GI Physiology Research

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Course-learning outcomes (CLOs)

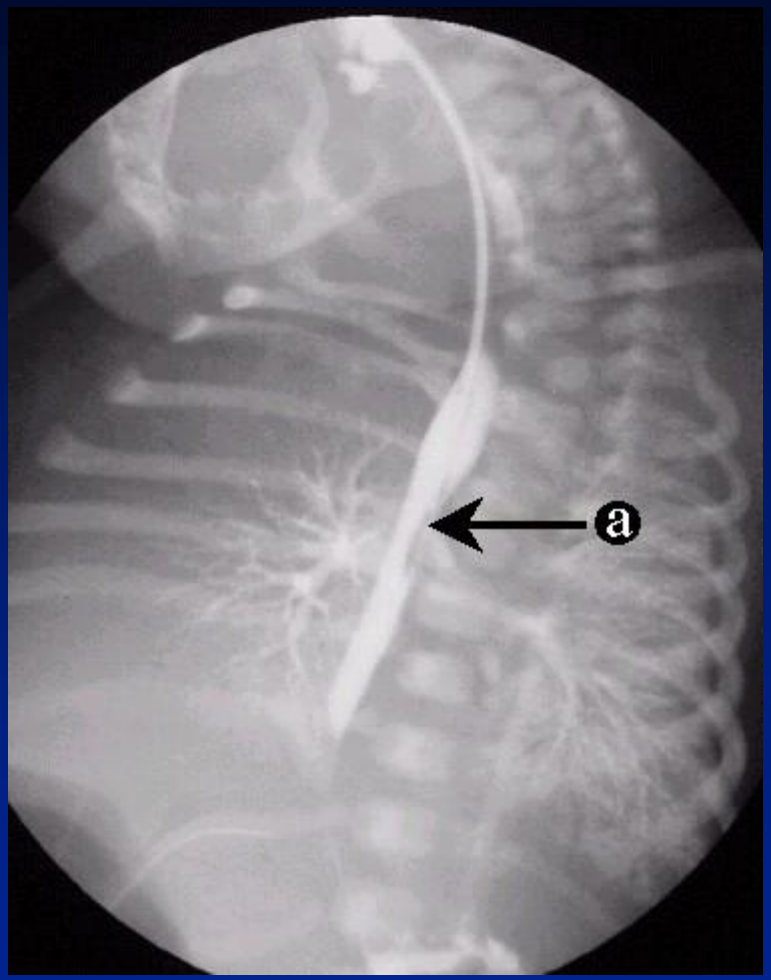
1. Explain the following aspects of experimental methods used in physiological research: Principles, Methods, Interpretation, Advantages and Disadvantages
2. Apply the knowledge to choose appropriate methods in experimental designs and appraise the choice of methods employed in literatures

Gastrointestinal (GI) functions

- Motility
- Secretion
- Digestion
- Absorption

Motility

- **Testing of the esophagus**


a

- **Esophagogram**

- An esophagram is a radiographic study of the esophagus

- Patient swallows barium

(a contrast agent) and the radiologist visualizes the esophagus and stomach under fluoroscopy.

- **Esophagogram**

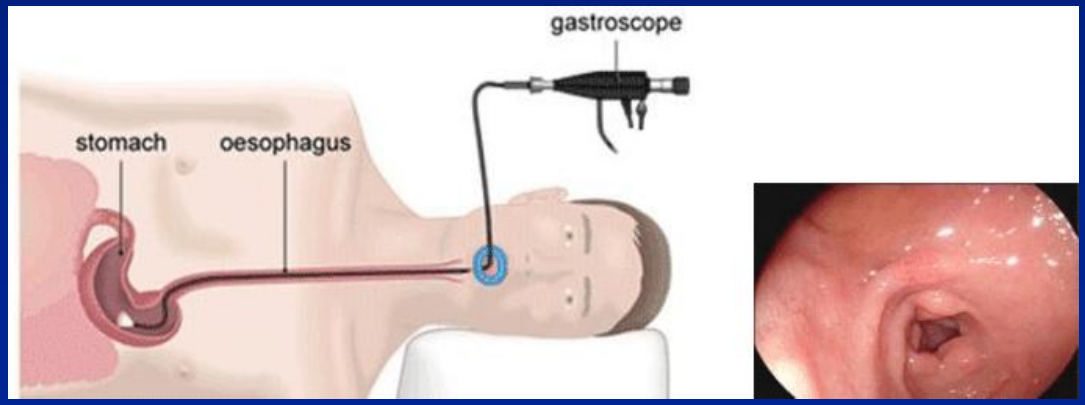
- This test can help detect if there is a problem with a stricture (narrowing) in the esophagus or if a hiatal hernia is present.

- It can also give a rough estimate of the degree of esophageal muscle contractions.

- **Upper endoscopy**

- A test that allows direct visualization of the lining of the esophagus, stomach, and upper portion (duodenum) of the small intestine

by the use of an endoscope passed through the mouth.


gastroscope
stomach
oesophagus

- **Esophageal manometry**

- Esophageal manometry involves

a small diameter tube passed through the nose into the esophagus.

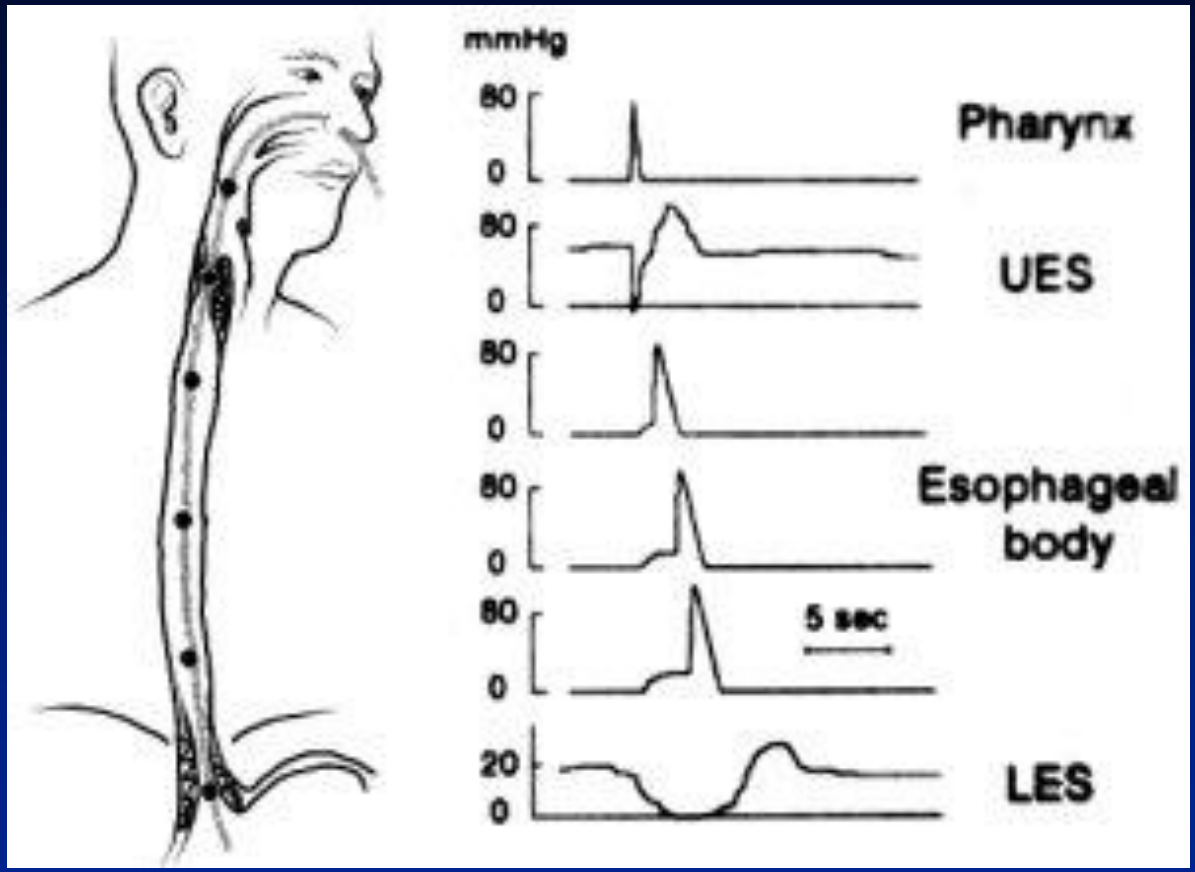
- The nose and throat of the patient are numbed prior to this procedure.

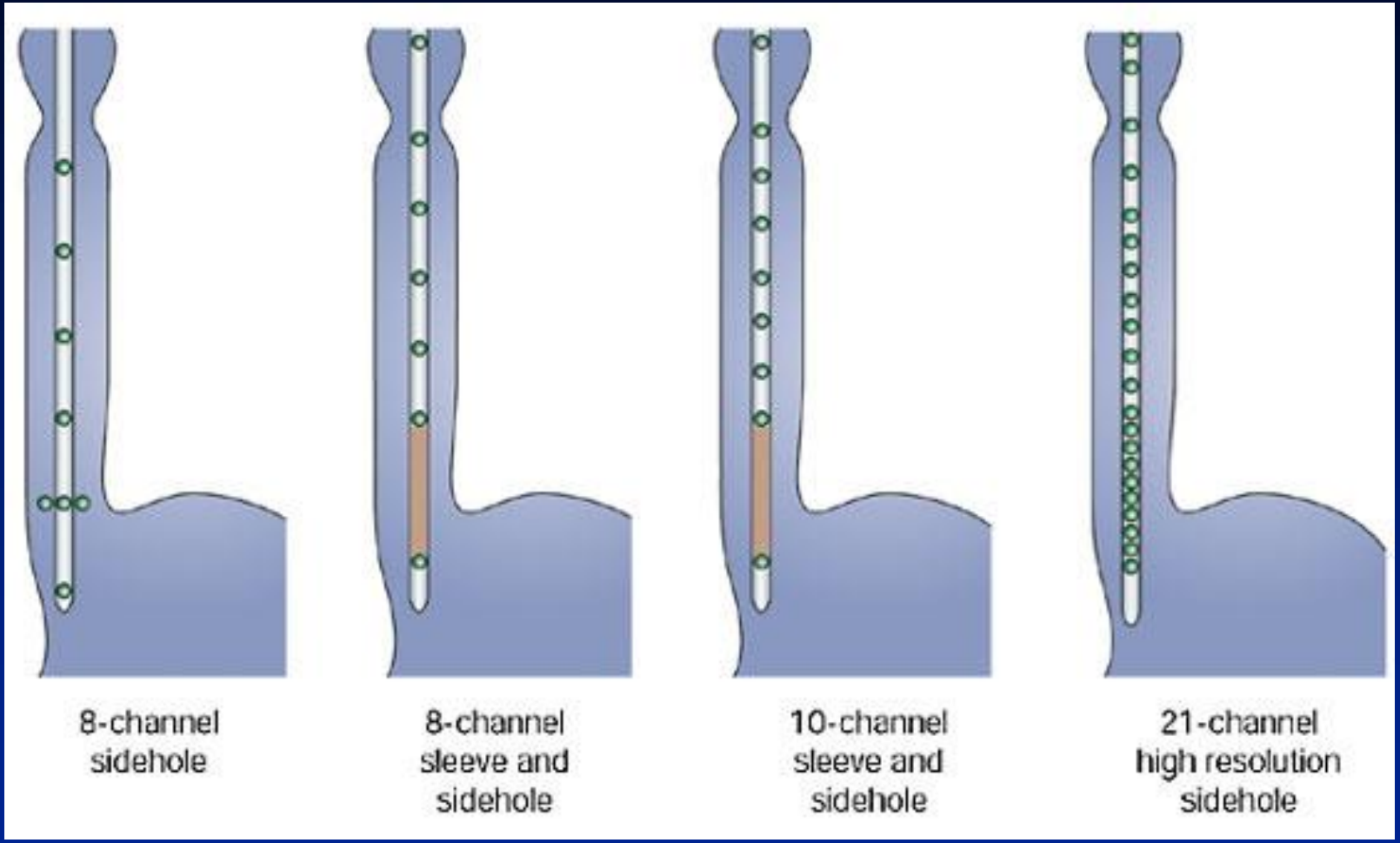
- Once the tube is in position, the patient is asked to swallow.

