CLINICAL BIOCHEMISTRY OF THE GASTROINTESTINAL SYSTEM

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2 major functions – digestion and absorption of food

- **digestion -** dietary components are broken down to smaller molecules and
- **absorption** of these digested constituents from the gut then occurs

- Efficient ***gut motility*** is essential to bring about mixing and forward propulsion of the gut contents and processes leading to absorption are integrated by ***hormonal and neuronal mechanisms.***

Carbohydrate digestion and absorption

- **digestion** starts in ***the mouth*** with the ***salivary* α-amylase (α-1,4-glukosidase)**
- continues with ***pancreatic* α-amylase**, resulting in **formation of oligosaccharides** (especially **maltose**)
- these oligosaccharides are cleaved by **α1,4-glukosidase and disaccharidases** (lactase, maltase, isomaltase, sucrase, and trehalase) within ***the brush border of the enterocytes***
- the resulting **monosaccharides (glucose, galactose, and fructose) are then absorbed**

Protein digestion and absorption

- **digestion** starts in ***the stomach*** with protein denaturation by **HCl**. HCl also activates gastric pepsinogen to proteolytic **pepsin.**
- digestion is continued in ***the duodenum*** by ***proteases secreted from the pancreas***. These are **trypsin, chymotrypsin, elastase, and carboxypeptidase** which are all secreted as inactive proenzymes. An enterokinase from the brush border activates the trypsinogen to trypsin which then activates the other proenzymes.
- **peptidases within the brush border** complete the protein digestion and a combination of **amino acids, di- and tripeptides are absorbed**

Fat digestion and absorption

- **digestion** begins with **emulsification** resulting from ***chewing and stomach*** motility (the **bile stabilises** this emulsion)
- **pancreatic lipase** hydrolyses triglycerides to release free fatty acids and monoglycerides
- **pancreatic phospholipase and esterase** hydrolyse phospholipids and cholesterol esters, respectively
- products (**cholesterol, monoglycerides, and free fatty acids**), together with bile salts, form mixed **micelles**
- ***within enterocytes*** these are reformed into **chylomicrons** and **absorbed**

LABORATORY INVESTIGATION OF DISORDERS OF GASTROINTESTINAL FUNCTION

- **According to organs:** **stomach, pancreas, intestine**
- **According to nutritional components:** **saccharides, proteins, lipids, vitamins**

THE STOMACH

- ***gastroscopy***
- **pH-METRY**
- **pH electrode indwelling within the stomach**
- **monitoring of pH changes during 24 h**

THE STOMACH

- **Pentagastrin test** **(formerly used)**
- measurement of **HCl** in gastric fluid aspirated through a nasogastric tube **before and after admission of pentagastrin** (a synthetic analogue of gastrin; stimulates the gastric secretion)
- ***hypersecretion:*** **gastrinoma (Zollinger-Ellison sy), duodenal ulcer**
- ***hyposecretion:*** **atrophic gastritis, gastric ulcer, late gastric carcinoma**

THE STOMACH

- **Serum pepsinogen**
- **↓: atrophic gastritis and late gastric carcinoma**
- **↑: duodenal ulcer**

- **Plasma gastrin**
- **ref. value 5 - 115 ng/l**
- **↓: duodenal ulcer**
- **↑: gastrinoma, atrophic gastritis and during therapy by H2- and proton pump blockers**

THE STOMACH

- **Detection of Helicobacter pylori**

- **urease activity** ($H_2N\text{-}CO\text{-}NH_2 \xrightarrow{H_2O} 2\ NH_3 + CO_2$)

- breath test with C* labeled urea
- microbiological testings in stomach mucosa biopsy

THE PANCREAS

- **2 indications:**
- ***acute pancreatitis*** **(necrosis of the cells)**
- ***chronic pancreatitis*** **(disorder of the secretory function → maldigestion → malabsorption)**

Acute pancreatitis

- **Serum amylase**
- **physiological value AMS /S, P < 1.67 μkat/l**
- increases 5 and a number of times (100)
- maximal activity within 24 - 48 h, returns within 72 hours
- **pancreatic izoenzyme** improves the diagnostic specificity **- 0,2 - 1 μkat/l**
- **activity /U < 7,67 μkat/l**

Acute pancreatitis

- **Serum lipase**
- **physiologically < 1 or 3 μkat/l (according to methodology)**
- less sensitive
- more specific (isn`t produced by the salivary glands)

- **Plasma trypsin**
- **ref. value /P ~ 272 μg/l**

Chronic pancreatitis

- *direct tests of pancreatic function* - analysis of fluid aspirated from the duodenum
- **secretin-cholecystokinin test**
- or analysis of stools
- ***elastase***

