

## Lecture-5

### Biochemical aspects of digestive disorders

Stomach is major organ of digestion and performs the following functions.

1. Stomach is a reservoir of ingested foodstuffs.
2. It has a great churning ability which promotes digestion.
3. Stomach elaborates HCl and proteases, which are responsible for the initiation of digestive process.
4. The products obtained in the stomach (peptides and amino acids) stimulate the release of pancreatic juice and bile.

#### Secretion of gastric HCl :

The parietal cell of gastric glands produce HCl. A unique enzyme  $K^+$  activated ATPase present in the parietal cells is connected with the mechanism of HCl secretion. The process involves an exchange of  $H^+$  ions (of the parietal cells) for  $K^+$  ions (of the lumen). This is coupled with the consumption of energy, supplied by ATP. The  $H^+$  are continuously generated in the parietal cells by the dissociation of carbonic acid. The bicarbonate ions liberated from the carbonic acid dissociation, enter the blood in exchange for  $Cl^-$  ions. The latter diffuse into the gastric lumen to form HCl. Gastric peptide hormone of gastro-intestinal tract stimulates HCl secretion.

Following a meal, there is a slight elevation in the plasma bicarbonate concentration which is linked with gastric HCl secretion. This is referred as alkaline tide.

#### **Tests to assess gastric function**

##### 1. Pentagastrin stimulation test:

Pentagastrin” is a Synthetic peptide which stimulates the gastric secretion on in a manner Similar to natural gastrin. The stomach contents are aspirated by Ryle’s tube in a fasting condition. This is referred to as residual juice. The gastric juice elaborated for the next one hour is collected and pooled which represents the basal secretion. Pentagastrin (5 pg/kg body weight) is now given to stimulate gastric secretion. The gastric juice is collected at 15 minute intervals for one hour. This represents the maximum secretion. Each sample of gastric secretion collected is measured for acidity by titration the samples with N/10 NaOH to pH 7.4. The end point may be detected by an indicator (phenol red) or a pH meter.

## Pancreatic function tests

The pancreas is a specialized organ with exocrine and endocrine functions. The exocrine functions involve the synthesis of pancreatic juice containing several enzymes and bicarbonate. The major enzymes of pancreatic juice are trypsin, chymotrypsin, Carboxy-peptidase, amylase and lipase.

### **Pancreatic enzymes in serum**

Serum lipase and amylase are commonly employed to assess pancreatic function. Both these enzymes activities are elevated in acute pancreatitis, obstruction in intestine and/or pancreatic duct.

### **Determination of Serum Amylase Activity by Sterkel and Kirsner method:**

**Principle:** Starch is incubated with serum at a controlled pH for a standard period of time. The serum amylase activity is then destroyed by the addition of tungstic acid and the reducing substances present before and after incubation determined by the method of Folin and Wu.

**Procedure:** Take two test tubes (20 X 200 mm) and place 5 ml of starch solution and 2ml of sodium chloride solution. In one tube place 1 ml of non-hemolysed serum and mix well. Incubate both the tubes at exactly 37°C for exactly 30 minutes. Place 3 ml of distilled water and 8 ml of 0.085 N Sulphuric acid into each tube. Add 1ml of non-hemolyzed serum to the second tube (control) and mix well. Add 1ml of sodium tungstate to both the tubes, mix and let stand for several minutes until precipitation is complete. Filter and determine the reducing sugar content on 2ml of each filtrate, using Folin-Wu method.

### **Calculation:**

$$\begin{aligned} & \text{mg\% sugar in test} - \text{mg\% sugar in control} \times 2 \\ & = \text{Serum amylase activity in somogyi units/100 ml serum} \end{aligned}$$

**Interpretation:** The normal range for serum amylase activity varies with the method used for determining reducing sugars. Serum amylase values rise within several hours after the onset of acute pancreatitis, reaching peak values within 24 hrs and returning to normal in 3 to 6 days. Pancreatitis may be extra pancreatic in origin as in acute appendicitis or biliary obstruction or intrapancreatic as in cancer of hepato pancreatic ampulla. Increased values are observed in appendicitis. In chronic pancreatitis, acute attacks are associated with similar elevation but the return to normal is often slower. After repeated acute attacks in chronic pancreatitis, destruction of tissue may become widespread as to prevent measurable production of the enzyme. In these instances increased serum amylase activity may not be observed.

### **Determination of Serum Lipase Activity by Cherry and Crandall Method:**

**Principle :** Serum is incubated with an olive oil emulsion and fatty acid produced are titrated with sodium hydroxide.

**Procedure :** Into each of two tubes or flasks, place 3ml distilled water and 1ml serum. Place one tube (control) into boiling water for 5 minutes and cool. Add 0.5 buffer solution and 2ml of olive oil emulsion to both tubes, shake well and incubate at 37°C for 24 hrs. Then add 3ml of 95% alcohol and 2 drops of phenolphthalein indicator and mix. Titrate each tube with 0.05N sodium hydroxide until the appearance of a permanent pink color (pH, 10).

#### **Calculation :**

$$\text{ml NaOH for unknown} - \text{ml NaOH for control} = \text{units lipase activity/ml serum}$$

**Interpretation:** The normal serum lipase activity by this method is upto 1.5 units. The determination of serum lipase activity is complementary to the serum amylase determination, since elevations of serum lipase disappear much more slowly. Greater organ specificity is achieved using olive oil emulsion, thus permitting differentiation between pancreatitis and appendicitis. Elevations of serum lipase often occur in chronic pancreatitis after the condition has reached a state where elevations of serum amylase activity no longer occur.

**Basal Acid Output (BAO) :** Refers to the acid output (millimole/hour). Under the basal conditions i.e. basal secretion. In normal conditions it is 4-10 m mole/hr.

**Maximal Acid Output (MAO) :** Represents the acid output (millimole/hour) after the gastric stimulation by pentagastrin i.e. maximum secretion. In normal conditions it is 20-50 m mole/hr.

#### **Insulin test meal :**

This is also known as Hollander's test it is mainly done to assess the completeness of vagotomy (vagal resection). Insulin (0.1 unit/kg body weight) is administered intravenously, which causes hypoglycemia (blood glucose about 40 mg/dl), usually within 30 minutes in normal persons. If the vagotomy operation is successful, insulin administration does not cause any increase in the acid output compared to the basal level.