderate forms)

**Clinical value:**
- early diagnosis of exocrine pancreatic failure in children with cystic fibrosis (confirmation of the diagnosis).

C. STOOL examination

- **Macroscopic examination** – can entail:
  - abundant, soft, light-yellow, shiny, greasy-like, rancid smell stools (due to steatorrhea)
  - undigested food

- **Microscopic examination** – can entail:
  - neutral fatty drops (Sudan III stain)
  - undigested muscle fibers (creatorrhea)
  - alkaline reaction of the stool

- **The lipid digestion test:**
  - during a 3 day period, the patient receives a regimen with 100-130 g of lipids/day
  - lipid stool levels are determined (normal value: < 2-6 g/day)
  - over 7 g/day = steatorrhea
  - the test does NOT quantify the severity of the pancreatic lesions, because chronic pancreatitis can exist without steatorrhea.

- **Stool nitrogen determination**
  - protein malabsorption induces an increase in stool nitrogen elimination
  - as with steatorrhea and creatorrhea, nitrogen appears in the stool only in advanced stages of pancreatic failure (over 70% damage of the pancreas)
1. Which of the following is considered the golden standard for the diagnosis of esophageal (acid) reflux?
   A. Esophageal endoscopy
   B. Barium meal performed in supine position
   C. Barium meal performed in Trendelenburg position
   D. Esophageal pH determination
   E. Esophageal manometry

2. Which of the following tests is used to monitor treatment efficiency in Helicobacter pylori (HP) infection?
   A. HP determination in gastric biopsies obtained thru endoscopy
   B. Serum anti-HP antibodies determination
   C. Stool HP antigen determination
   D. Urea breath test
   E. Urease test

3. Which of the following is mandatory in order to certify the cause of a malabsorption syndrome?
   A. Stool examination
   B. Bacterial proliferation determinations
   C. Computed virtual endoscopy
   D. Intestinal mucosa biopsies
   E. Fecal occult bleeding determinations

4. Which of the following are correct regarding the Hemocult test?
   A. It becomes positive in upper gastrointestinal bleeding
   B. It is considered a screening test that indicates which patient needs a colonoscopy
   C. It always requires a thorough preparation of the patient, with a “white diet” involved
   D. It is mandatory once a year in patients over 45-50 years old
   E. It represents the golden standard for early detection of colon cancer

5. Which of the following regarding serum amylase are true?
   A. Increased levels are major and early, but also transitory
   B. Increased levels appear late, but are very persistent
   C. Serum levels is corelated with the severity of pancreatitis
   D. Persisting increased levels can indicate an active process
   E. It can follow a transitory renal impairment that stimulates amylase tubular reabsorption
CASE STUDIES

1. A 55 years old male patient, with chronic alcoholism, is brought to the emergency room with severe epigastral pain, nausea, vomiting, severely altered state.

   - Erythrocytes = 4,500,000/mm³
   - Hb = 13 g/dL
   - Ht = 43%
   - Leukocytes = 16,000/mm³
   - Glucose level = 200 mg/dL
   - Serum calcium = 8 mg/dL
   - Serum amylase = 520 U/L
   - Urea = 41 mg/dL
   - Creatinine = 1,2 mg/dL

   **What diagnosis (diagnoses) can be considered?**
   **What other tests can be ordered?**
   **Give arguments for your answers.**

2. A 47 year old female patient consults a specialist due to chest pain and burning sensation, that worsens in supine position, after meals and during the night. The patient is also obese and smokes a packet of cigarettes per day. Most recently, she was also diagnosed with gall-bladder stones, for which she receives an antispastic treatment.

   **What diagnosis (diagnoses) can be considered?**
   **What other tests can be ordered?**
   **Give arguments for your answers.**