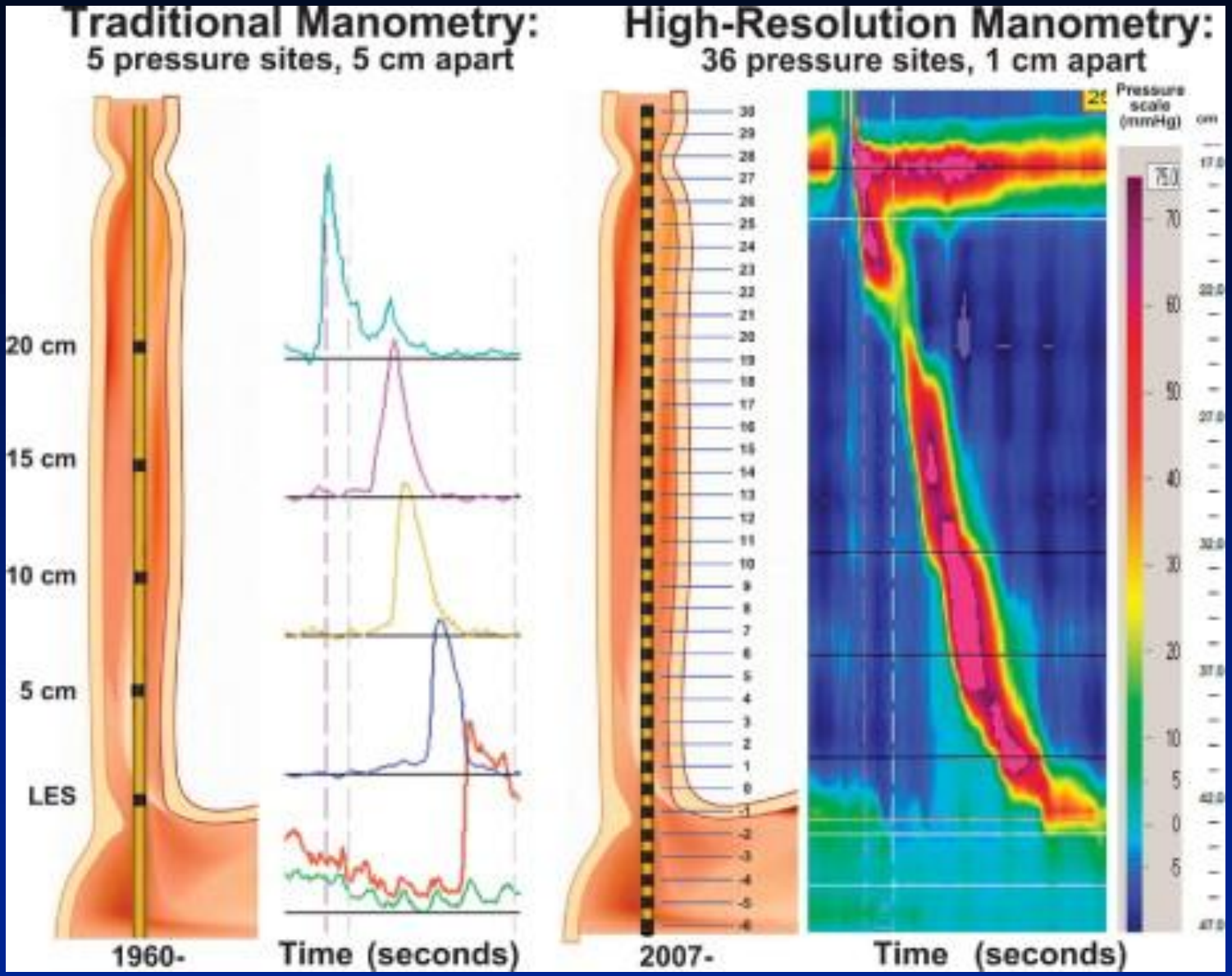
- **Esophageal manometry**

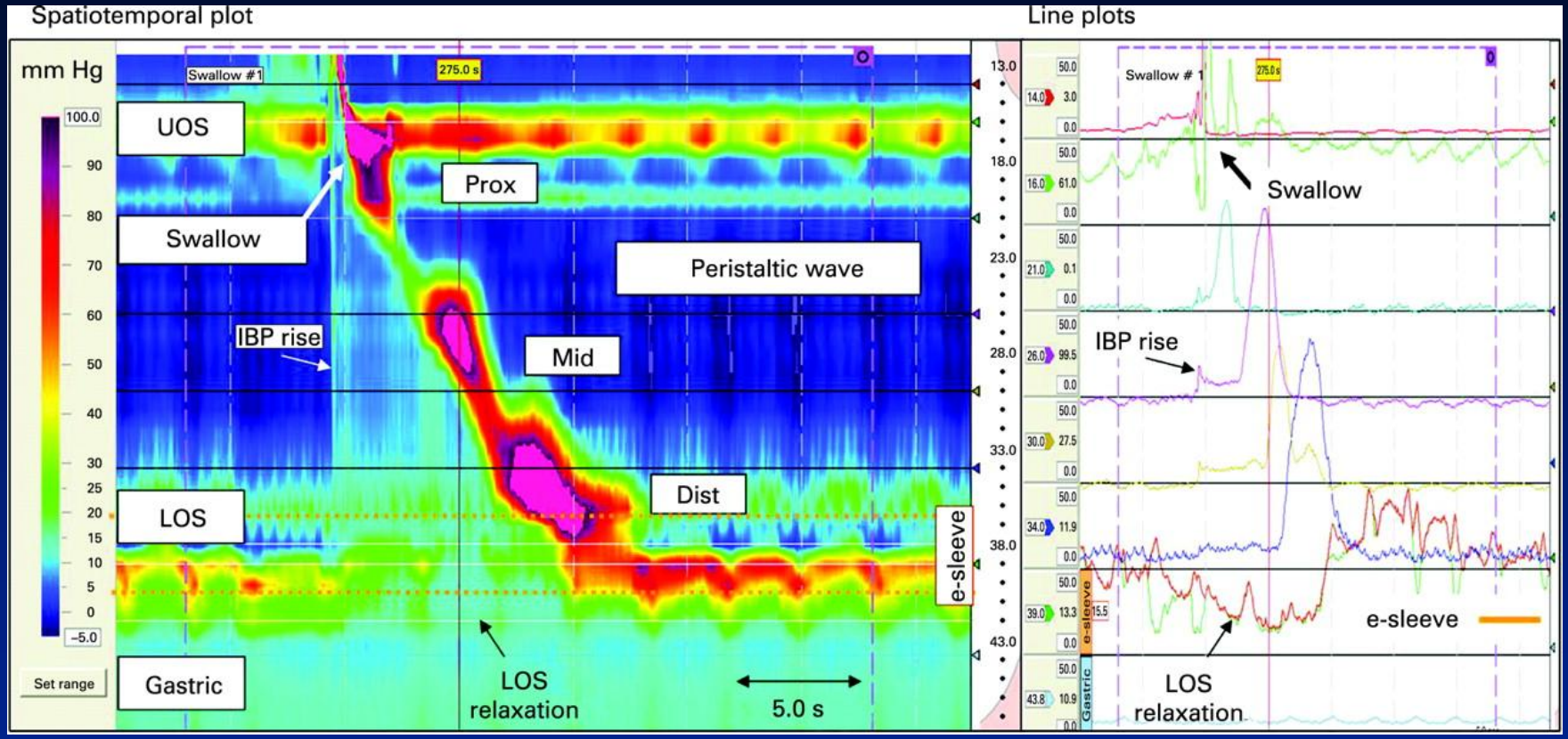
- **Measurements of esophageal function are made by the use of pressure readings of the muscle contractions (motility) of the esophagus.**

- **Lower esophageal sphincter muscle pressure can also be taken.**


mmHg
80
0
Pharynx
80
0
UES
80
0
80
0
Esophageal body
80
0
5 sec
20
0
LES


8-channel sidehole
8-channel sleeve and sidehole
10-channel sleeve and sidehole
21-channel high resolution sidehole


Traditional Manometry:
5 pressure sites, 5 cm apart
20 cm
15 cm
10 cm
5 cm
LES
1960-
Time (seconds)
High-Resolution Manometry:
36 pressure sites, 1 cm apart
2007-
Pressure scale (mmHg)
Time (seconds)


Spatiotemporal plot
Line plots
mm Hg
Swallow #1
275.0 s
UOS
Prox
Swallow
Peristaltic wave
IBP rise
Mid
Dist
LOS
Gastric
LOS relaxation
5.0 s
e-sleeve
Set range
Swallow # 1
Swallow
IBP rise
e-sleeve
LOS relaxation

24 hr pH monitoring

-A test that consists of a small tube passed through the nose into the esophagus at the level of the LES.

-A pH sensor at the tip of the tube allows measurements of acid exposure in the esophagus to be collected on a portable computer.

24 hr pH monitoring

-The pH probe is worn for 24 continuous hours.

-This is considered the "gold standard" for determining if the patient has reflux disease, or GERD.


Sleuth

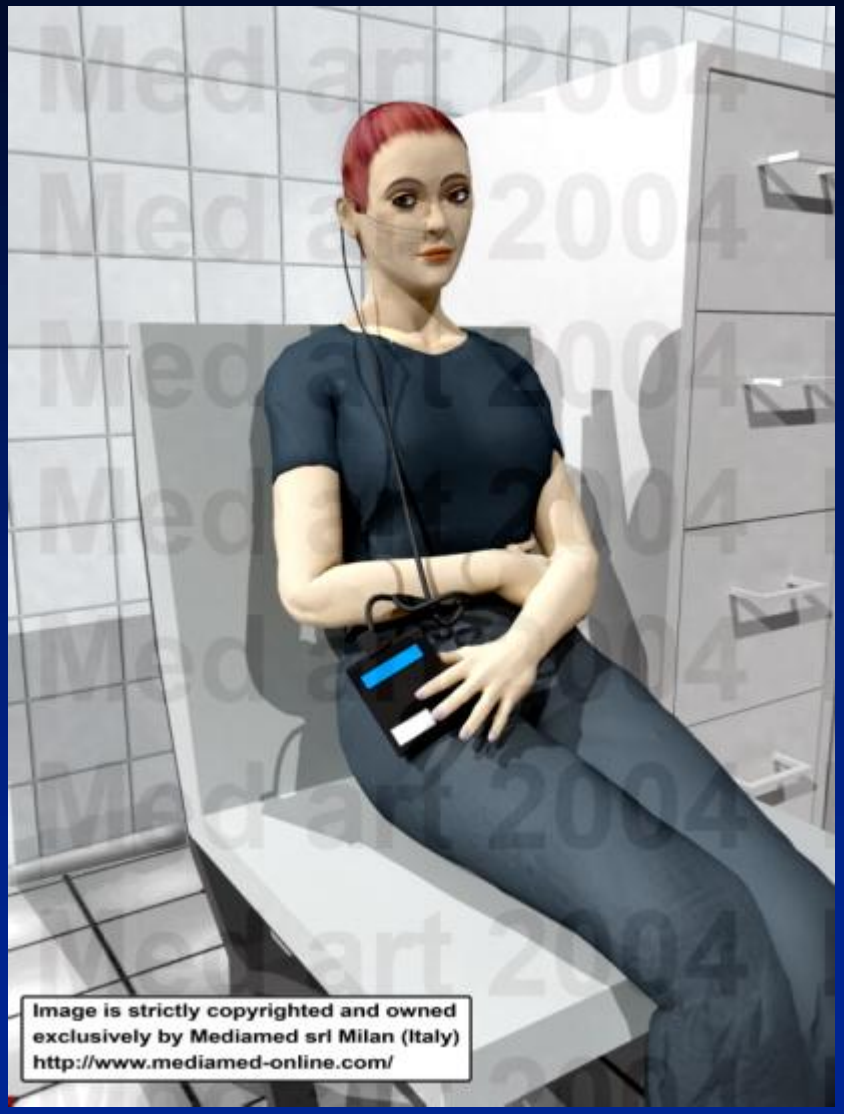
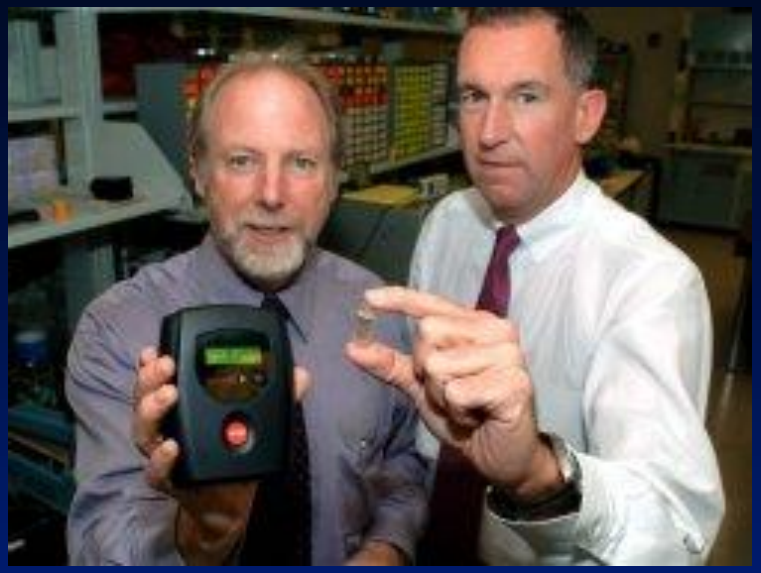


Image is strictly copyrighted and owned
exclusively by Mediamed srl Milan (Italy)
http://www.mediamed-online.com/

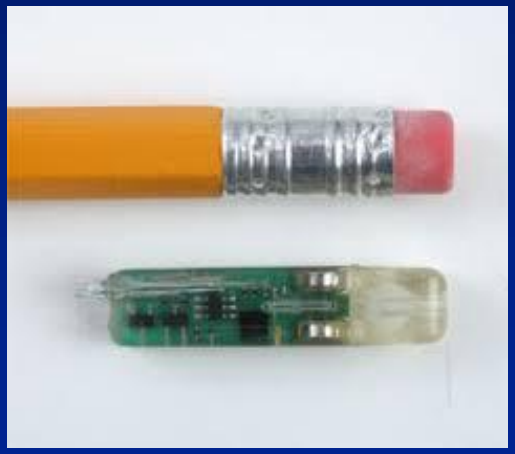
24 hr pH monitoring

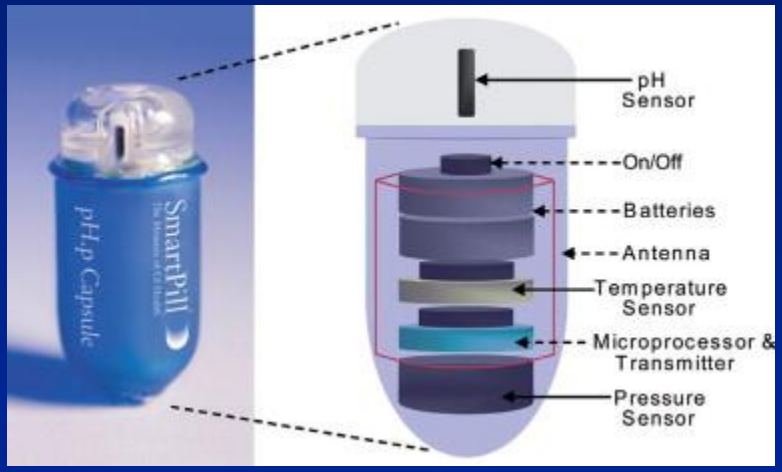
- A special pH-measuring device more recently has been developed that is clipped to the lining of the esophagus.

-The pH sensor sends a message to a portable computer that collects data about esophageal acid exposure over 24 hours.




SmartPill
pH,p Capsule




SmartPill
pH,p Capsule
pH Sensor
On/Off
Batteries
Antenna
Temperature Sensor
Microprocessor & Transmitter
Pressure Sensor

24 hr pH monitoring

-The clipped probe in the esophagus slowly detaches itself from the esophagus and is ultimately passed in the stool and discarded.

Impedance

- It measures liquid movement from the stomach into the esophagus.

- This test may be important for people with reflux symptoms who are having bile reflux, not acid reflux, and therefore have normal results from a 24-hour pH probe.

Motility

- **Testing of the stomach**

Gastric emptying test

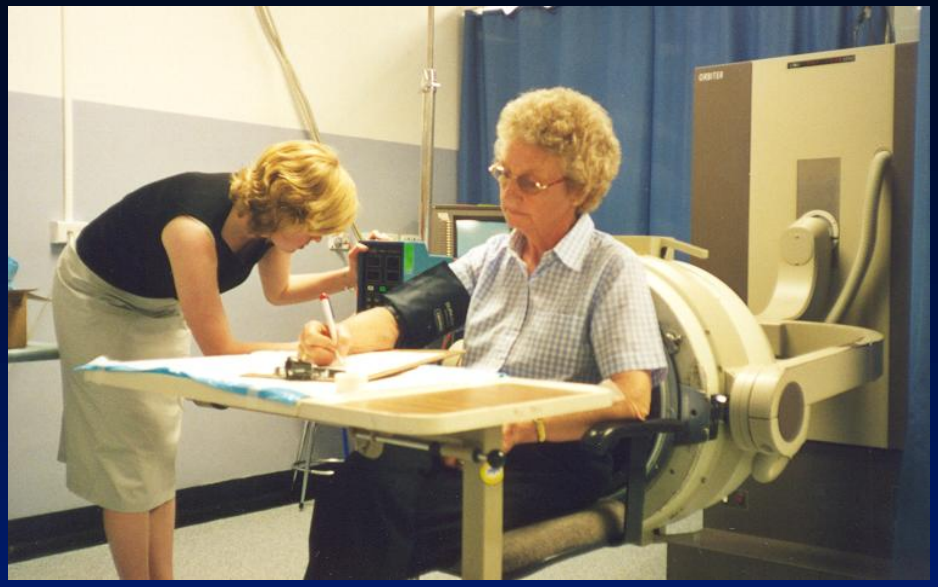
- Tests used to evaluate patients with delayed or altered gastric emptying

- Scintigraphy (a nuclear medicine study) to measure how quickly food leaves the stomach.

Gastric emptying test

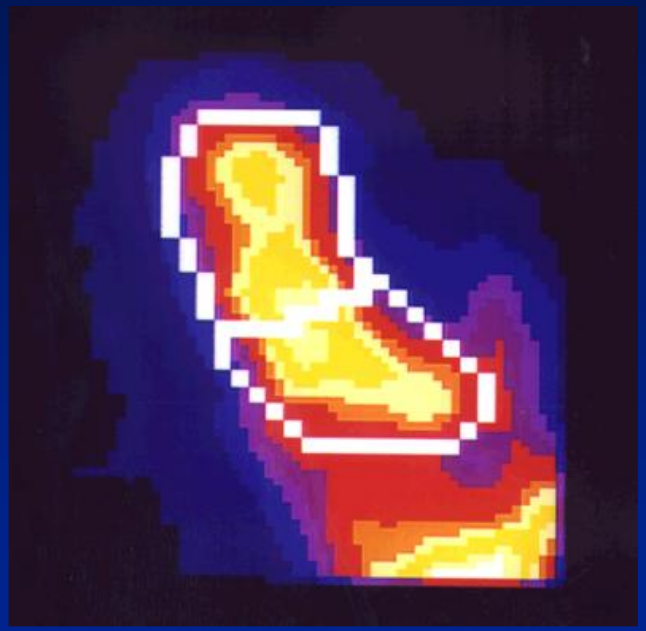
-The test of gastric emptying involves eating food that has a radioactive substance added to it,

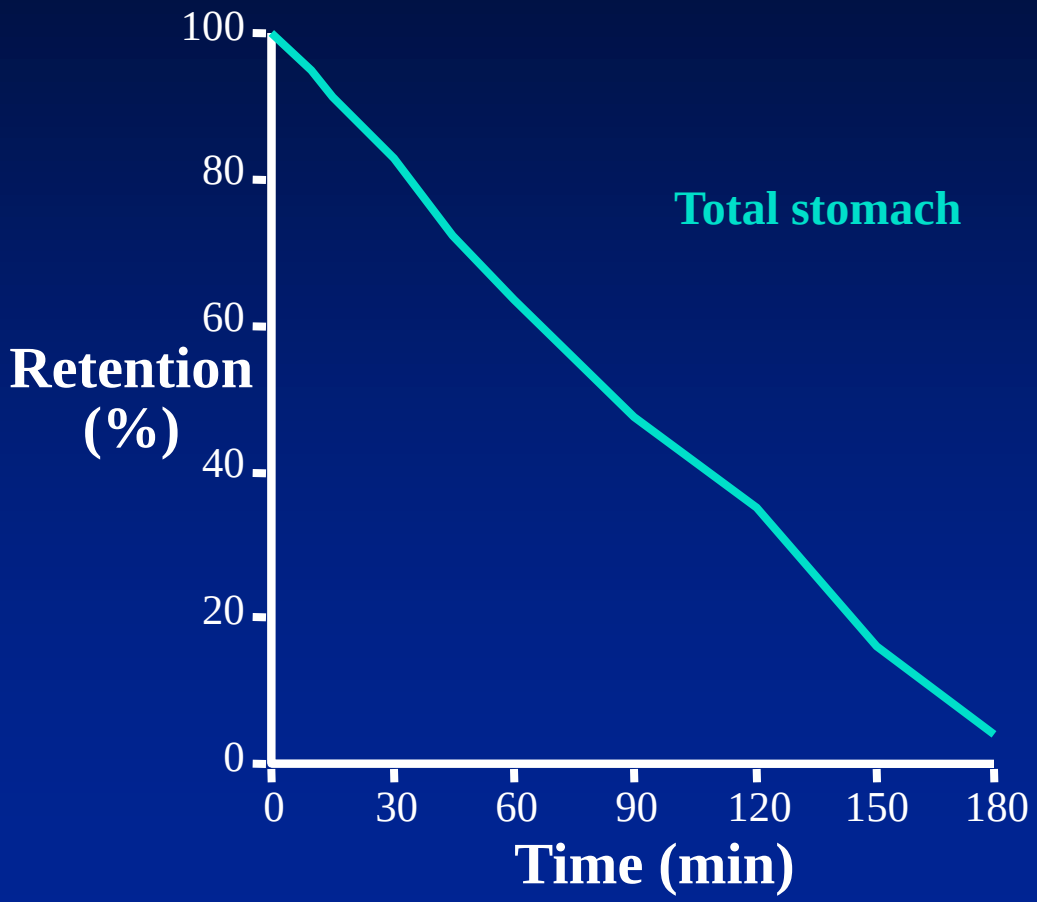
so that the rate of emptying of the stomach can be measured with a special camera (Gamma camera).



