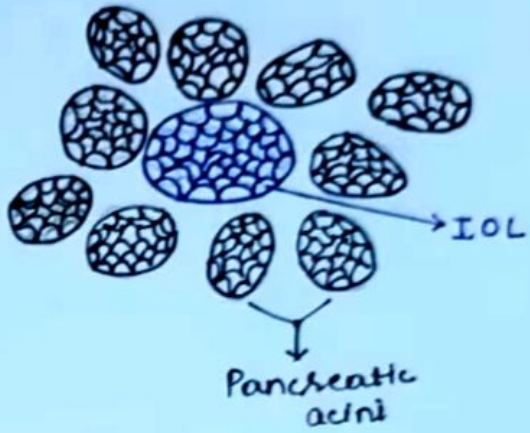
PANCREAS :-

Pancreas → Acini → Secretes digestive juices to duodenum

Pancreas → Islet of Langerhans → Secretes Insulin & Glucagon to blood.



4 types of cells.

α cells	= 25%	= Glucagon
β cells	= 60%	= Insulin, Amylin
δ cells	= 10%	= Somatostatin
PP cells	= 5%	= Pancreatic polypeptide

These cells have effective cell-to-cell communication

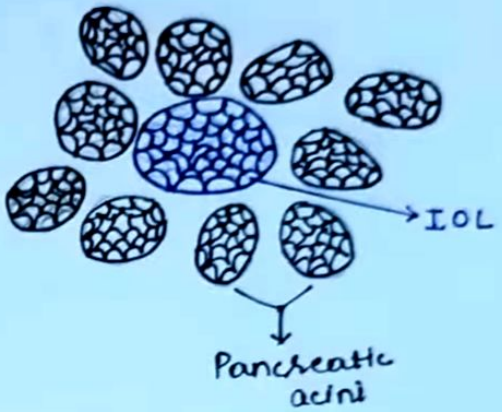
Insulin → ⊖ Glucagon secretion

Amylin → ⊖ Insulin secretion

Somatostatin → ⊖ Both Glucagon & Insulin secretion.

PANCREAS :-

Pancreas
- → Acini → Secretes digestive juices to duodenum
- → Islet of Langerhans → Secretes Insulin & Glucagon to blood.



4 types of cells.

α cells	= 25%	= Glucagon
β cells	= 60%	= Insulin, Amylin
δ cells	= 10%	= Somatostatin
PP cells	= 5%	= Pancreatic polypeptide

These cells have effective cell-to-cell communication

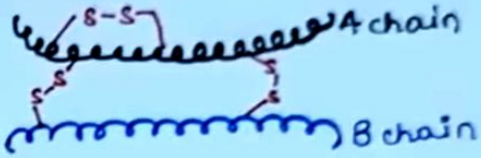
Insulin → ⊖ Glucagon secretion

Amylin → ⊖ Insulin secretion

Somatostatin → ⊖ Both Glucagon & Insulin secretion.

INSULIN :-

- First isolated from pancreas by Banting & Best
- Human insulin have 2 AA chain connected by disulfide linkage



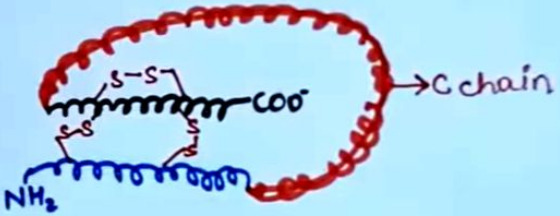
Synthesis of Insulin :-

Preproinsulin

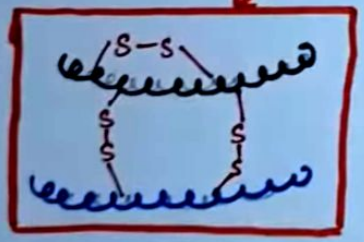
ER ↓ cleavage

Proinsulin

GA ↓ cleavage



Insulin + Connecting peptide (C peptide)



→ Packaging of Insulin & C peptide in secretory granules

↓

Secreted in equimolar amount.

Final secretary product :-

5-10% Proinsulin → No activity

Insulin → ✓

= C-peptide

- Activation of
  - $Na^+ - K^+$ ATPase
  - Endothelial Nitric Oxide Synthase
- Application :-
  [Measured by RadioImmunoAssay]
  To get estimate of natural Insulin secreted.

Metabolism of Insulin :-

➡ Remains in blood in unbound form.

➡ $t_{1/2}$ = 6min ∴ Degraded completely within 10-15 mins
[those that are not bound to receptors]

➡ Degraded by enzyme known as Insulinase
present in (Liver), kidney, muscles.

