Insulin deficiency

- There are tissues in which insulin doesn't facilitate glucose uptake, and these are vital organs such as: brain, kidney tubules, intestinal mucosa and red blood cells.
- Half lie of insulin:1 hour to 6 minutes.
- The homeostasis of glucose: 90% of population have glucose concentration in blood ranging between 90-100 mg/dL, rare below that up to 70 mg/dL, very rare above 100 till 110 mg/dL (there is something wrong in the metabolism of glucose).
- Brain doesn't need insulin, 30-40% of glucose transferred to adipose tissue, 5 % to the liver and the remaining to the muscle and other tissues.
- There's no glucose in urine unless glucose concentration exceeded 180 gm\dl which is the renal threshold leading to glycosuria.
- Deficiency of insulin lead to abnormality or disorder in metabolism of carbohydrates, lipids and proteins, the combination of the disorders of carbohydrate, fat and protein metabolism at diabetic leads to specific micro vascular lesion in the retina, renal glomerulus and peripheral nerves.
- National health and nutrition organization survey: 2/3 of the adults (men and women) in USA with diagnosis of diabetes have Body Mass Index (BMI) more than 27 (high percentage in obese or individuals).
    - Symptoms of diabetic patients (used for diagnosis of diabetes) :
    1. Urination.
    2. Increased food consumption.
    3. Weight loss.

❖ The effect of insulin deficiency on carbohydrate metabolism :

- If you consider a patient with 300 mg/dL glucose concentration there will be :
    - Hyperglycemia and there is a disorder in blood glucose homeostasis.
    - However brain isn't affected it takes glucose spontaneously.
    - Entering to adipose tissue is affected.
    - Some enzymes are activated.
    - Glucose coming from liver more than that transferred into the liver.
    - Glucose transferring into muscles and other tissues are affected.
    - Glucose will be seen in urine (glycosuria) because concentration of glucose is above 180 mg/dL which is above renal threshold.

❖ The effect of insulin deficiency on lipid metabolism :

- The lipid metabolism is affected and the most important effect is that the enzyme **Hormone Lipase Sensitive** is activated causing hydrolysis of the stored triglyceride and a lot of fatty acids and glycerol are released into circulation.
- At this stage (insulin lack) the body totally depends on the energy from these free fatty acids, but when there is a lot of free fatty acids utilizing there will be production of Ketone Bodies.
- Ketone Bodies are: 1. Beta-hydroxybutyric acid. 2. Acetone. 3. Acetoacetic acid.
- When Ketone Bodies are produced it is called **acidosis**.
- Another problem that makes acidosis even more serious that Ketone Bodies are excreted in the urine sometimes combined with Na+, Na+ excreted is replaced by H+.
  - ➔ Then two factors for making acidosis in diabetic patients more serious :
    1. Production of Ketone bodies.
    2. Replacement of Na+ by H+.

❖ The effect of insulin deficiency on protein metabolism :

- Protein catabolism will release high number of amino acids into the blood.
  - ➔ Amino acids either →utilized for energy.
    Or →utilized for production of glucose (even this glucose can't be utilized).
- The resulted protein wasting is one of the most serious effects of severe diabetes mellitus.
  - ➔ It can lead to: 1. Extreme weakness.
    2. Many deranged functions of organs.

➢ To sum up the results of insulin deficiency :

1. On carbohydrates metabolism (decreased glucose uptake) :
   1- Hyperglycemia.
   2- Glycosuria.
   3- Osmotic Diuresis: which is increased concentration of glucose in renal tubules, resulting in:
      → Reabsorbing water can't be done and water will be excreted.
      →Increased osmotic pressure.
   4- Electrolytes depletion.
2. On proteins metabolism (increased protein catabolism) :

1- Increased amino acids in blood.
2- Nitrogen loss.
3- Increase uria.

3. On lipids metabolism (increased lipolysis) :
    1- Increased fatty acids and glycerol in blood.
    2- Ketogenesis.
    3- Ketonuria.
    4- Ketonemia.
    - All results will lead to acidosis then dehydration (increased urination) that lead to coma and this can lead to death.

❖ There are 4 causes of coma that can occur due to complication of diabetes :

1. Acidosis and dehydration.
2. Hyperosmolar coma: in which glucose will be elevated to such a degree that (independent of the pH) leads to coma.
3. Lactic acidosis: where there is accumulation of the lactate in blood, also may cause diabetic ketoacidosis if the tissue become hypoxic.
4. Brain edema: occurs in 1% of children with ketoacidosis and can cause coma.