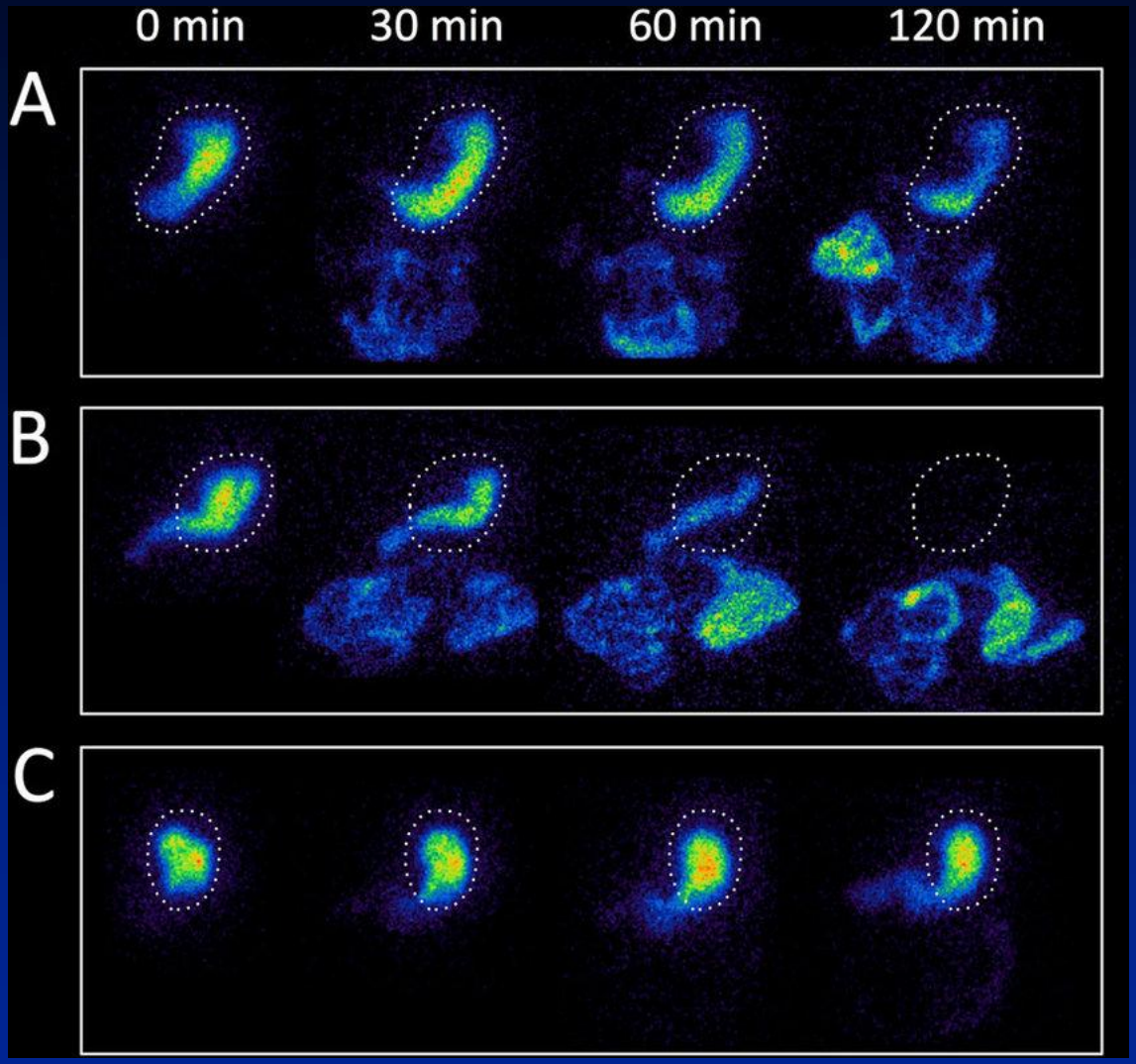
Scintigraphy

Scintigraphic measurement of gastric emptying





Gastric emptying scintigraphy images at 0, 30, 60, and 120 min after radioactive meal ingestion.



A: Healthy control with normal gastric emptying time (T 1/2 72 min).

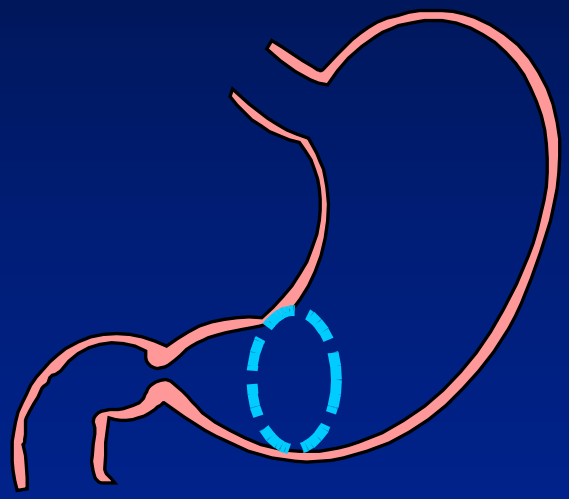
B: Patient with rapid gastric emptying time (T 1/2 26 min).

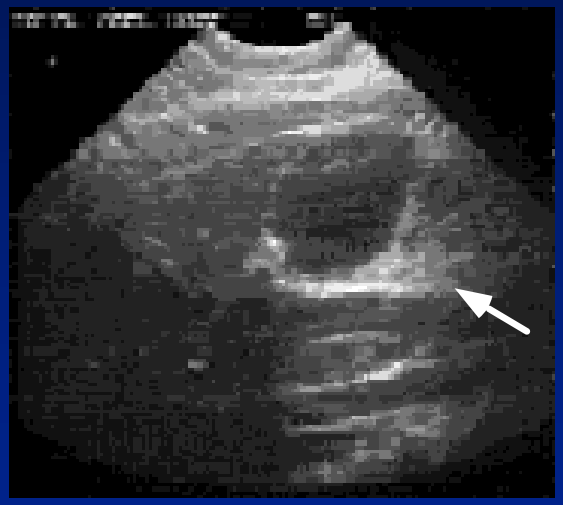
C: Vagotomized patient with severely delayed gastric emptying time (T 1/2 > 180 min)

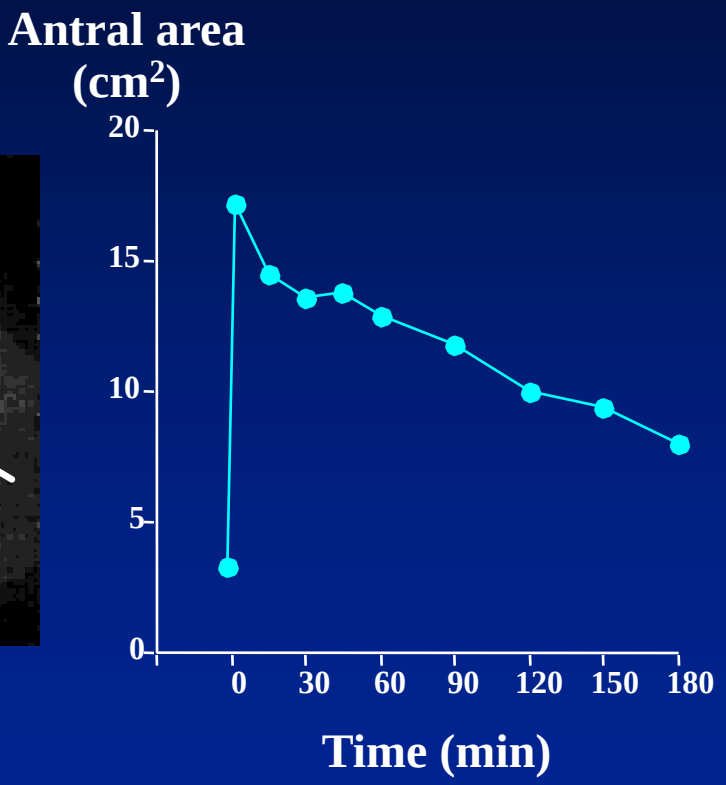
The dashed line designates the stomach.

Borghammer P, Knudsen K, Fedorova TD, Brooks DJ. Imaging Parkinson's disease below the neck. NPJ Parkinsons Dis. 2017 Apr 25;3:15.

Measurement of gastric emptying with 2D ultrasound

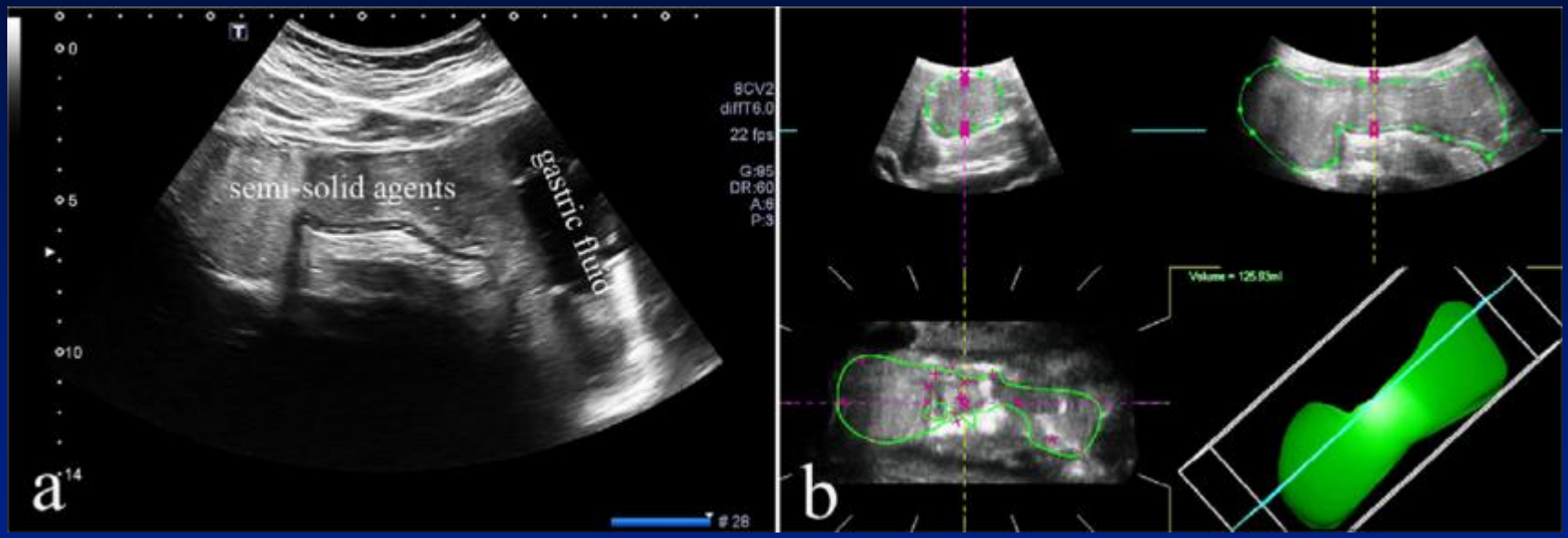






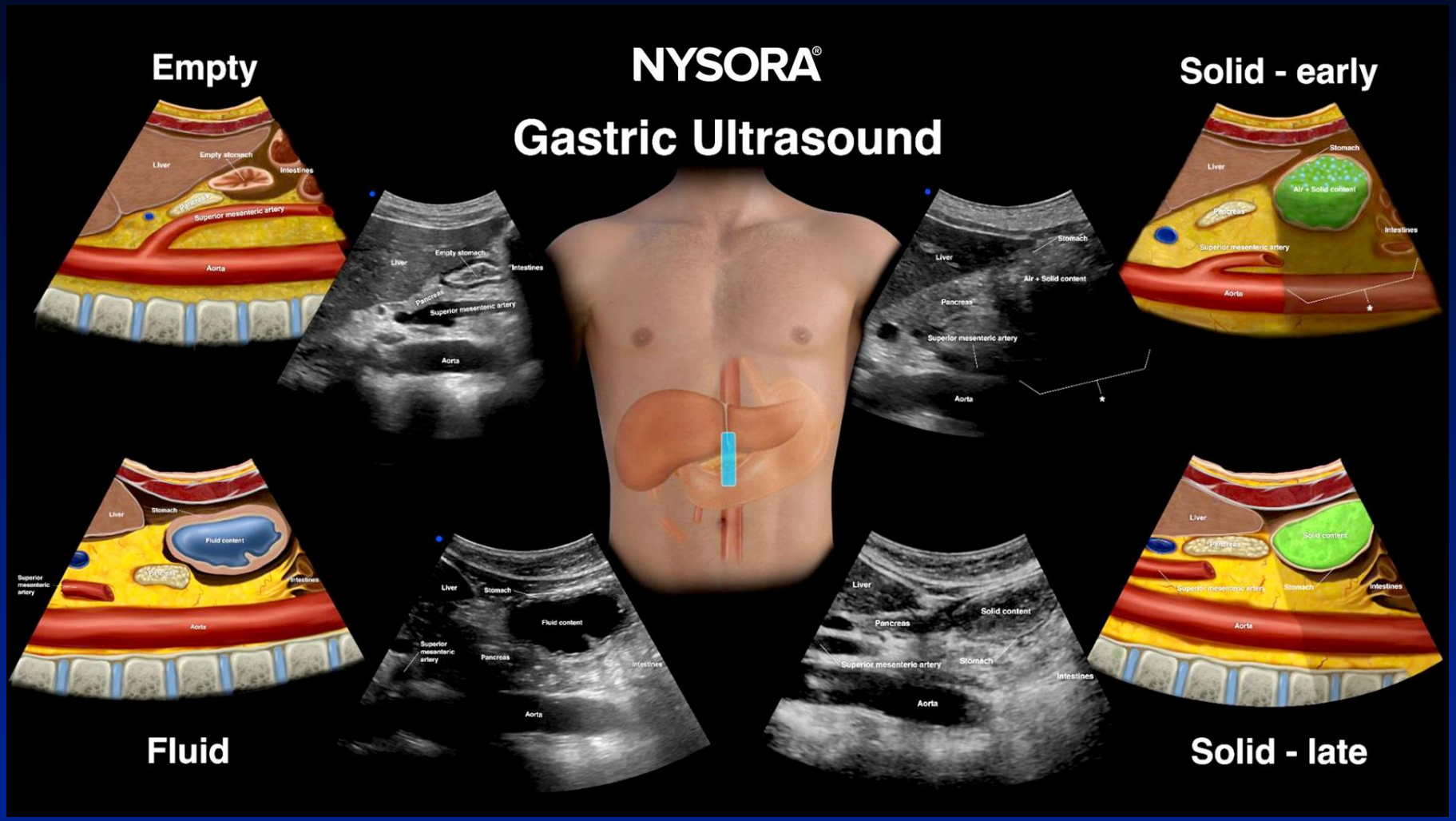
(Hveem et al 1996)

Measurement of gastric emptying with 3D ultrasound



Ultrasonography image of gastric ultrasound agents within the stomach.
(a) In this cardiac portion of the stomach (b) After observation of all regions in which agent was present in all 2-D ultrasound images one by one, the total volume of agent within the stomach was calculated automatically by 3-D data reconstruction.

Liu Z, Liu Z, Li Y, Guo J, Li J, Ren W, Tang S, Xie L, Huang Y, Huang L, Sun S, Zhao Y. Evaluation of Gastric Emptying by Transabdominal Ultrasound after Oral Administration of Semisolid Cellulose-Based Gastric Ultrasound Contrast Agents. Ultrasound Med Biol. 2018 Nov;44(11):2183-2188.



https://www.nysora.com/education-news/evaluating-preoperative-gastric-ultrasound-in-diabetic-patients-with-dysautonomia/

Gastric contraction test

Electrogastrography (EGG)

A non-invasive diagnostic technique used to evaluate gastric myoelectrical activity.

Surface electrodes are placed on the abdominal wall to record electrical signals generated primarily by the interstitial cells of Cajal (ICCs), which function as gastric pacemaker cells.

The recorded signal, known as the electrogastrogram, reflects the underlying slow-wave activity of the stomach.

EGG provides information regarding the frequency (2.4–3.7 cycles per minute (cpm)), amplitude and regularity of gastric electrical rhythms.

Clinically, it is applied in the assessment of disorders such as gastroparesis, functional dyspepsia, chronic nausea, and vomiting.