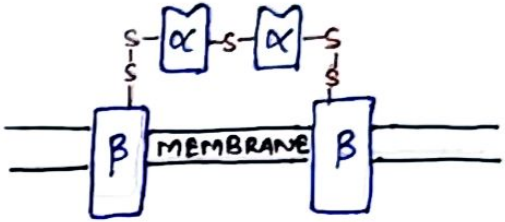
Action of Insulin On Target Cell

Insulin Receptor

↳ Made up of 4 subunits

(2α), (2β) → penetrate membrane protruding into cytoplasm

lies outside membrane



↑ Glucose uptake

Glucose

Mobilisation & Transportation of Glucose Transporters ↑

P

TK

Phosphorylation of multiple Enzymes i.e. Insulin Receptor Substrates (IRS)

Increases permeability for
- AA
- K^+
- phosphate

Fat metabolism → Fat synthesis

Protein metabolism → Protein synthesis

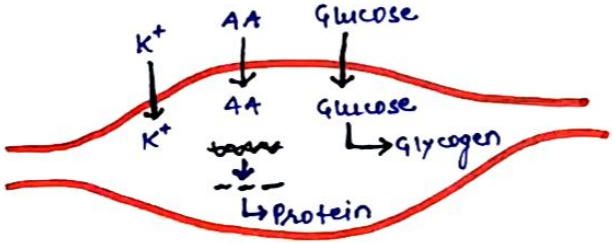
Carbohydrate metabolism → Glycogen synthesis

Effect of Insulin

- On Muscle
- On Liver
- On Adipose Tissue

Insulin deficiency or fat & protein metabolism.

Effect of Insulin On Muscle



- ⊕ Glucose uptake by muscle cells
- ⊕ Muscle glycogen synthesis
- ⊕ Protein synthesis
  - → AA transport to interior of cell
  - → ⊕ Transcription & Translation
  - → ⊖ Catabolism of muscle protein
- ⊕ Transport of K^+ into cells
  - [⊕ Na^+-K^+ ATPase activity]

Resting muscle (Most of time) ➡ uses FA for its energy
[less permeability of muscle fibre for glucose]

Case #01 :- Heavy or moderate exercise

Muscle contraction

⬇

Translocation of GLUT-4 ↑ses

⬇

Muscle fibre permeability to glucose ↑ses

⬇

Glucose uptake

Case #02 :- Few hrs after meal

Blood glucose↑

⬇

Insulin secretion↑

⬇

Glucose uptake & utilisation ↑

⬇

Glucose preferred over FA for energy

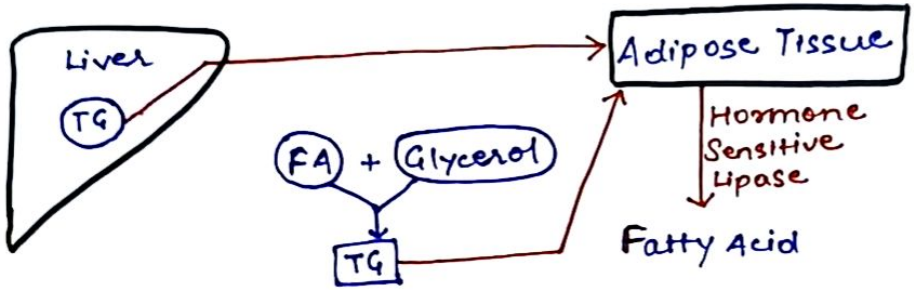
→ If this glucose not used for energy

⬇

Then stored in form of glycogen

Effect of Insulin On Adipose Tissue

⇒ It ↑ fat storage in adipose tissue



→ ⊖ Hormone Sensitive Lipase
↳ ⊖ of release of FA

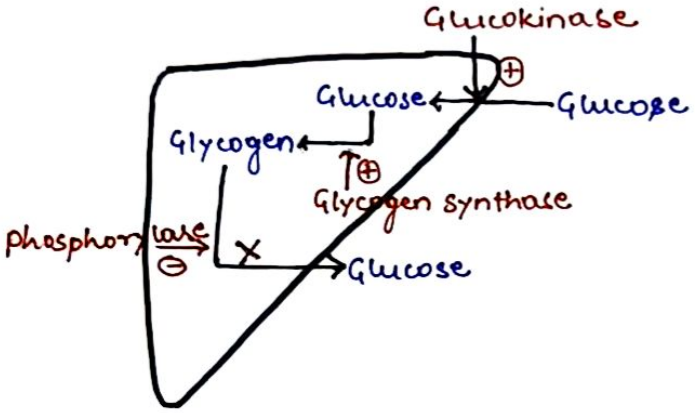
→ ⊕ Glucose transport to adipose cell
↓
conv. to fat in adipose cell

→ Glucose
↓
α-Glycerol phosphate
↓
(FA) binds to glycerol to form TG
↓
Stored as fat

→ ⊕ TG formation in liver
⇓
Transported to adipose tissue

→ ↑ transport of K^+ ion into adipose tissue cells.

Effect of Insulin on Liver :-



➡ ↑ Amount of glycogen in liver.