- *indirect tests of pancreatic function* - assessment is made without intubation
- **NBT-PABA test**
- **fluorescein-dilaurate test**
- **breath tests**

Secretin - CCK test (formerly used)

- secretin stimulates the pancreatic fluid secretion
- CCK = pancreozymin (PZ) increases the pancreatic enzymes secretion and stimulates the gall-bladder contraction
- **assessment of total fluid volume and HCO_3^- amount after secretin administration**
- **assessment of pancreatic enzymes activity after administration of CCK**
- all measured parameters are **decreased in chronic pancreatitis**

NBT-PABA test

- **N-benzoyl-tyrosyl-p-aminobenzoic acid** is administred with meal in order to stimulate the pancreatic secretion
- NBT-PABA is split by **chymotrypsin** to yield ***PABA*** which is absorbed and excreted ***in the urine***
- **PABA / S > 25 μmol/l**
- **PABA / U > 30% of administered dose**

Fluorescein - dilaurate test

- fluorescein-dilaurate is hydrolysed by the pancreatic **cholesterolesterase** and ***fluorescein*** is absorbed and excreted ***in the urine***

Other tests of pancreatic function

- ***trypsin /S*** **after meal stimulation (↓)**
- ***chymotrypsin / faeces*** **(↓)**
- ***elastase / faeces*** **(<100 μg/g, ELISA, instead of SCCKT)**

Breath tests of pancreatic function

- **given substrate cleaved by lipase, cholesterol esterase or chymotrypsin, absorbed and metabolized → CO_2**
- **substrates used: triglycerides, cholesterol esters, acyl-Tyr-PABA**
- **for example Triolein test = MTG test (mixed triglyceride)**
- **measurement of CO_2^* in breath**

THE SMALL INTESTINE

- **Tests for malabsorption of**
  - **fats**
  - **carbohydrates**
  - **vitamin B_{12}**

Fat malabsorption

- **Faecal fat excretion**
- **replaced by:**

- **Triolein breath test = MTG test**
- **labeled triolein (^{14}C) is absorbed and metabolised, *$^{14}CO_2$ is measured in breath***

- **Serum β-carotene**
- **physiological value = 0,7 - 2,9 mg/l**
- **severe malabsorption < 0,3 mg/l**

Carbohydrate malabsorption

- **Xylose absorption test**
- administration of xylose (25 g p. o., children 5 g)
- assessment of **xylose /S after 2 hours > 300 mg/l**
  1 h children > 200 mg/l
- assessment of **xylose amount in 5-hour urine collection**
  > 20% administered xyl (both adults and children)

Carbohydrate malabsorption

- **Disaccharidases deficiencies tests**
- **enzymes within the brush border of the enterocytes:**
- ***lactase:*** **lac → gal + glc**
- ***saccharase:*** **sac → glc + fru**

- ***maltase:*** **mal → glc + glc**
- ***izomaltase:*** **→ glc + glc**
- ***trehalase:*** **tre → glc + glc**

Carbohydrate malabsorption

- **Disaccharidase deficiencies tests**
- administration of the given disaccharide
- **evaluation: a) measuring of the blood glucose response (↓)**
- **b) measuring of the faecal pH (↓)**
- **c) breath hydrogen test (its presence in expired air is a result of the bacterial fermentation of the unabsorbed sugar)**
- assessment of activity of the relevant disaccharidase in biopsy tissue may be helpful

Carbohydrate malabsorption

- ***Lactose* load test performance**
- measuring of **glc /P**
- ***lactose* administration** (50 g p. o., children older than 2 years 4 g/kg)
- measuring of **glc /P after 30, 60, 90, 120´**
- **next day administration of** 25 g **glc +** 25 g **gal**
- measuring of **glc /P after 30, 60, 90, 120´**
- **in healthy pac. ↑ glc /P more than > 1,1 mmol/l**
- **in deficiency** **lower ↑ after *lactose* admin.**
  normal ↑ after monosaccharides admin.
  rate of ↑ < 0,4
- false positive in DM and glc tolerance impairment

Protein malabsorption

- is not usually specifically investigated

- however there are **tests of protein-losing enteropathy:**
- **i.v. administration of radio-labelled protein** (^{51}Cr, ^{59}Fe or ^{131}I labelled albumin, dextran or polyvinylpyrolidon)
- **measurement of faecal radioactivity**
- **↑ if loss of proteins from the gut is present**

Other test of protein-losing enteropathy is:

Intestinal clearance of α1-antitrypsin

- **72 h collection of faeces** (storage -4°C or -20°C)
- **assessment of AAT/ faeces**
- **every day assessment of AAT /S**

- **clearance =** $\frac{V \cdot F}{S}$

V – Ø faeces volume, ml/d
F – Ø AAT /faeces, mg/d
S – Ø AAT /S, mg/d

- **physiologically < 35 ml/d**

LAMA-test

- **examination of intestinal permeability**

- **administration** of test solution with **lactulose and mannitol**
- **6 h collection of urine**
- **assessment of lactulose and mannitol /U**

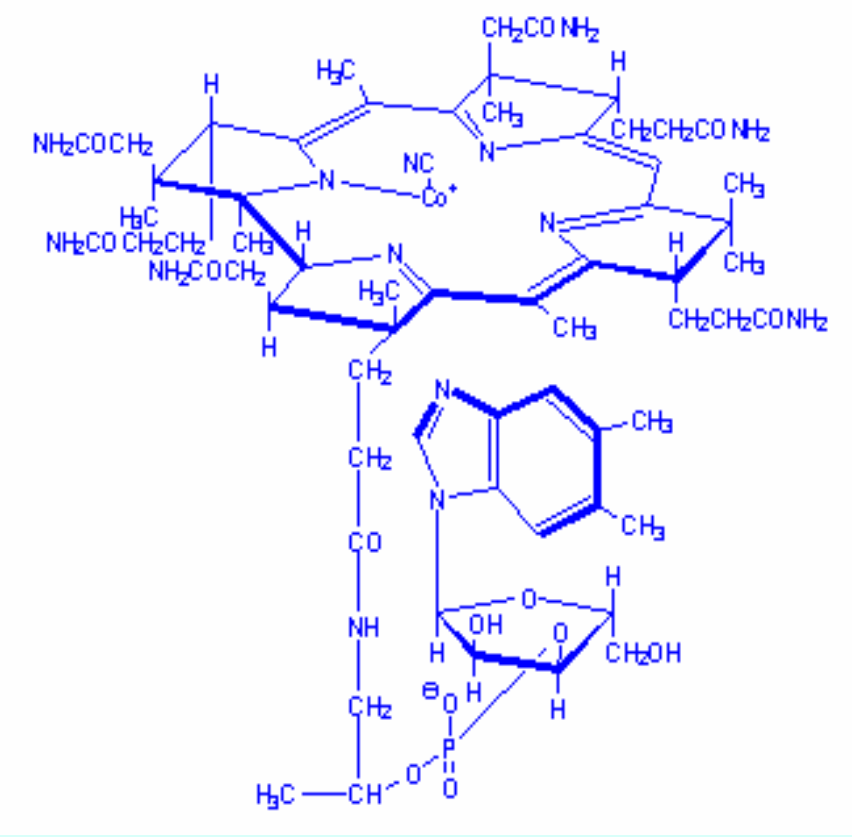
Vitamin B_{12} malabsorption

- **Schilling test**
- **examined in:**
- **↓ B_{12} /S**
- **suspicion of chronic atrofic gastritis** (insufficient production of intrinsic factor - IF)
- **suspicion of terminal ileus disease** (where the complex B_{12}-IF is absorbed)
- **pernicious anemia** (result of ↓ B_{12})

Schilling test with radio-labelled B_{12}

1. **administration of ^{57}Co or ^{58}Co labelled B_{12}**
2. **measuring of $*B_{12}$ /U in 24 h**

- **with and without oral administration of intrinsic factor**



Schilling test without radio-labelled B_{12}

1. measuring of **B_{12} /S**
2. **p.o. 1 mg B_{12}**
3. measuring of **B_{12} /S after 4 h**
4. **idem with simultaneous administration of 35 mg IF**

- **ref. value B_{12} /S = 220 – 1130 ng/l**
- **atrofic gastritis: ↓**
  after IF admin. normal
- **terminal ileus disease: ↓**
  after IF admin. ↓

Blood in stools tests

- **gFOBT (guaiac based faecal occult blood test)**
- **screening**
- **chemical demonstration of heme´s peroxidase activity:**

  achromatic chromogene $H_2A + H_2O_2 \rightarrow$ color chromogene A + 2 H_2O

- **cut-off of positivity = 5 mg Hb /g stools**
- **need of bloodless diet 3 days before the test performing**
- **bleeding may be intermitent → examination during 3 days**

Blood in stools tests

- **iFOBT (immunochemical Fecal Occult Blood Test)**

- **immunochemical demonstration of globin**
- **species specific → no need of the diet**

- **cut-off of positivity < 0,1 mg Hb /g stools**