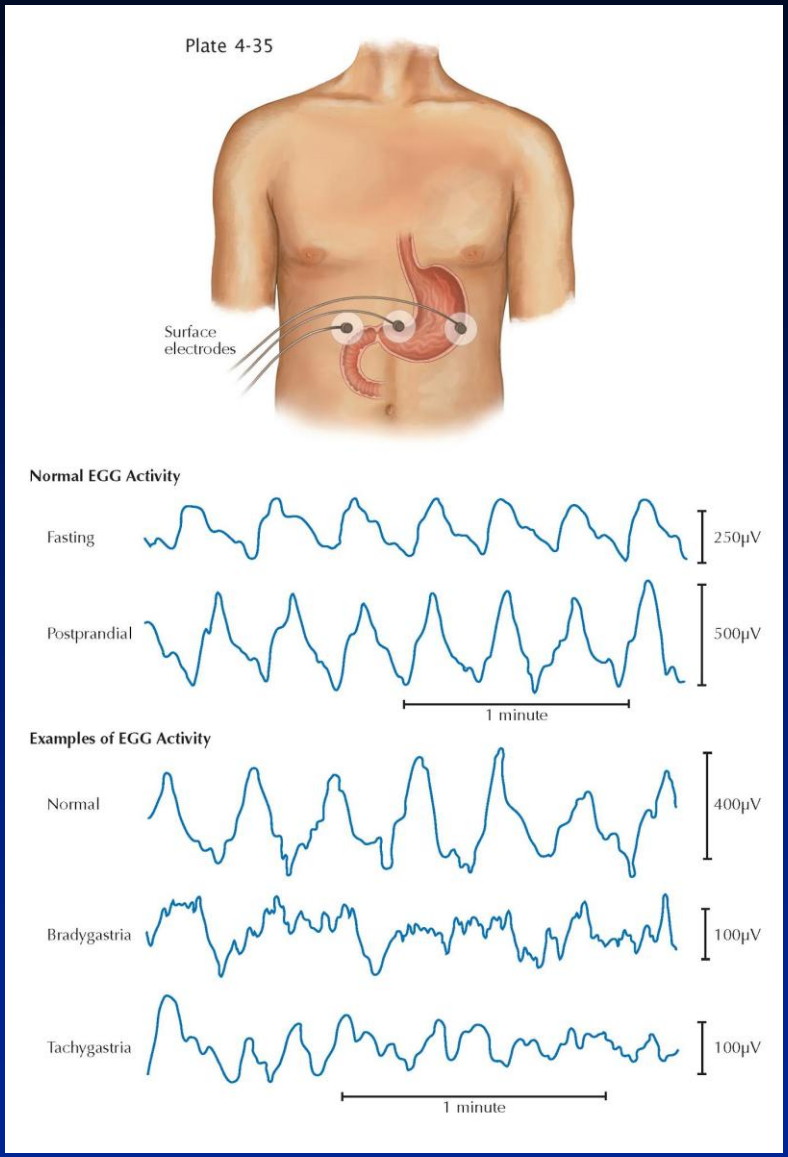
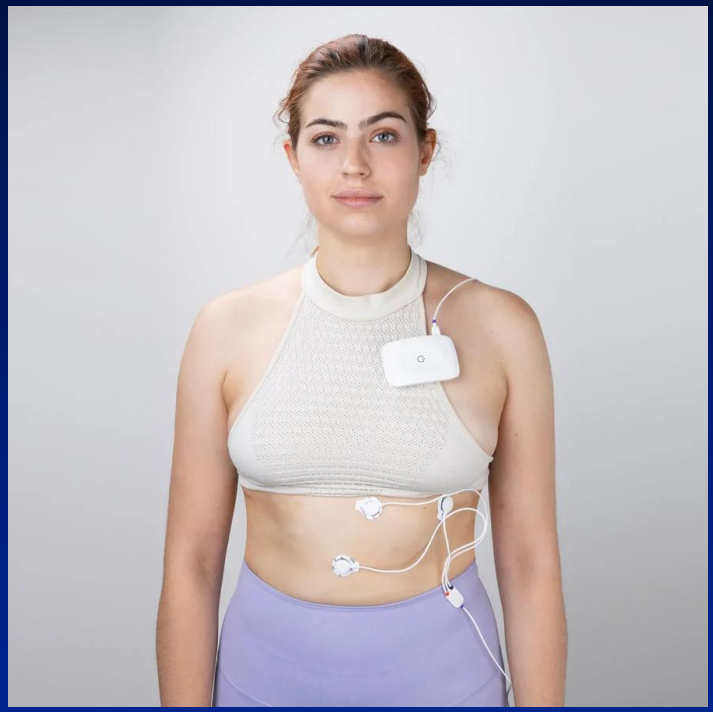


Plate 4-35
Surface electrodes
Normal EGG Activity
Fasting
250μV
Postprandial
500μV
1 minute
Examples of EGG Activity
Normal
400μV
Bradygastria
100μV
Tachygastria
100μV
1 minute

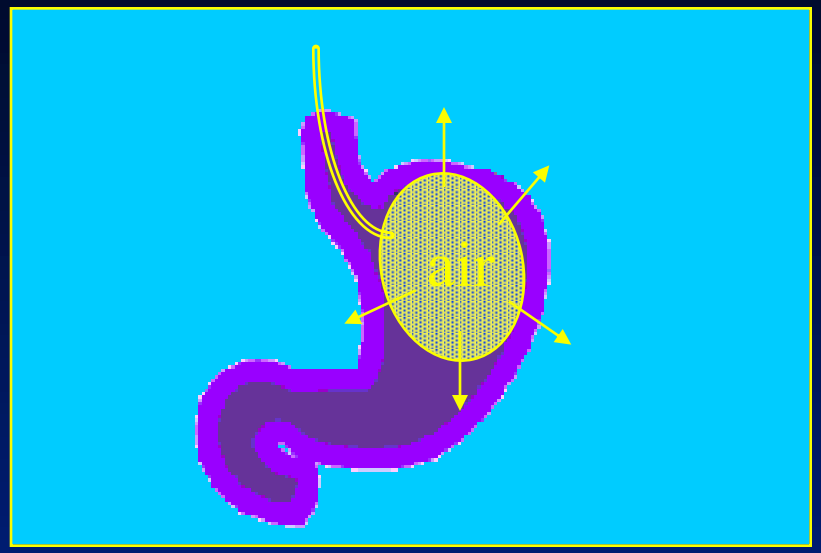


The gastric barostat

To record intraluminal pressures after meals.

The barostat balloon was designed to measure changes in tone (or gastric relaxation) and volume in the spherical areas of the proximal stomach

The gastric barostat



pressure distension

pressure

volume

time

volume distension

volume

pressure

time

Motility

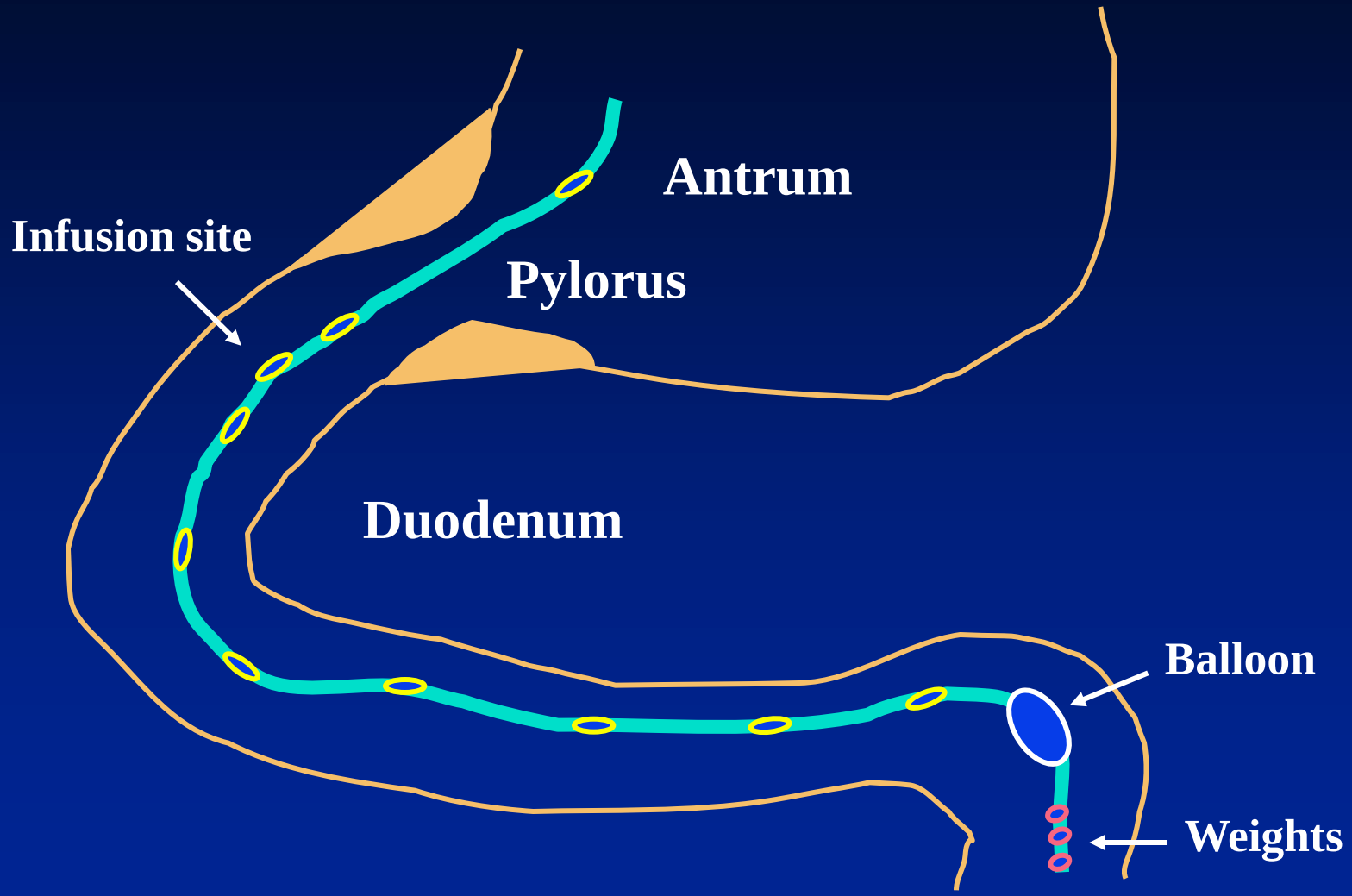
- **Testing of the small intestine**

Small bowel manometry

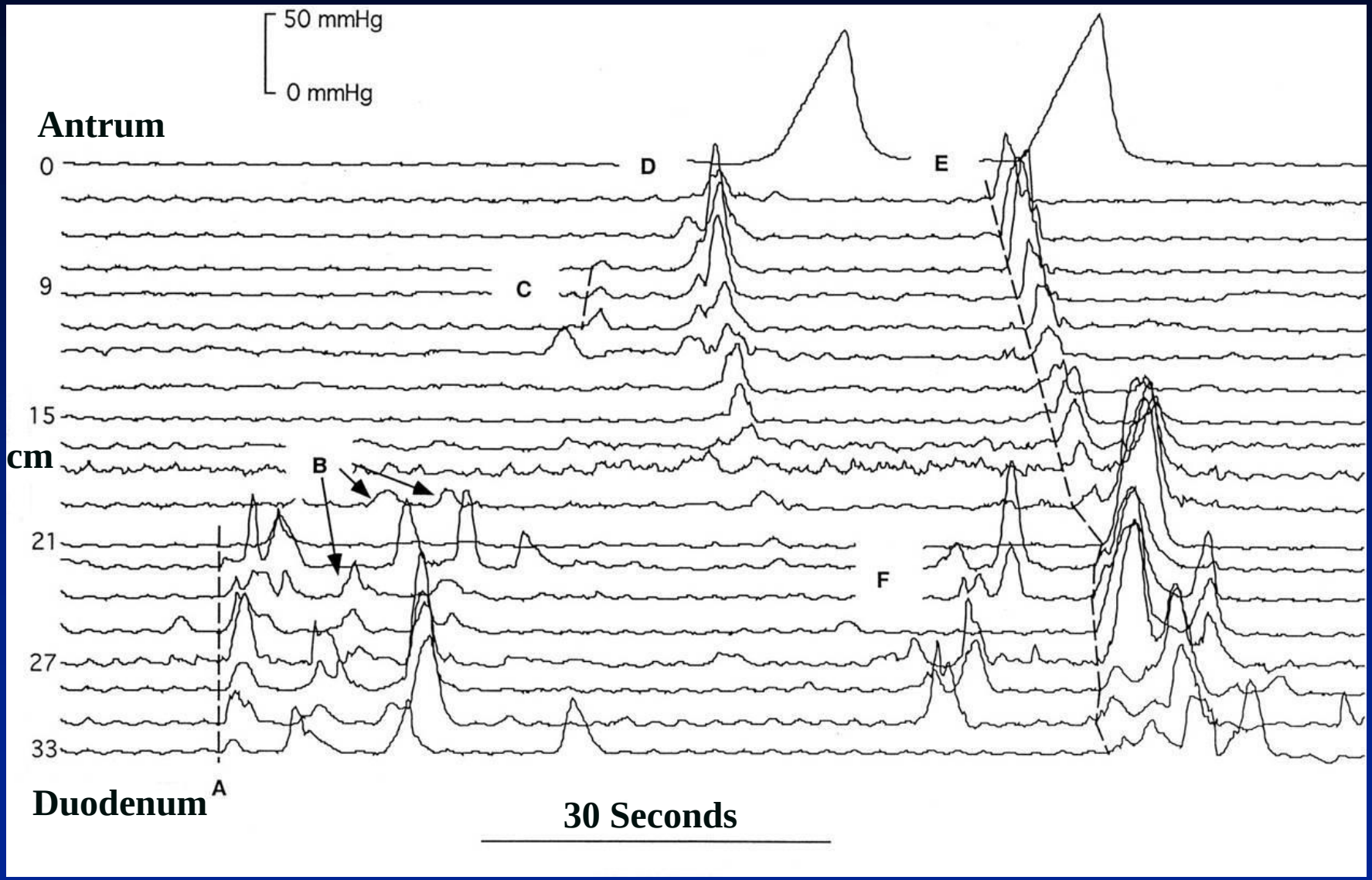
- A test that is used to detect intestinal motility abnormalities (antroduodenal manometry).

-This involves placing a long tube with pressure sensors on it
that passes through the stomach
and into the small intestine.

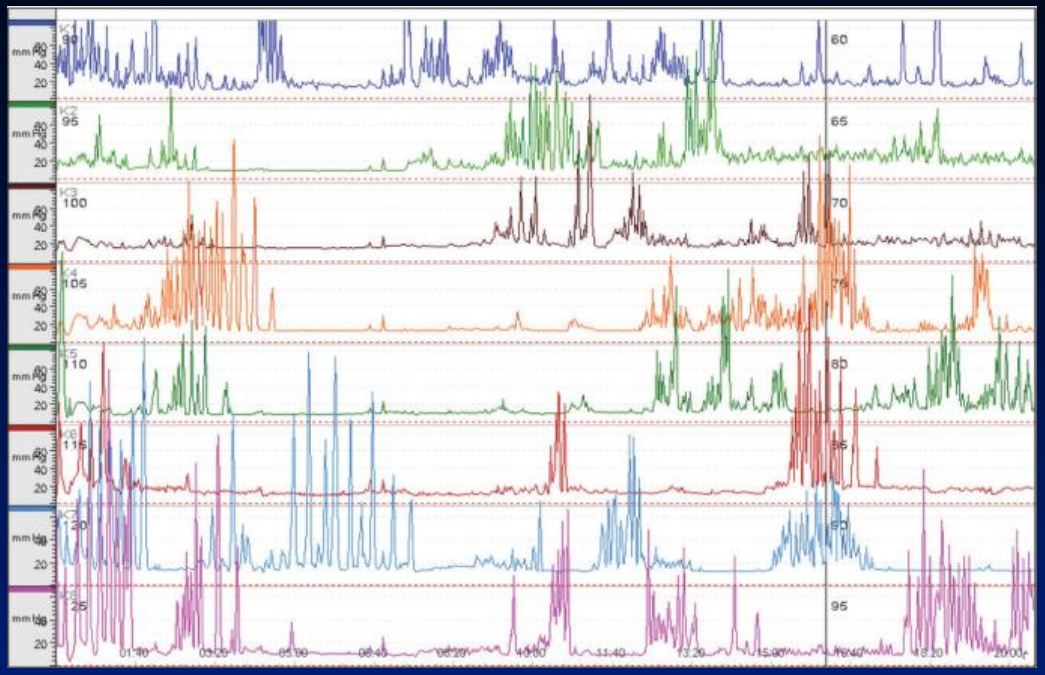
Small intestinal manometry

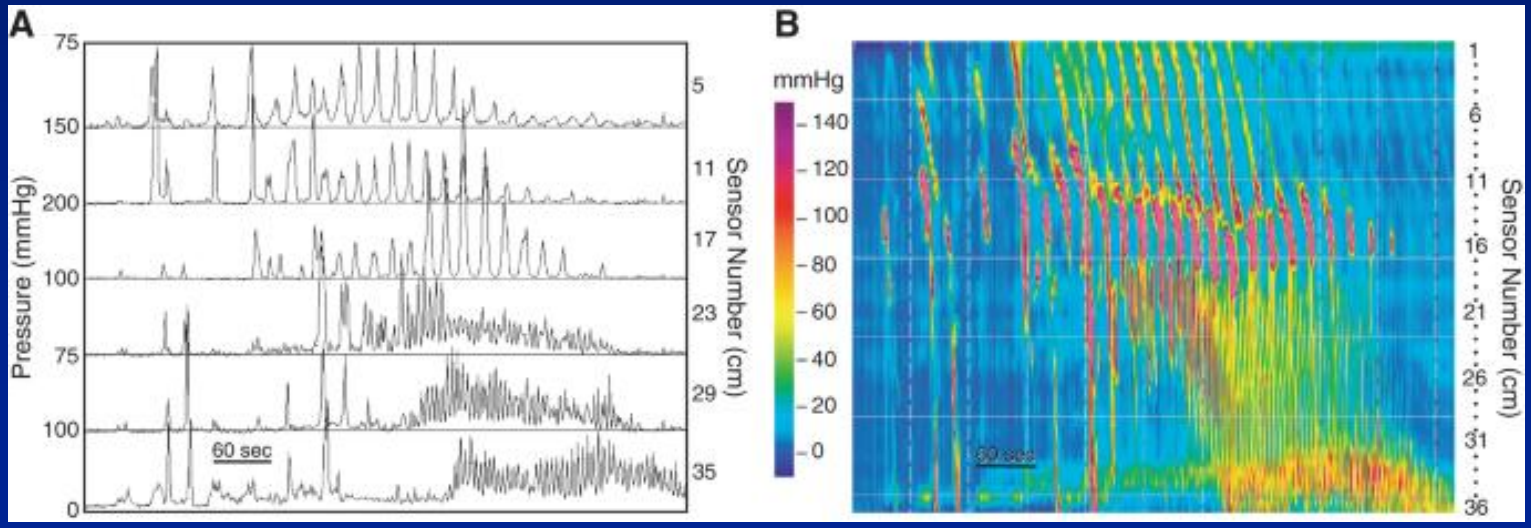


Postprandial small intestinal pressures



Andrews et al. 2000




A
Pressure (mmHg)
75
150
200
100
75
100
0
60 sec
5
11
17
23
29
35
Sensor Number (cm)
B
mmHg
140
120
100
80
60
40
20
0
1
6
11
16
21
26
31
36
Sensor Number (cm)

