Diabetes Mellitus

[DEPTH OF BIOLOGY]

- In this condition the body is in trouble to remove glucose from blood into cell
- Leads to high level of glucose in blood not enough in cells (&cell need glucose as a source of energy [DEPTH OF BIOLOGY]
- Insulin & glucagon control glucose level in blood and cells
- Insulin- reduce blood glucose level
- Glucagon- increase blood glucose level

[DEPTH OF BIOLOGY]

- Both of these hormones are produced by cluster of cells in the pancreas called ISLETS OF LANGERHANS [DEPTH OF BIOLOGY]

1. glucagon=α

2.insulin= β

- Insulin reduce the amount of glucose in blood by binding to insulin receptor embedded in cell membrane of various insulin responsive tissue like muscle cell & adipose tissue [DEPTH OF BIOLOGY]
- When activated, the insulin receptor cause vesicles containing glucose transporter that are inside the cell to fuse with the cell membraneallowing glucose to be transported into the cell

[DEPTH OF BIOLOGY]

- Glucagon is exactly opposite- it raises the blood glucose level by getting the liver to generate new molecule of glucose from other molecule & breakdown of glycogen to glucose. [DEPTH OF BIOLOGY]

- Diabetes mellitus is diagnosed when blood glucose level rises.

- Around 10% of world population suffer from it [DEPTH OF BIOLOGY]

TYPE-1

- Cannot be prevented
- 10% affected
- In this condition body doesnt makes enough insulin.....WHY?

-there are 4 type of hypersensitivity response or a cell mediated immune response where a person's own T cell attack the pancreas

- In general our body does not attack our self cells called ***SELF TOLERANCE***

[DEPTH OF BIOLOGY]

TYPE-2

- Can be prevented [DEPTH OF BIOLOGY]
- 90% people affected
- Body makes insulin but the tissue does not reponse well to it. (reason not fully understood)
- Body provide normal insulin but the cells do not move their glucose transporter to their membrane in response & its important to fuse to get insulin in the cell
- This cells therefore have insulin resistance
- Some risk factor for insulin resistance obesity, lack of exercise, hyper tension etc.

- When genetic abnormality occurs it damages self tolerance among the T cell that specifically targets **β- cell antigen**
- Losing self tolerance means these T cells are allowed to recruit other immune cells & co-ordinate an attack on **β cells**.
- If ~~**β cells**~~ ~~insulin~~ glucose in blood rises
- Because it cannot enter in cells.
- Important gene involved in regulation of the immune response is the human leukocyte antigen system or HLA system [DEPTH OF BIOLOGY]

- Excess of adipose tissue or fat is thought to cause the release of frequent fatty acid &so called adipokines ***(which are signaling molecule that can cause inflammation which seems to related to insulin resistance)*** [DEPTH OF BIOLOGY]

[DEPTH OF BIOLOGY]

DEPTH OF BIOLOGY

- It's basically this group of gene on chromosome six encode the major histocompatibility complex or MHC which is a portion that is extremely important in helping the immune system recognize foregin molecules, as well as maintaining self tolerance

[DEPTH OF BIOLOGY]

- MHC is like servicing platter that antigen are presented to the immune cells [DEPTH OF BIOLOGY]

- In this type of diabetes (mellitus-1) destruction of beta cells usually starts in early life

- But sometime upto 90% of the beta cell are destroyed before symptoms crop up

[DEPTH OF BIOLOGY]

SYMPTOMS OF UNCONTROLLED DIABETES

1. ***Polyphagia*** (eating a lot)
2. ***Glycosuria*** (glucose in urine)
3. ***Polyuria*** (a lot urine)
4. ***Polydipsia*** (a lot thirst)

Increased glucose blood= low glucose in cell (lead to cell starve for energy)

Adipose tissue	Muscle tissue
Start breaking down fat (lipolysis)	Start breaking down protein

- Both of it result in weight loss; in some people with uncontrolled diabetes, this catabolic state leaves people feel hungry also known as polyphagia.

[DEPTH OF BIOLOGY]

- ***Increased glucose blood=*** glucose filtered through kidneys, some of it start to spill in urine called ***GLYCOSURIA.***

- Since glucose is osmotically active water tends to flow it; it results in an increase in urination or polyuria [DEPTH OF BIOLOGY]

- Finally after so much urination people become dehydrated & thirsty ***(POLYDIPSIA)***

[DEPTH OF BIOLOGY]

- Even though people with diabetes are not able to produce their own insulin, they can still respond to insulin [DEPTH OF BIOLOGY]
- So treatment involves life long therapy of insulin to regulate their blood glucose level & basically enable their cells to use glucose [DEPTH OF BIOLOGY]
- One serious complication of type 1 diabetes mellitus are ketoacidosis ***(diabetic ketoacidosis).***

TYPE 2

- However many obese people are not diabetic; so genetic factor play a major role as well
- Now INSULIN⇑⇑ =to move

glucose out of blood.

[DEPTH OF BIOLOGY]

WHY???