➔ The 4 types of coma cause unsettled but serious complications with mortality rate about 25%.

- There is a coma because of hypoglycemia (diabetic cause).

→Coma occurs if blood glucose become below 40 mg/dL usually between 30-40 mg/dL, and that depends on individual, sometimes reach 25 mg/dL without coma, and sometimes coma can occur even when it is about 45-50 mg/dL.

❖ Types of diabetes mellitus:

➢ There are 2 types of diabetes mellitus:

1. Type 1: - it is genetic.
    -Insulin-dependent diabetes or Juvenile diabetes mellitus.
    -it can be associated with children because it is genetic.
2. Type 2: - non-insulin dependent.
    - Obesity onset diabetes.
    - Maturity onset diabetes.
    - The difference between 2 types: 1. Age. 2. Body mass. 3. Plasma insulin 4. Plasma glucose. 5. Insulin sensitivity.

- You must advice the old obese individual to:
  1. Exercise. 2. Control their diet. 3. Lose their weight.
  → They will cure 100%.

- We must give them drugs , these drugs depend on the tissue that we want to affect.
  →The available oral anti-diabetic drugs can be divided by mechanism of action to:
  1- Insulin sensitizer with primary action on liver.
  2- Insulin sensitizer with primary action on peripheral tissues.
  3- Insulin secretagogues: stimulate insulin secretion. (most common)
  4- Agents that slow absorption of carbohydrates.
  →Usually we use one of them, rarely use two.
  →So these drugs action depends on liver or muscle to prevent absorption of glucose.

➔ Sometimes all these drugs will not treat type 2 diabetic patients even with exercise, and then the last choice is to use insulin.
→Although insulin therapy apparently provides some benefit to type 2 diabetic
Patient, it has a limited effect on controlling the elevated glucose level or Controlling obesity corresponding to this disease.

❖ The complications of diabetes:

-are very serious even worse than cancer!!
- If untreated lead to: 1- renal failure.
2-increased risk of cancer.
3-primary coronary arterial disease.
-more than 65% of people with diabetes die from heart disease.
- Adults with diabetes have death rate due to heart diseases 2-4 times more than people without diabetes.
- Also strokes accounts for approximately 20% of diabetes related death, and risk of stroke is also 2-4 times higher among people with diabetes.

- Note: in obesity there will be increased fat cell size (not number).

❖ Measures of obesity:

1. Body Mass Index (BMI):
   -BMI = Mass (kg) / (Height (m)) ^2

- If it was → less than 18.5 → under-weight
  → 18.5-24.9 → normal
  → 25-29.9 → over-weight
  →More than 30 → obesity

2. The relationship between height and weight:
   -the normal weight is equal to →in males: weight = height - 100
   →In females: weight = height - 105
3. Measuring of waist:
   -in normal people waist measure must be less than the half of the height.
   -this is very important because people with long waist measure are exposed to stroke more than others because the fat in abdomen captures many vitamins (such as vit.D) .

❖ Glucagon: - a protein hormone (polypeptide).

-opposite to insulin.
-insulin is high when glucose is high (to low it), and glucagon is high when Glucose is Low (to raise it) the most potent hyperglycemic enzyme.
-the half-life of glucagon is 20 minutes.
-the main stimulator of glucagon secretion is ingestion of protein, although The Primary action of it is the metabolism of carbohydrate and lipid in liver.

Main function of glucagon:

1- Glycogenolysis
2- Gluconeogenesis
3- Ketogenesis
4- Lipolysis

- Stimulator of glucagon:
  1- Amino acids
  2- Hypoglycemia
  3- Acetylcholine
  4- Norepinephrine and Epinephrine
- Inhibitors of glucagon:
  1- Fatty acids
  2- Somatostatin
  3- Insulin

❖ The figure shows glucose uptake by different organs in different cases:

Organ / Case	Glucose taken by brain	Glucose taken by liver, muscle, fat cells
Rest	6 g	No change
exercise	6 g	46 g
Carbohydrate meal	6 g	44 g

- We see that glucose taken by the brain is not affected.

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THANK YOU MOHAMMAD SHAWAGFEH FOR HELPING :D

THE EXPERT IN ANYTHING WAS ONCE A BEGGINER