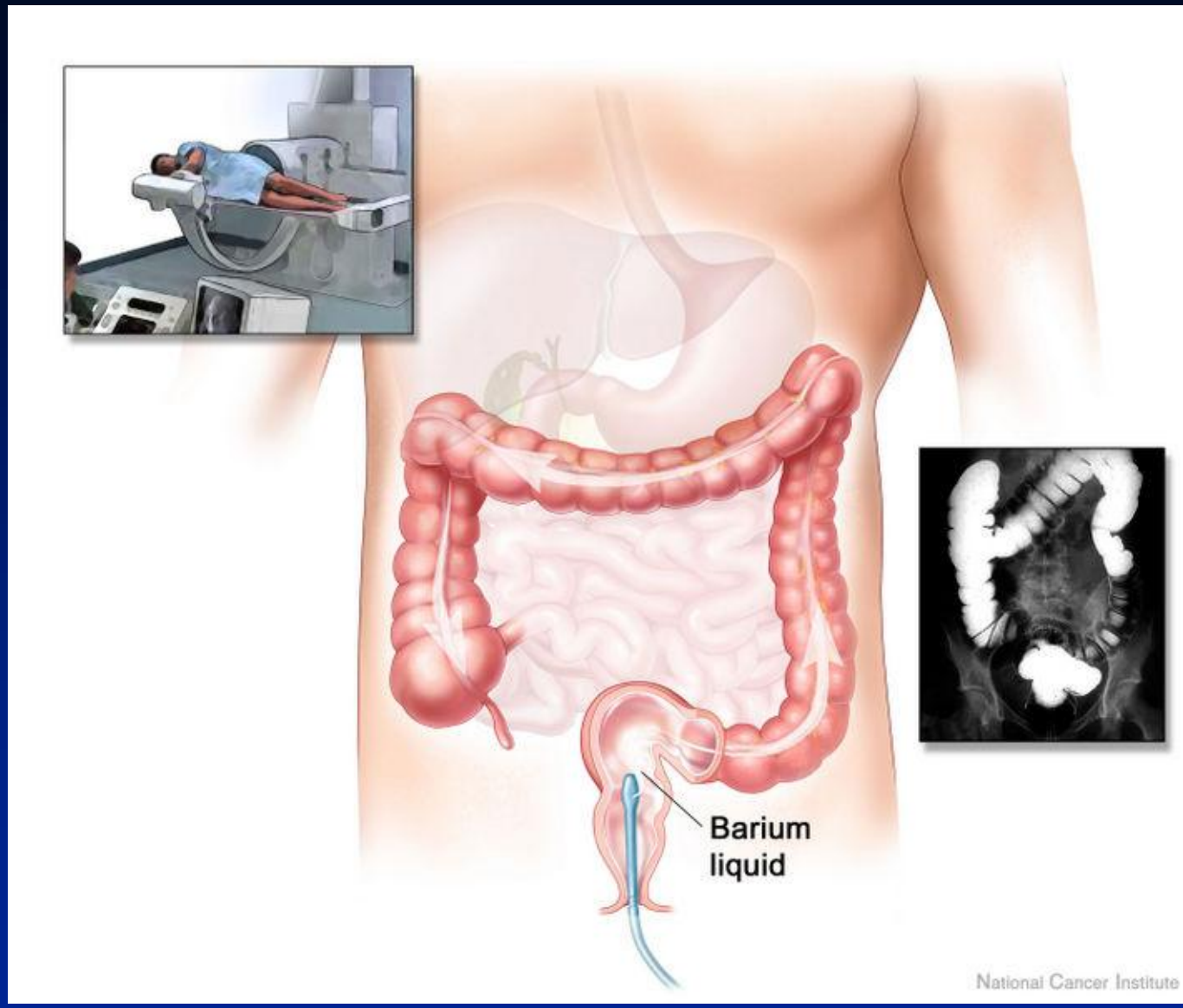
Motility

- **Testing of the large intestine**

Barium enema

- The method uses a contrast material that can be seen on x-ray (barium enema) to outline the anatomy of the colon.

- A barium enema consists of the injection of radiation-dense barium through the anus into the colon.


Barium
liquid
National Cancer Institute

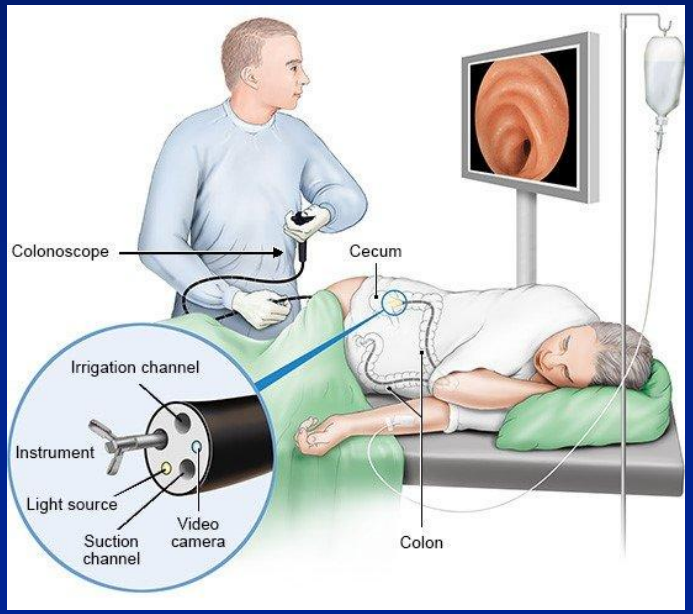

EVAC

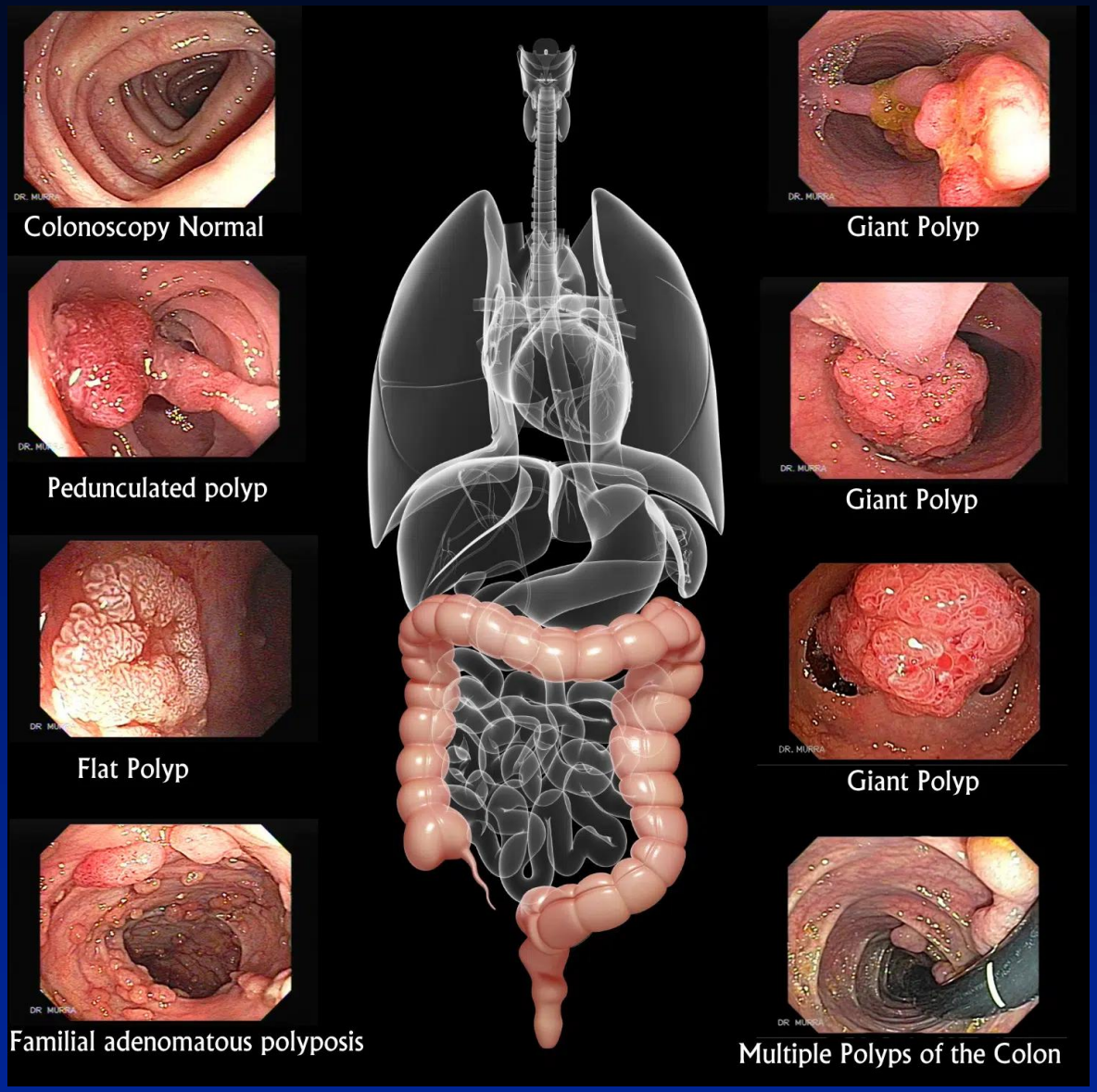
Sigmoidoscopy or colonoscopy

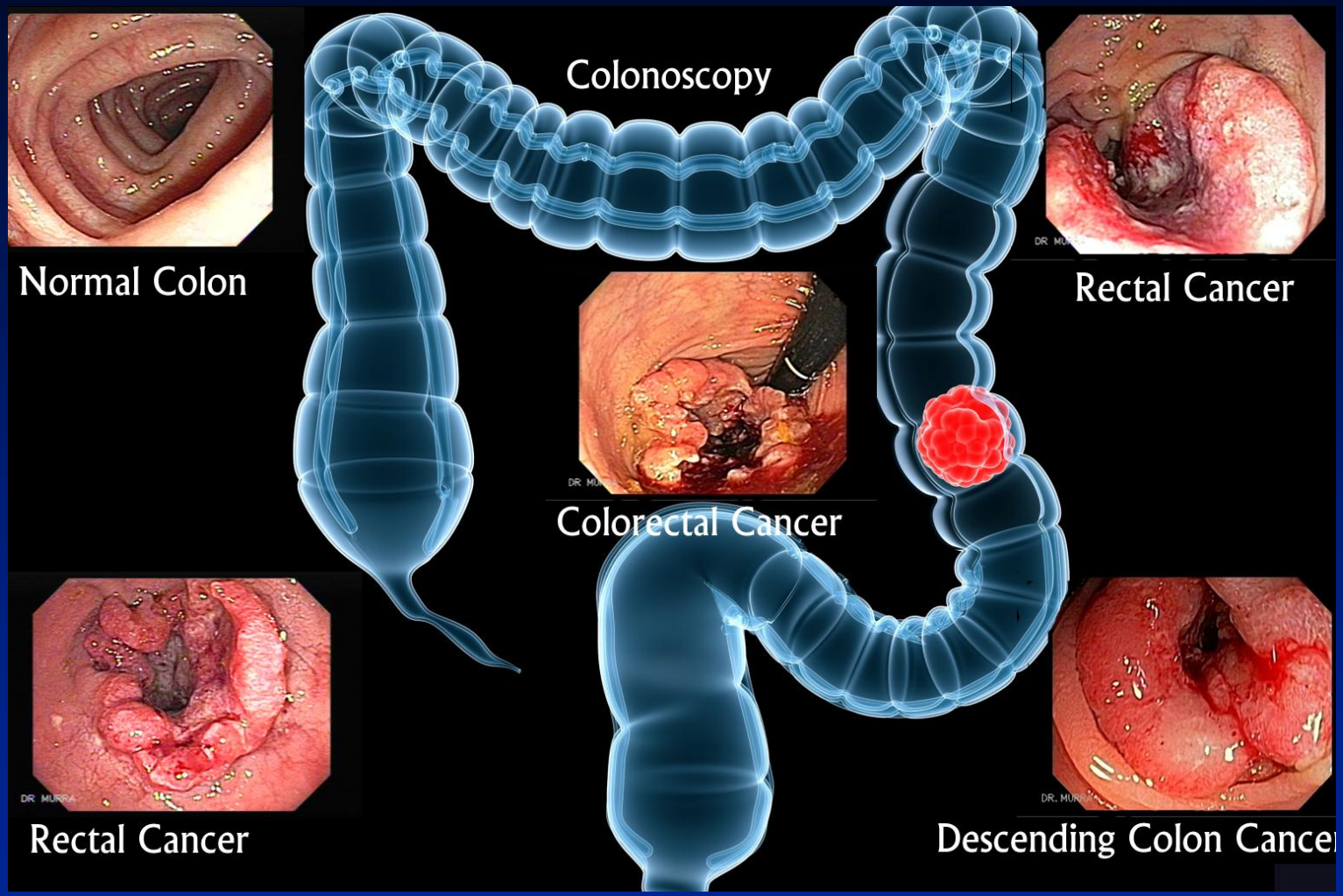
- Use a thin flexible tube with a video camera at its tip;

the tube is slowly inserted into the rectum and lets a doctor view the inside of the rectum and colon (sigmoidoscopy or colonoscopy).


doktor.is


Colonoscope
Cecum
Irrigation channel
Instrument
Light source
Suction channel
Video camera
Colon


Colonoscopy Normal
Pedunculated polyp
Flat Polyp
Familial adenomatous polyposis
Giant Polyp
Giant Polyp
Giant Polyp
Multiple Polyps of the Colon


Colonoscopy
Normal Colon
Rectal Cancer
Colorectal Cancer
Rectal Cancer
Descending Colon Cancer

Colonic transit time (sitzmark study)

- A simple but effective method of studying how well the bowel propels food along.

- Three capsules containing small markers are swallowed, one on each of three successive mornings (Days 1, 2 & 3).

-On the following day (Day 4) and three days later (Day 7) a plain x-ray of the abdomen is taken.