Because we think that glucose is not entering cell so we increase the secretion of insulin through β cell hyperplasia

DEPTH OF BIOLOGY

- β cell hyperplasia takes place (size of beta cell increase. [DEPTH OF BIOLOGY]

- Now among with insulin, β cell also secrete **ISLET AMYLOID POLYPEPTIDE** or **AMYLIN**.
- So also increase amount of amylin

[DEPTH OF BIOLOGY]

- Over the time amylin builds up & aggregrate in the islets
- β cells get exhausted overtime and become dysfunctional ; undergo hypotrophy & smaller as well as hyperplasia & die off [DEPTH OF BIOLOGY]

- As β cells die- insulin level decrease- glucose level increase ***(HYPERGLYCEMIA).***

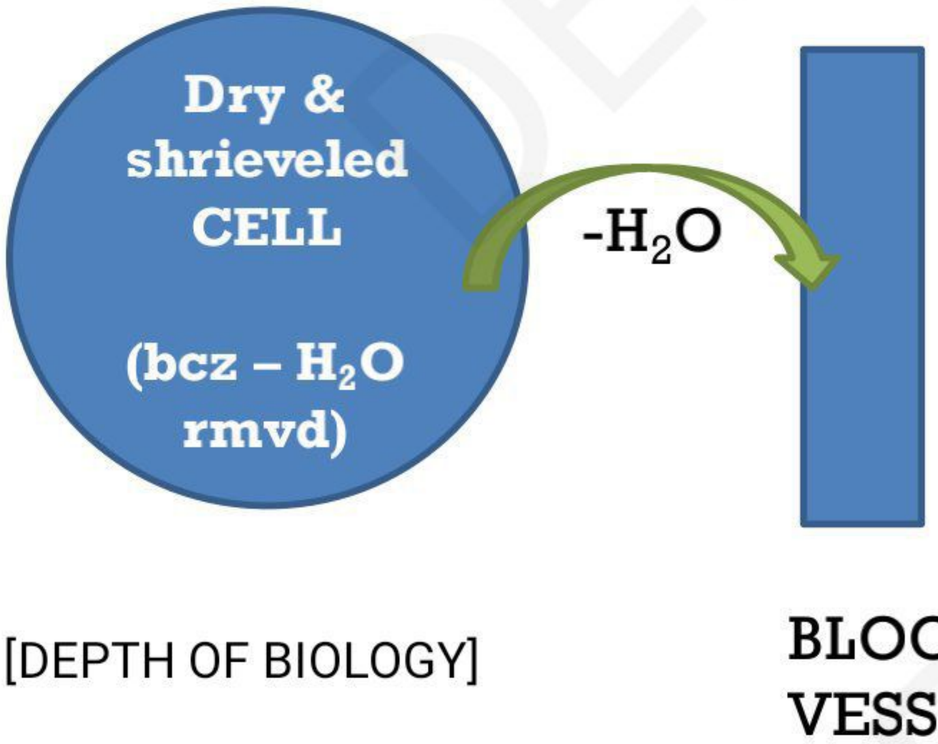
- There are some circulating insulin in type 2 diabetes from the beta cells that are trying to compensate for the insulin resistance

- In type 2 diabetes a complication called hypersomolar hyperglycemic state or HHS is much more common in type 2 instead of type 1.

- It cause increase in plasma osmolarity due to extreme dehydration & concentration of blood

- Glucose (polar molecule) does not passively cross the cell membrane

- It means that acts as solute
- When glucose increase in blood (hypersomolar state)



-H_2O in blood vessel increase leads to increase urination & dehydration

- It is very serious condition because cell shrink & if in brain area cell shrink then it can cause symptom including mental status change [DEPTH OF BIOLOGY]

* In HHS –mild ketonuria & acidosis is observed sometimes [DEPTH OF BIOLOGY]

DIABETES (Sub-Types)

a. *Gestational diabetes-* [DEPTH OF BIOLOGY]

Blood glucose level in pregnant women increases during 3rd trimester

b. Drug induce diabetes-

Medication side-effect increase blood glucose level [DEPTH OF BIOLOGY]

DIAGNOSIS

1. Fasting glucose test (common)-

Person doens't eats or drinks anything except water for 8 hours & then blood is tested for glucose level

100 to 125 mg/dL prediabetes

126 mg/dL diabetes.

2.Non fasting random glucose test-

(can be performed anytime)

≥200 mg/dl - red flag for diabetes

3.Oral glucose tolerance test-

When person is given glucose and then blood sample is taken at interval of 2 hours

140-199 mg/dl prediabetes

≥200 mg/dl- diabetes

4. HbA1c test

glucose- stick with protein

5. C-peptide test

TREATMENT

[DEPTH OF BIOLOGY]

For:

Type -1 diabetes= insulin

Type-2 diabetes =weight loss, exercise, also treated with insulin, oral anti diabetic medication

#RISKS- [DEPTH OF BIOLOGY]

insulin increase can cause hypoglycemia (weakness, hunger, shaking); loss of consciousness occur in severe cases

[DEPTH OF BIOLOGY]

If glucose increases it may lead to:

1. Damage tiny blood vessels called microvasculature.

2. **Arteriosclerosis** occur – wall of arteriole develops hyaline deposit which makes them hard & inflexible.

3. In capillaries the B. Membrane thicken & make it hard for oxygen to move from capillary to tissue causing hypoxia

1. Also lead to medium & large arterial damage

DEPTH OF BIOLOGY

5. Cause retinopathy & blindness in eye
6. Glomerulus , afferent & efferent arteriole damage lead to ***NEPHROTIC SYNDROME*** [DEPTH OF BIOLOGY]
7. Also affect the function of nerves (decrease in sensation of toes & fingers)
8. ANS malfunction [DEPTH OF BIOLOGY]