- ⊕ Glucokinase ⇒ ⊕ uptake of glucose from blood
- ⊕ Glycogen synthase ⇒ ⊕ Glycogen synthesis
- ⊖ Liver phosphorylase ⇒ ⊖ Glycogen breakdown
- ⊖ Gluconeogenesis

➡ Excess Glucose → Fatty Acid

[when Glucose is more than that can be stored as glycogen]

Fatty Acid ↓

Transported as TG in very low density lipoprotein ↓

To Adipose Tissue → Deposited as fat

➡ ⊕ Protein synthesis

Effect of Insulin deficiency on fat & protein metabolism

- Between Meals [Normal Insulin Level ↓]
- Diabetes Mellitus [Drastic Insulin Level ↓]

➡ Action of hormone sensitive lipase activated

⇩

Lipolysis of stored fat & Release of FFA

➡ [TG ↑
Plasma cholesterol ↑
Phospholipid ↑] ← can lead to atherosclerosis

➡ Due to excessive usage of fat → Ketosis & Acidosis

Fat

⇩

Acetyl CoA

- Energy
- Acetone & β-hydroxybutyric acid ⊕ Acetoacetic acid

⇩

Ketone Bodies

⇩

Ketosis → can lead to
- Acidosis
- Coma
- Death

➡
- AA transport ↓
- protein synthesis ↓
- Catabolism of protein ↑

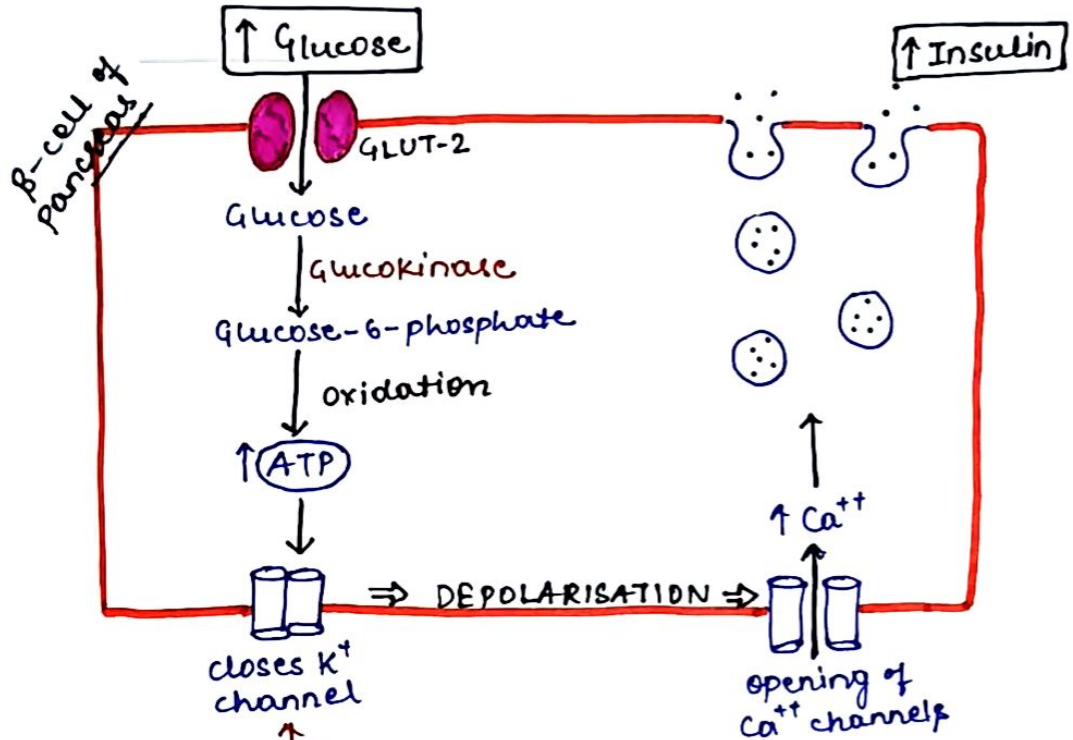
⇩

protein depletion & ↑ plasma AA

⇩

- protein wasting
- Extreme weakness

Mechanism of Insulin Secretion :-



Drug ➡ Sulfonylurea

↳ Stimulates insulin secretion by blocking activity of K^+ channel

↓

Depolarisation

↓

Insulin secretion ↑

Factors affecting Insulin Secretion :-

Factors stimulating Insulin secretion

- ↑ Blood glucose
- ↑ Blood free fatty acid
- ↑ Blood AA (Arginine & Lysine)
- GI hormones
  - Gastrin
  - Secretin
  - CCK
  - Glucagon-like Peptide-1 (GLP-1)
  - Glucose dependent Insulinotropic peptide (GIP)

  Most potent Insulin stimulators

  ↓ Aka

  Incretins
- Glucagon, GH, cortisol
- Parasympathetic stimulation; Ach
- β-Adrenergic stimulation

Factors inhibiting Insulin secretion

- ↓ Blood glucose
- fasting
- Somatostatin
- α Adrenergic activity
- Leptin
- Insulin resistance, obesity
- Sulfonylurea drugs (Glyburide, Tolbutamide)