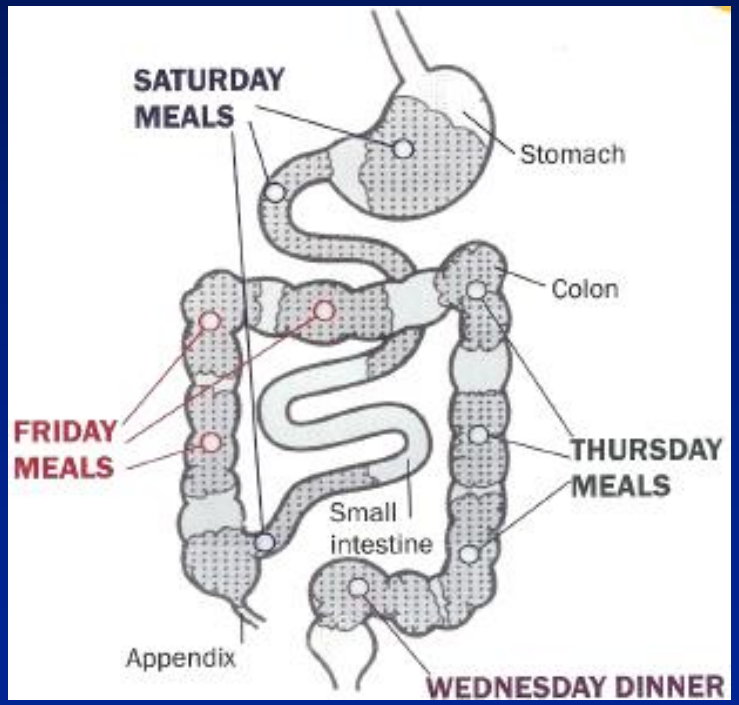
Colonic transit time (sitzmark study)

- All of the markers seen on the x-rays of each day are counted and added together.

- This number is the total transit time.

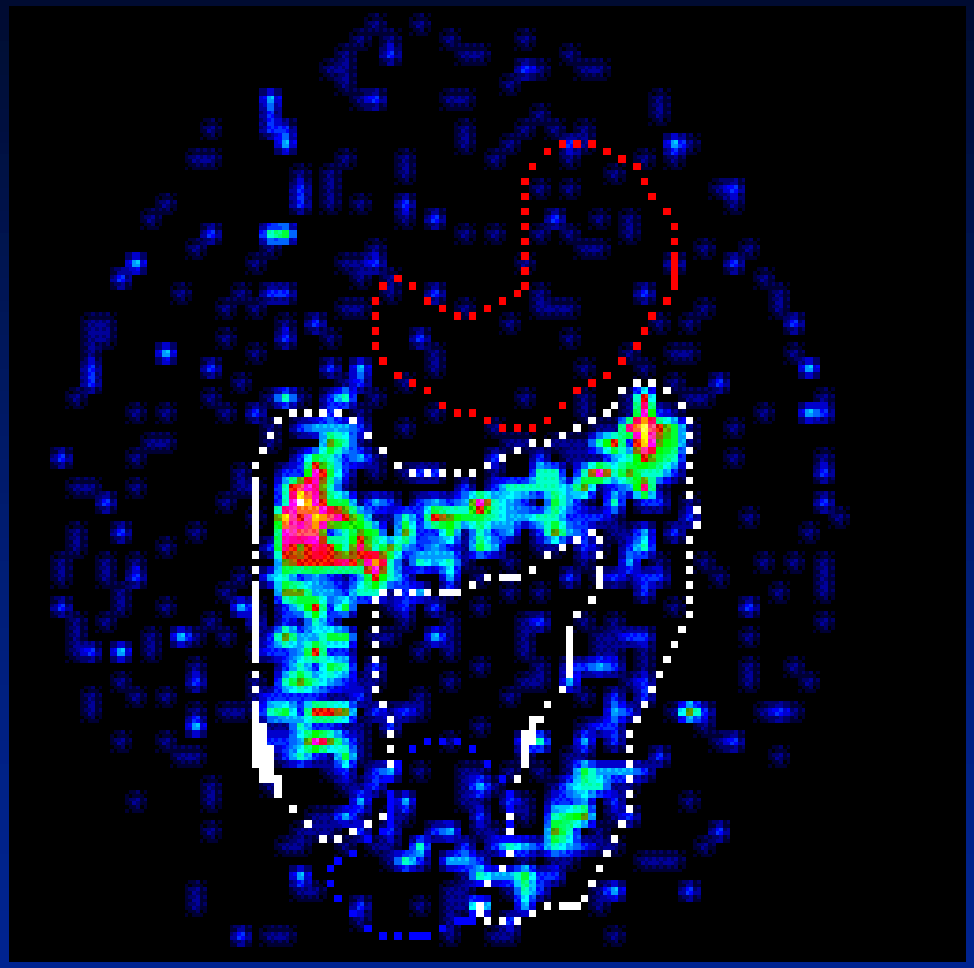
- This test is very useful for detecting different types of constipation.


Kolomark™
Sitzmarks®


SATURDAY MEALS
Stomach
Colon
FRIDAY MEALS
THURSDAY MEALS
Small intestine
Appendix
WEDNESDAY DINNER

Scintigraphic emptying and transit

- The emissions from the isotope are picked up by a special camera and the data is analyzed by a computer.



Motility

- **Testing of Anorectal and Pelvic Floor area**

  Defecography

  Manometry

Defecography

-The rectum is filled with a semi-solid paste with a consistency of soft stool containing contrast.

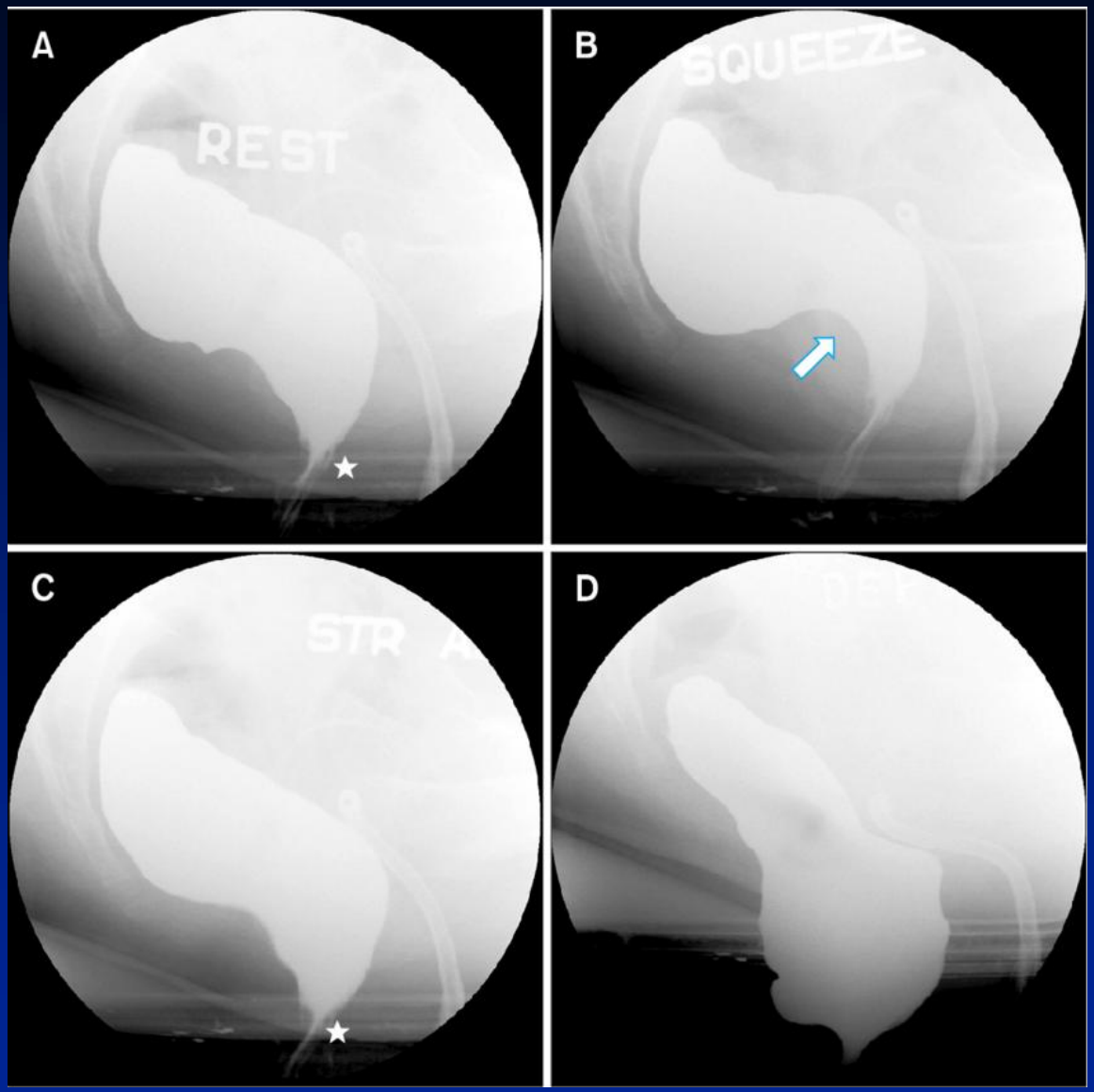
-The individual sits on a commode within an x-ray machine, then asked to relax, to squeeze, to tense the abdomen and to evacuate the material.

Defecography

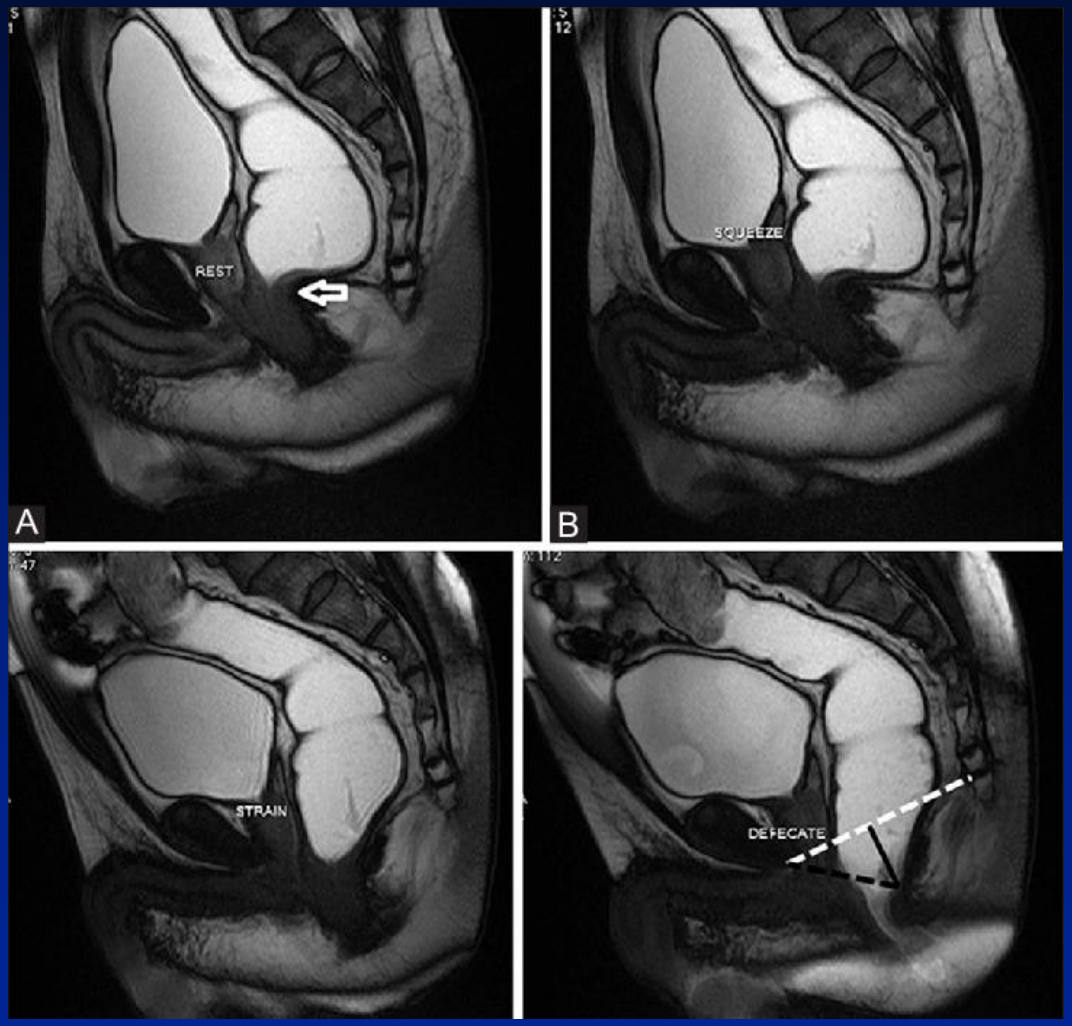
- X-ray films and video are taken during each phase.

-The study is then analyzed for anatomic defects such as rectal prolapse, anorectal angles and function of the puborectalis muscle

- This study is particularly useful when evaluating complaints of constipation and difficult evacuation.

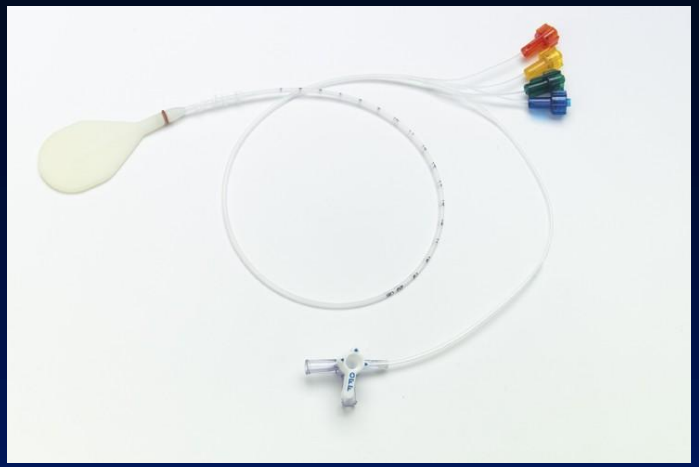

A
REST
B
SQUEEZE
C
D

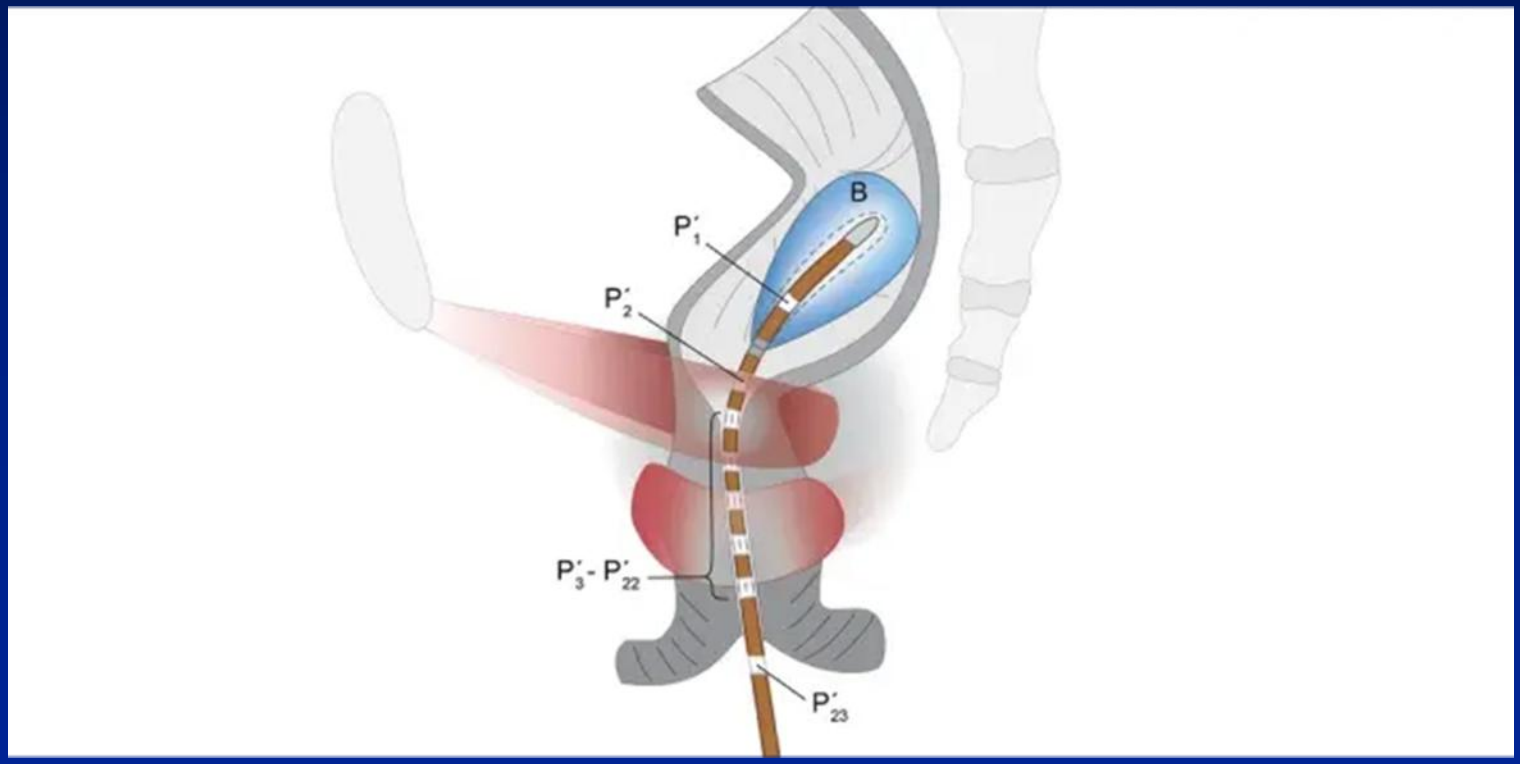
Magnetic resonance imaging (MRI) defecography

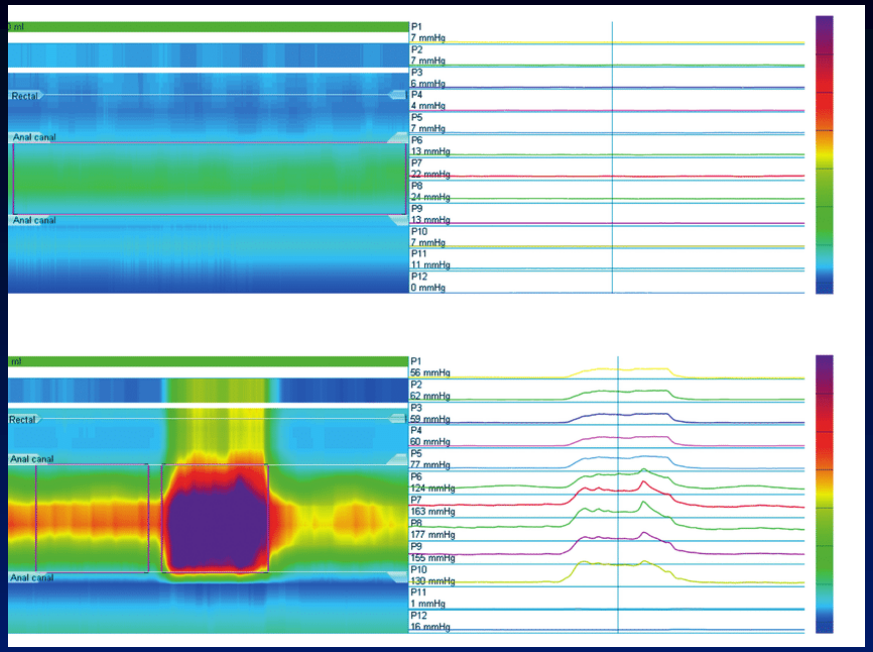


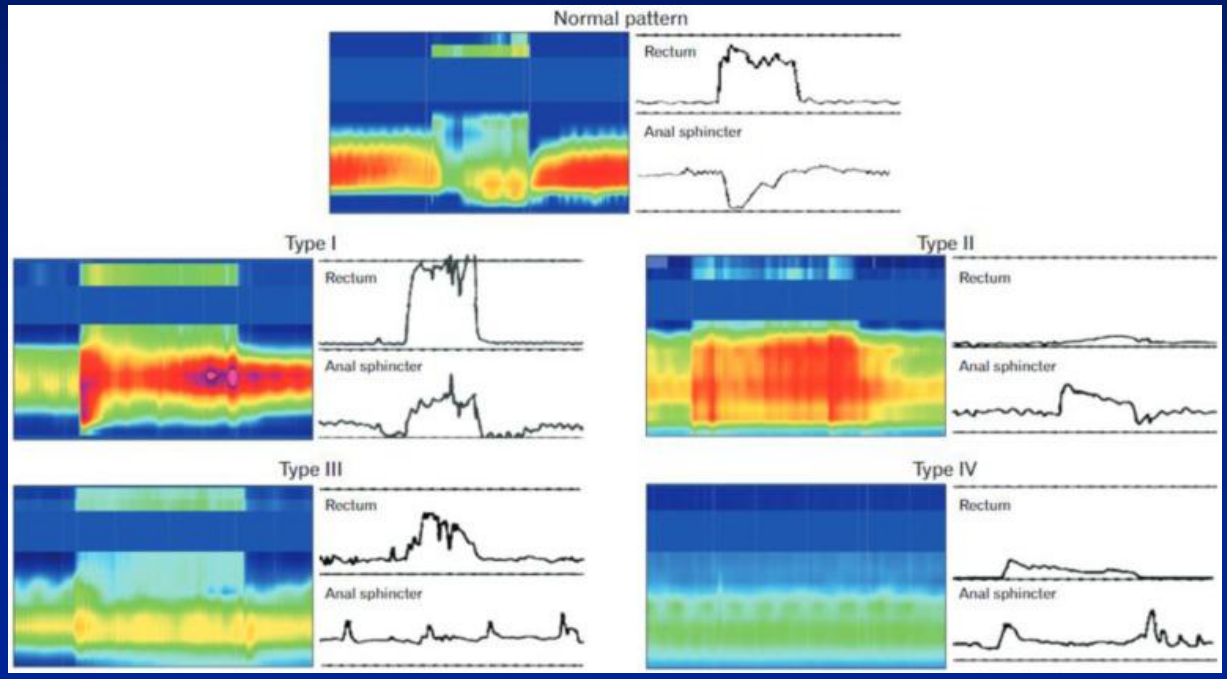
Anorectal manometry

- Tests the anal canal and provides information about the strength of the anal sphincter muscles and the sensation and reflex activity of the rectum.




B
P'1
P'2
P'3 - P'22
P'23


Rectal
Anal canal
Anal canal
P1 7 mmHg
P2 7 mmHg
P3 6 mmHg
P4 4 mmHg
P5 7 mmHg
P6 13 mmHg
P7 22 mmHg
P8 24 mmHg
P9 13 mmHg
P10 7 mmHg
P11 11 mmHg
P12 0 mmHg
Rectal
Anal canal
Anal canal
P1 56 mmHg
P2 62 mmHg
P3 59 mmHg
P4 60 mmHg
P5 77 mmHg
P6 124 mmHg
P7 163 mmHg
P8 177 mmHg
P9 155 mmHg
P10 130 mmHg
P11 1 mmHg
P12 16 mmHg


Normal pattern
Rectum
Anal sphincter
Type I
Rectum
Anal sphincter
Type II
Rectum
Anal sphincter
Type III
Rectum
Anal sphincter
Type IV
Rectum
Anal sphincter

Balloon capacity and balloon evacuation study

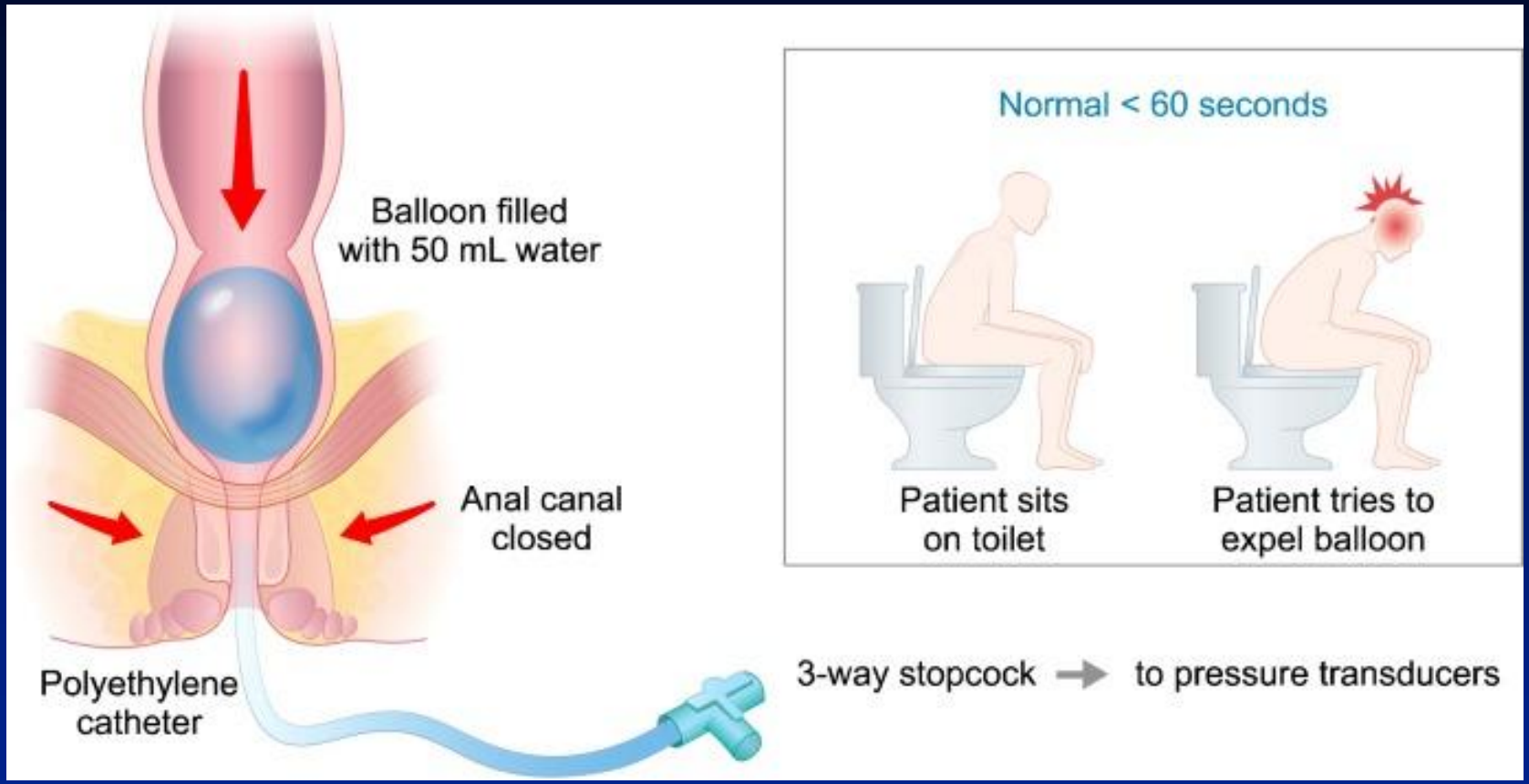
- Studies the function of the rectum and its ability to expand and contract.

-An empty, soft, latex balloon attached to a thin plastic catheter is lubricated and gently placed through the anus into the rectum.

-The balloon is slowly filled with warm water while measurements of volume and pressure are recorded.

A balloon evacuation study

- A study tests pelvic floor relaxation and opening of the anal canal. It is useful in determining how easy or difficult it is to pass a bowel movement.


Balloon filled
with 50 mL water
Anal canal
closed
Polyethylene
catheter
Normal < 60 seconds
Patient sits
on toilet
Patient tries to
expel balloon
3-way stopcock
to pressure transducers

Secretion

- **Urease test**
- **Fecal elastase**
- **Hydrogen breath test**

Urease test

- Used for the presumptive evidence of the presence of *Helicobacter pylori* in tissue biopsy material.

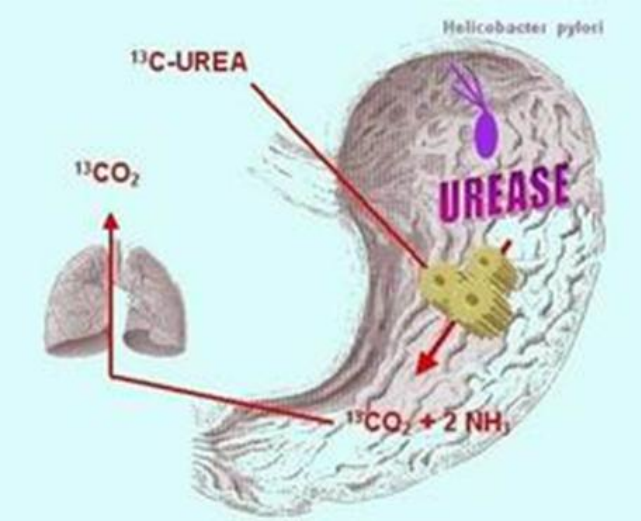
- A positive urease test is considered presence of *Helicobacter pylori*.

Urea breath test

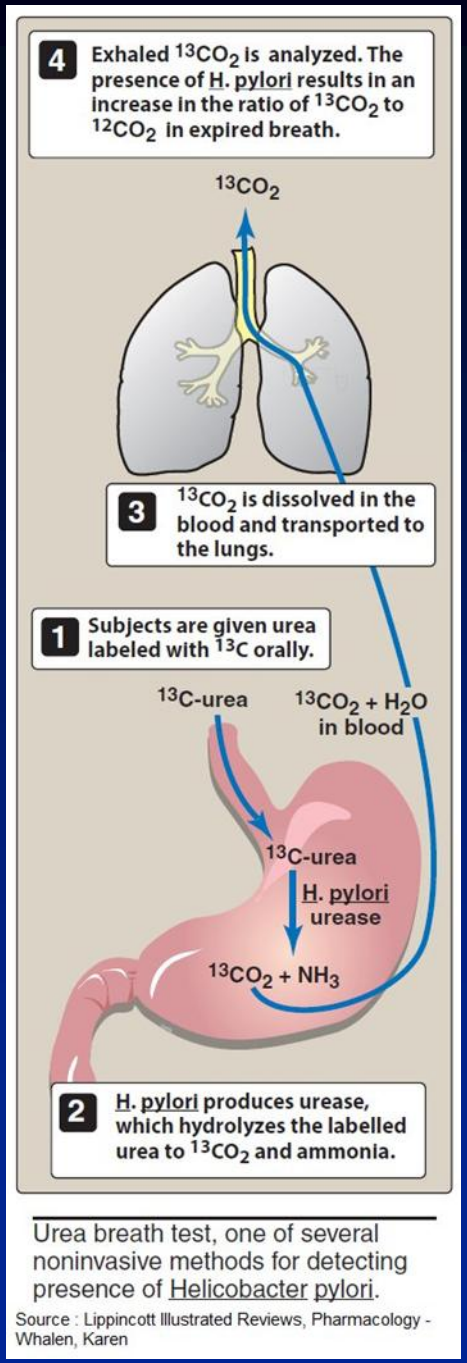
- A common noninvasive test to detect *Helicobacter pylori* also based on urease activity.

- This is highly sensitive and specific test.

- Patient ingests radioactively labeled (13C) Urea.



- If infection is present, the urease produced by *Helicobacter pylori* hydrolyzes the urea to form ammonia and labeled bicarbonate that is exhaled as CO_2.



Urea breath test, one of several noninvasive methods for detecting presence of Helicobacter pylori.

Source : Lippincott Illustrated Reviews, Pharmacology - Whalen, Karen

Fecal elastase

- Evaluate exocrine pancreatic secretion

- Measure elastase in feces

- Normal > 200 µg/g stool if not pancreatic insufficiency

Digestion

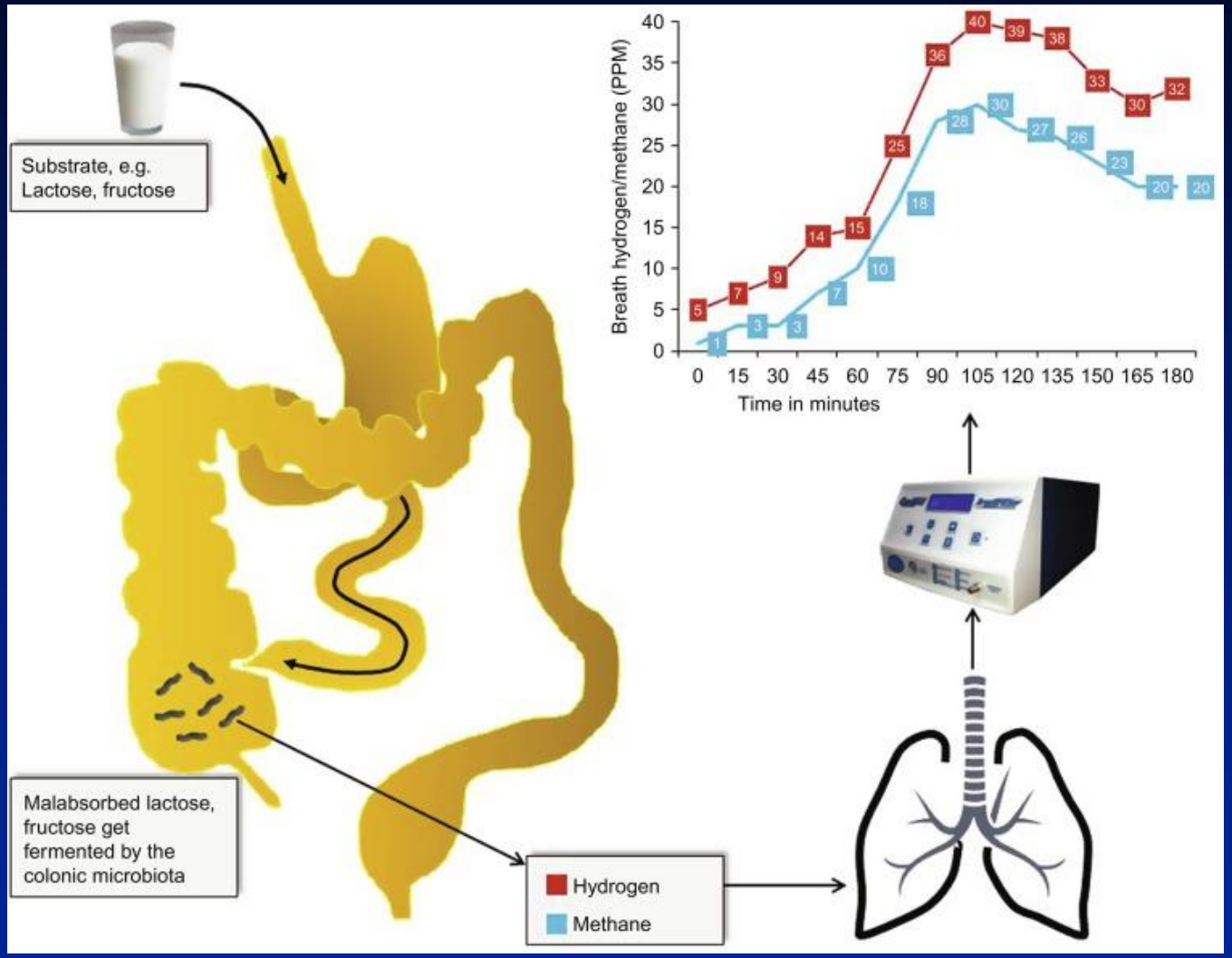
- **Hydrogen breath test**

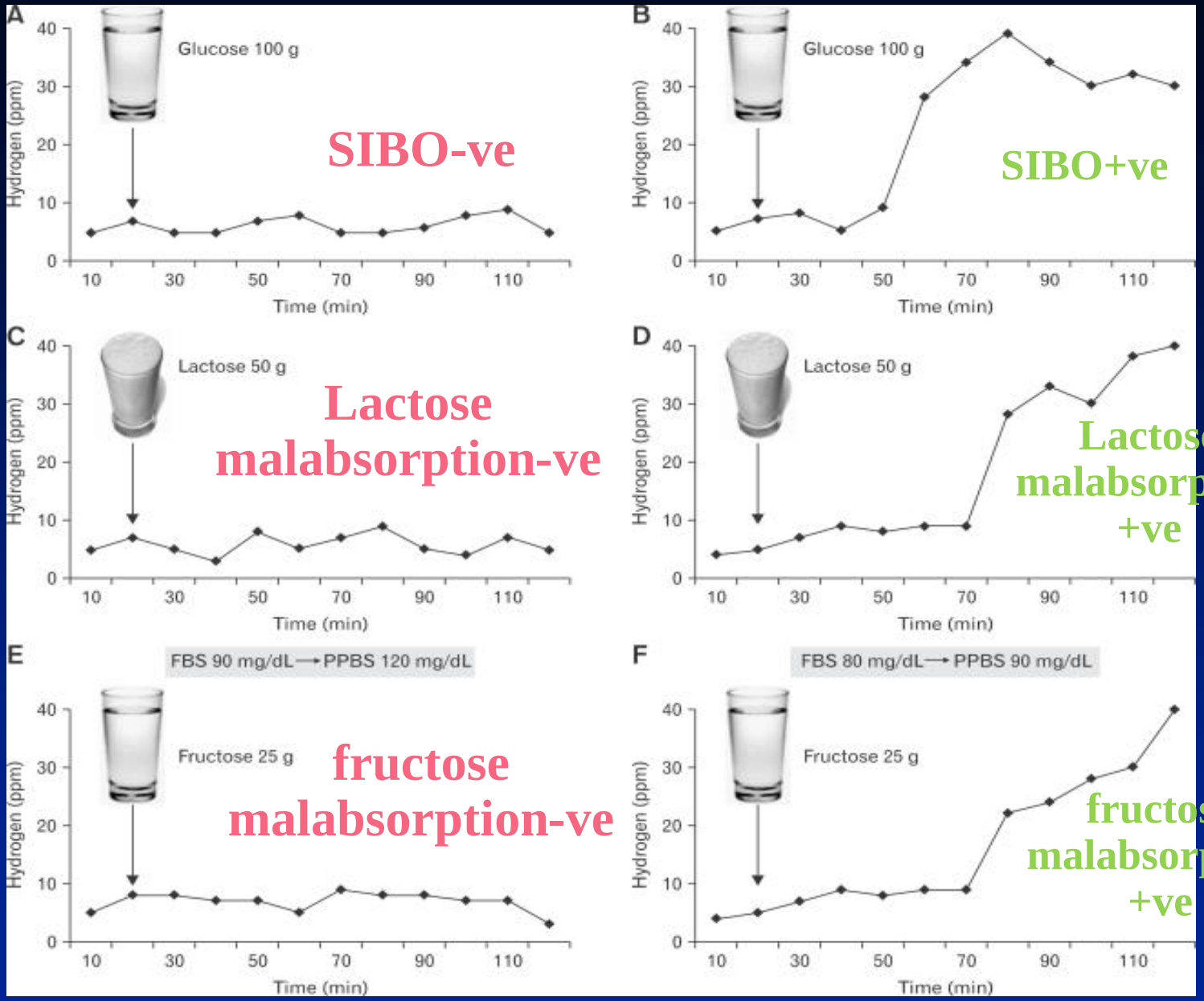
- **This test help to diagnose either intolerance to sugars or small intestinal bacterial overgrowth (SIBO).**

- **The test measures how the amount of hydrogen present in the breath changes after consuming a sugar solution.**

- **The patient drinks a sugar solution and breathes into a bag every 15 minutes for two hours.**

Hydeogen breath test




A
Glucose 100 g
SIBO-ve
B
Glucose 100 g
SIBO+ve
C
Lactose 50 g
Lactose malabsorption-ve
D
Lactose 50 g
Lactose malabsorption +ve
E
FBS 90 mg/dL → PPBS 120 mg/dL
Fructose 25 g
fructose malabsorption-ve
F
FBS 80 mg/dL → PPBS 90 mg/dL
Fructose 25 g
fructose malabsorption +ve
Hydrogen (ppm)
Time (min)
0
10
20
30
40
10
30
50
70
90
110

Absorption

- **Schilling test**
- **Fecal fat**
- **Intestinal mucosal biopsy**

Schilling test

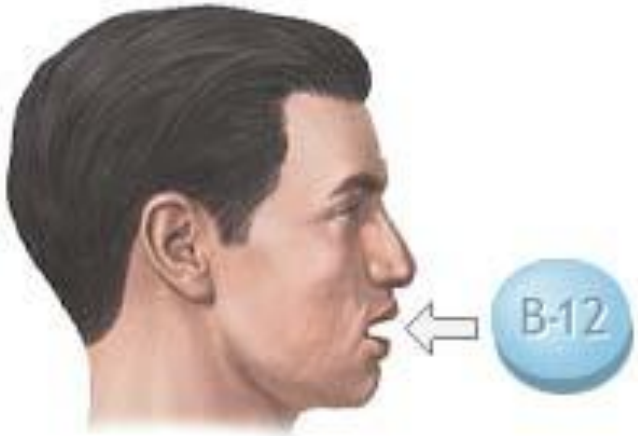
Stage 1: oral vitamin B_{12} plus intramuscular vitamin B_{12}

-In the first part of the test, the patient is given radiolabeled vitamin B_{12} to drink or eat.

(The most commonly used radiolabels are ^{57}Co and ^{58}Co).

-An intramuscular injection of unlabeled vitamin B_{12} is given an hour later.

Injection of nonradioactive vitamin B12 given



Radioactive B12 ingested

Urine samples are collected

Schilling test

The purpose of the single injection is to

- temporarily saturate B_{12} receptors in the liver with enough normal vitamin B_{12} (to prevent radioactive vitamin B_{12} binding in body tissues (especially in the liver))

-So that if absorbed from the G.I. tract, it will pass into the urine.

-The patient's urine is then collected over the next 24 hours to assess the absorption.

Schilling test

Normally, the ingested radiolabeled vitamin B_{12} will be absorbed into the body.

Since the body already has liver receptors for transcobalamin/vitamin B_{12} saturated by the injection, much of the ingested vitamin B_{12} will be excreted in the urine.

A normal result shows at least 10% of the radiolabeled vitamin B_{12} in the urine over the first 24 hours.

Schilling test

- A normal result shows at least 10% of the radiolabeled vitamin B_{12} in the urine over the first 24 hours.

- In patients with pernicious anemia or with deficiency due to impaired absorption, less than 10% of the radiolabeled vitamin B_{12} is detected.

Schilling test

Stage 2: vitamin B_{12} and intrinsic factor

-If an abnormality is found, i.e. the B12 in the urine is only present in low levels, the test is repeated,

-This time with additional oral intrinsic factor.

- If this second urine collection is normal, this shows a lack of intrinsic factor production, or pernicious anemia.

Schilling test

- A low result on the second test implies abnormal

- intestinal absorption (malabsorption), which could be caused by coeliac disease, biliary disease, Whipple's disease, small bowel bacterial overgrowth syndrome, fish tapeworm infestation (Diphyllobothrium latum), or liver disease.

- Malabsorption of B_{12} can be caused by intestinal dysfunction

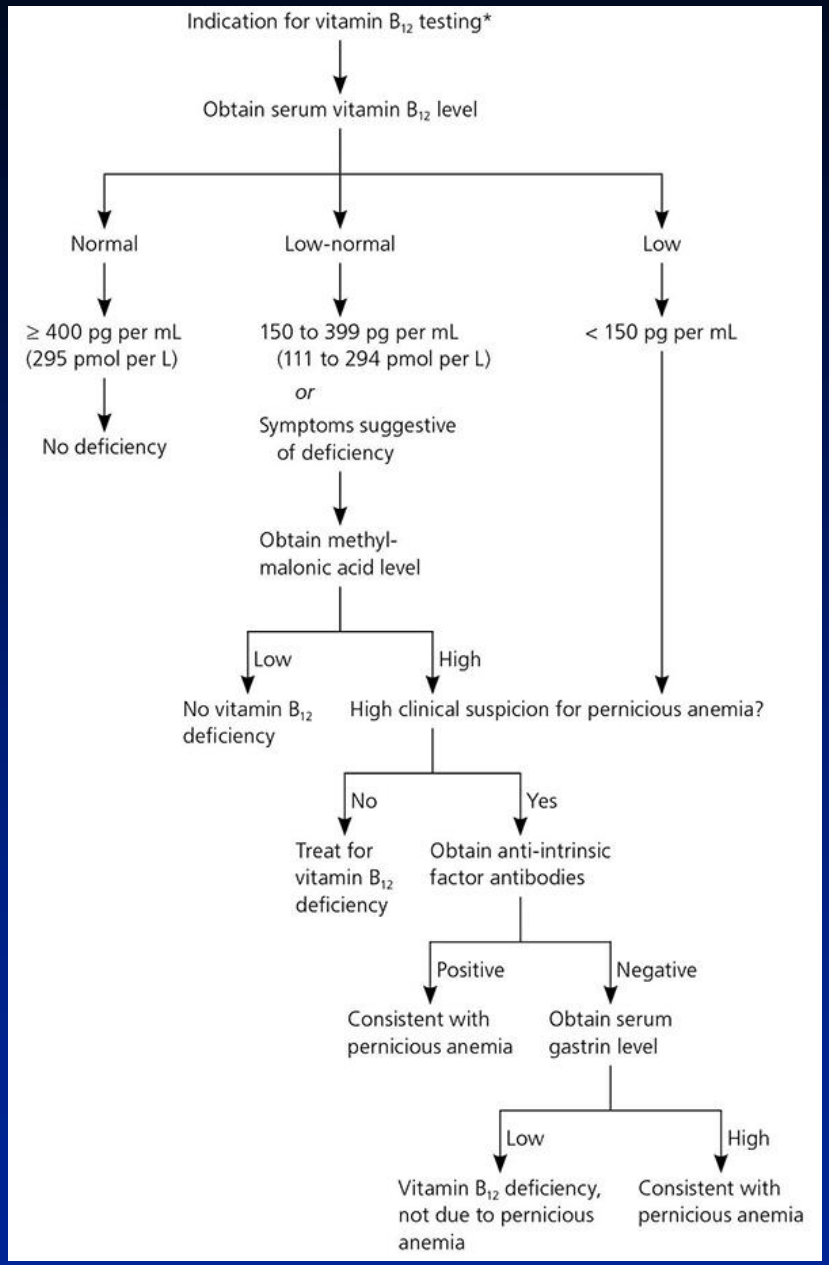
Schilling test

Stage 3: vitamin B_{12} and antibiotics
This stage is useful for identifying patients with bacterial overgrowth syndrome.

Stage 4: vitamin B_{12} and pancreatic enzymes
This stage, in which pancreatic enzymes are administered, can be useful in identifying patients with pancreatitis.

The Schilling test of vitamin B_{12} absorption is no longer available.

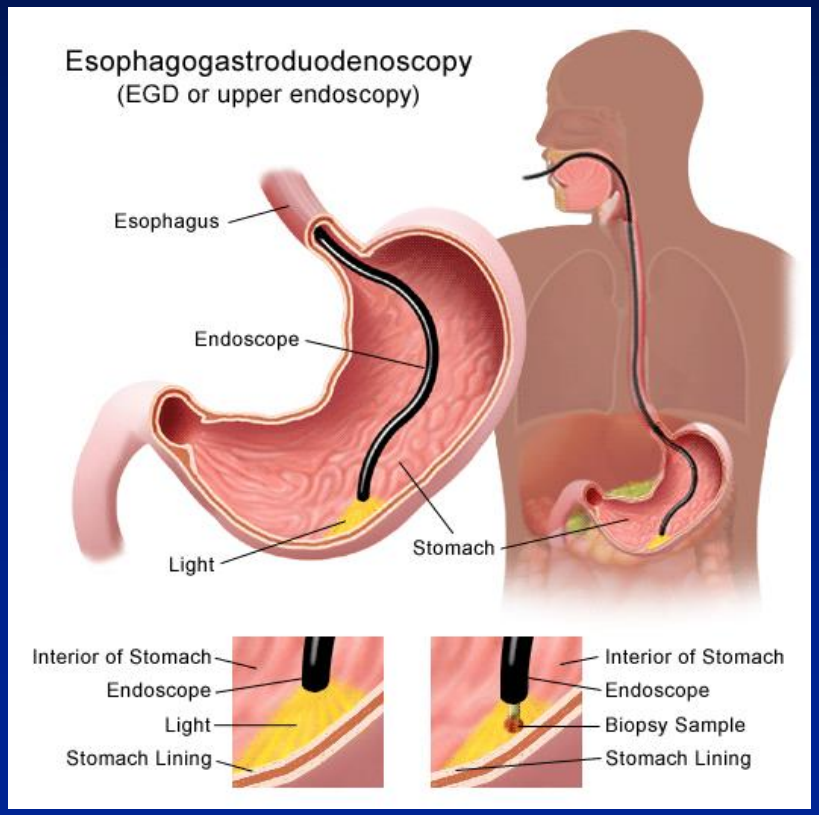
A potential replacement absorption test is under development wherein the increase in vitamin B_{12} absorption of holotranscobalamin is measured after several days of oral B_{12} loading



Serum vitamin B12 level test By Electrochemiluminescence immunoassay (ECLIA)

Biopsy

- A biopsy is a medical procedure that involves taking a small sample of body tissue so it can be examined under a microscope.



Glucose tolerance test

Fasting plasma glucose (measured before the OGTT begins) should be below 110 mg/dL.

-Fasting levels between 110 and 125 mg/dL are borderline ("impaired fasting glycaemia"),
-Fasting levels repeatedly at or above 126 mg/dL are diagnostic of diabetes.

A 2 hour OGTT glucose level below 140 mg/dL is normal, whereas higher glucose levels indicate hyperglycemia.

Glucose tolerance test

- Blood plasma glucose between 140 mg/dL and 200 mg/dL indicate "impaired glucose tolerance",

- Levels above 200 mg/dL at 2 hours confirms a diagnosis of diabetes.

Secretin test

- The secretin stimulation test evaluates how well the pancreas functions during digestion. It is also called the pancreatic function test.

-A doctor tests how the pancreas responds to secretin by inserting a tube through the nose into the esophagus and through the stomach until the tube reaches the duodenum.

-The doctor puts secretin into the body intravenously. If pancreatic fluid is released in response to the secretin, it will be removed through the tube within an hour or two.

Secretin test

- If the test results are abnormal,
: some degree of pancreatic insufficiency.

- Abnormal results may mean the patients have pancreatitis, or pancreatic cancer

- This test is invasive and conducted only when other evidence suggests you have pancreatic insufficiency.

Gastric acid stimulation test

- To evaluate gastric function by measuring the amount of acid as suctioned directly from the stomach.

- The complete gastric acid determination includes the basal gastric secretion test (measures acid secretion while in a fasting state) followed by the gastric acid stimulation test (measures the secretion of gastric acid for one hour after injection of pentagastrin or a similar drug that stimulates gastric acid output)

Gastric acid stimulation test

- The Gastric acid stimulation test is done when the basal secretion test suggests abnormalities in gastric secretion. It is normally performed immediately afterward.

Gastric acid stimulation test

- Elevated secretion may suggest different types of ulcers; when markedly elevated, Zollinger-Ellison syndrome is suspected.

- Depressed secretion can indicate gastric cancer, while complete absence of secretion (achlorhydria) may suggest pernicious anemia.

Future Studies

- **Genetic testing in gastroenterology**
- Genetic testing plays an important role in the diagnosis of many commonly encountered GI conditions including hereditary GI cancer syndromes, metabolic liver diseases, and inflammatory disorders.
- Genetic testing (ex. DNS sequencing) can be useful to screen pre-symptomatic relatives for disease.
- Tests that were once available only in research settings are increasingly available for clinical use.
- However, there are some limitations to genetic testing, and pre-test, counseling is recommended.
- The range of genetic test options will continue to increase in the future.

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