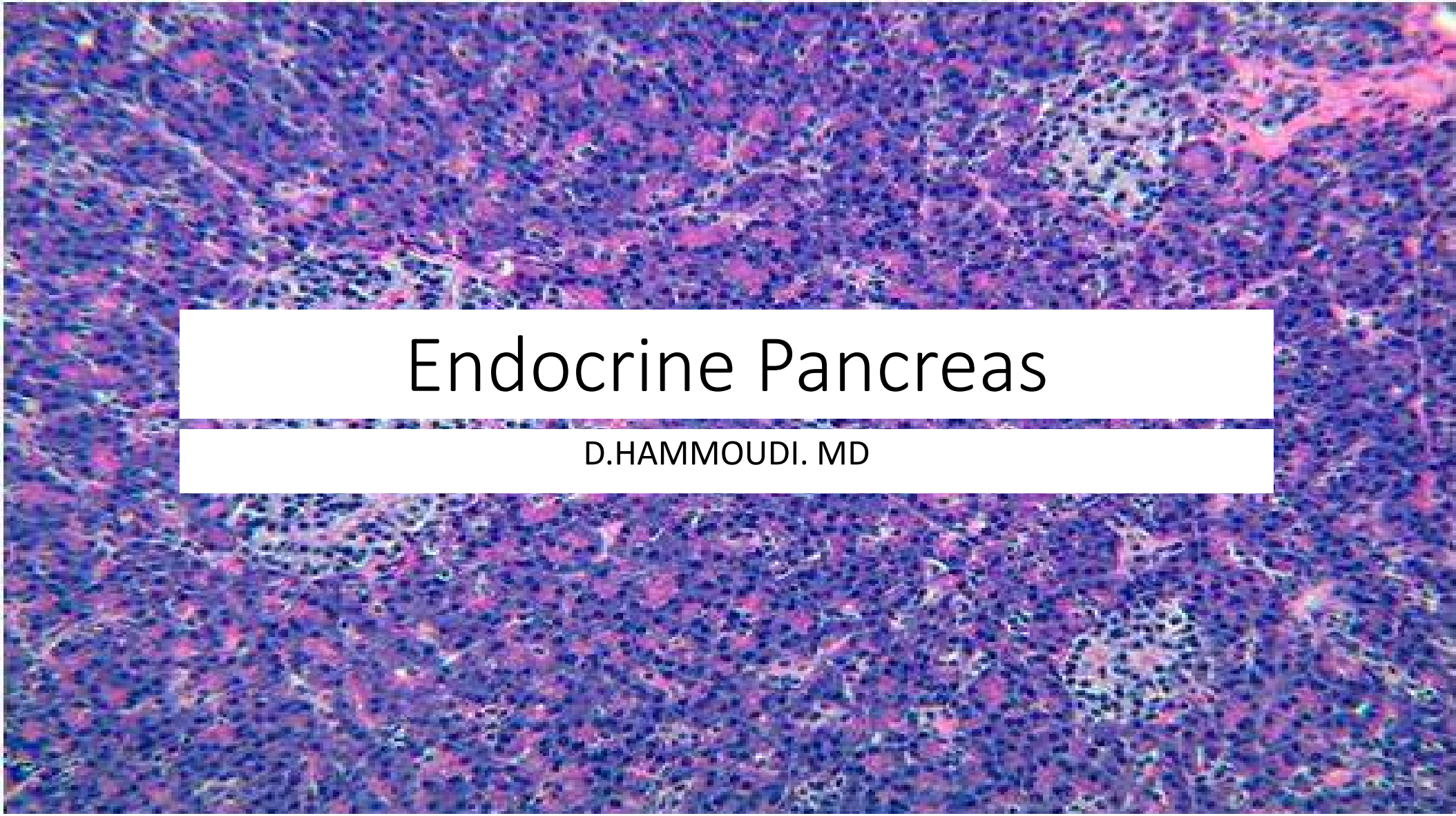


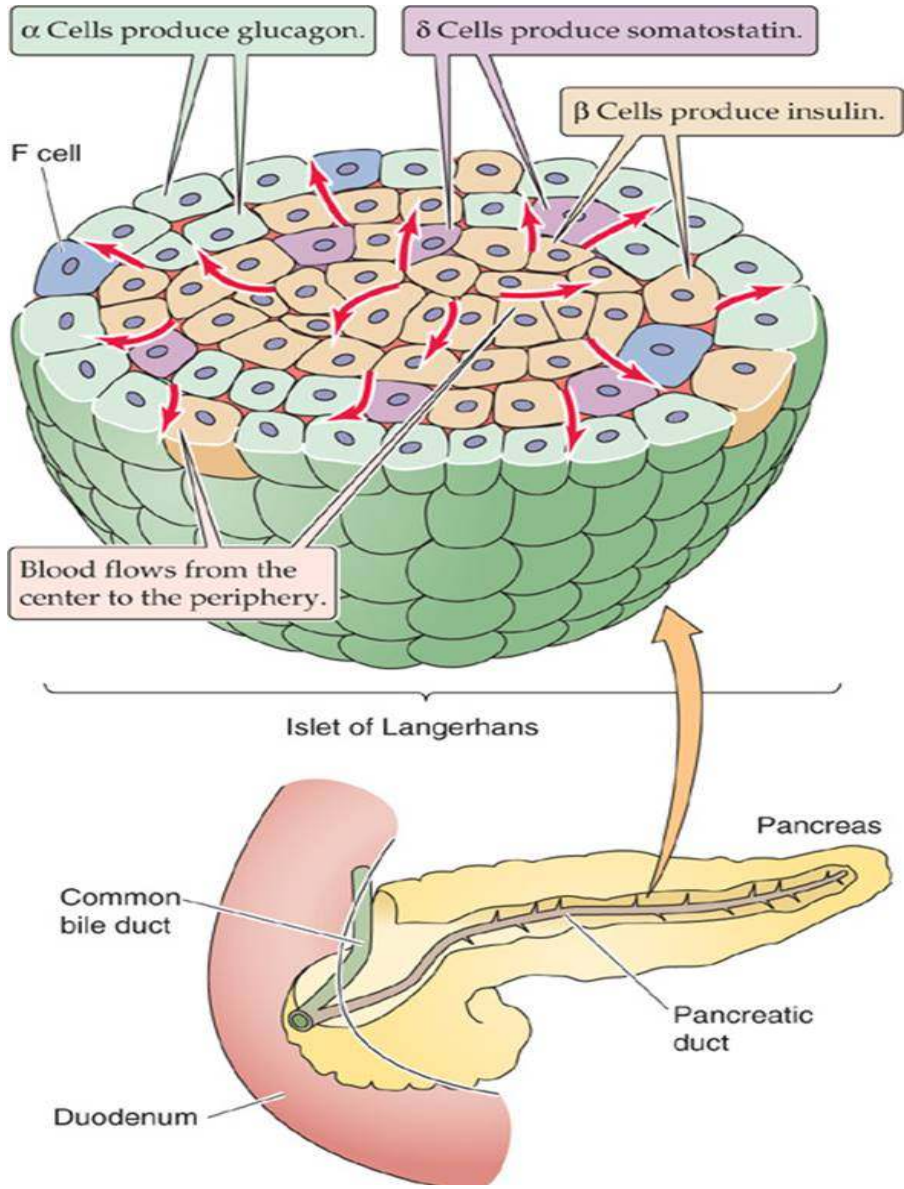
Endocrine Pancreas

D.HAMMOUDI. MD

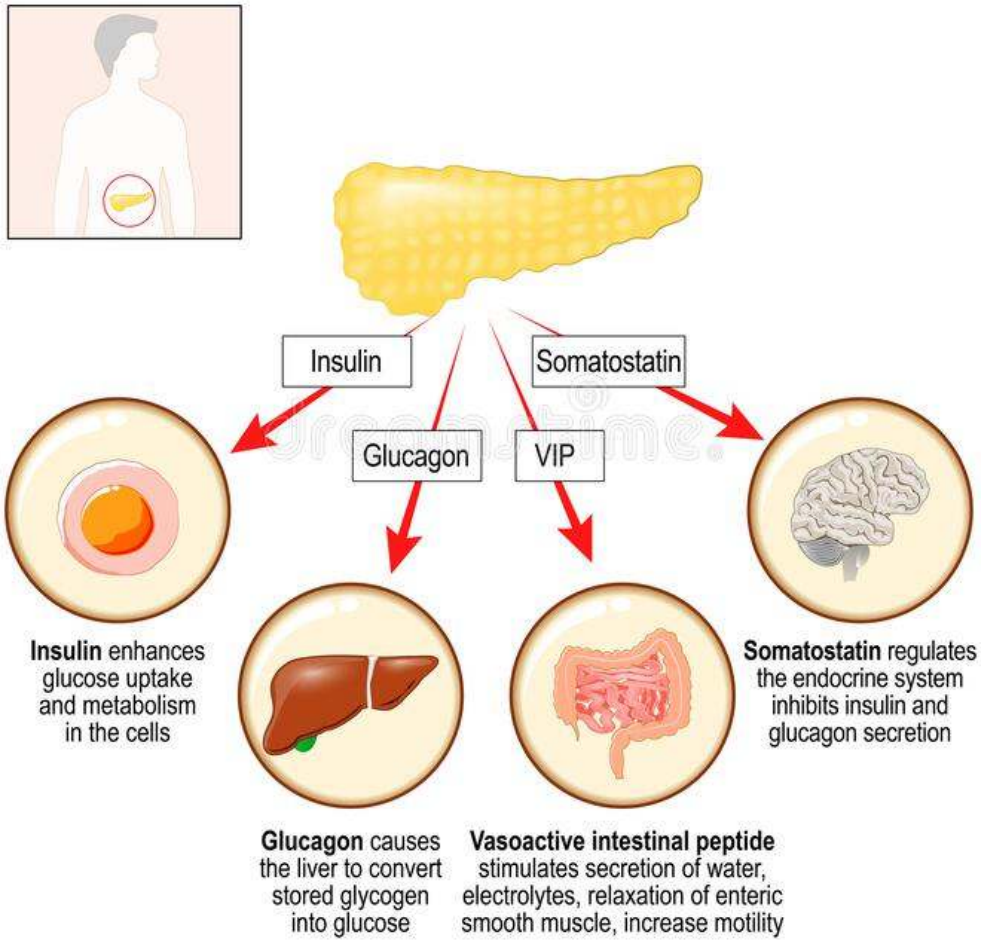
Pancreas

- Pancreas is having both Endocrine and Exocrine parts.
- The Endocrine part is made up of Islet of Langerhans which are aggregated in tail part of pancreas.
- Islet of Langerhans is an encapsulated structure bounded by thin capsule of reticular fibres.
- In the islet, following three different types of cells are mainly found. Alpha, Beta and D cells.

Beta (ß) cells produce INSULIN
- Alpha (a) cells produce GLUCAGON
- Delta (d) cells produce SOMATOSTATIN
- F cells produce PANCREATIC POLYPEPTIDE



Pancreas

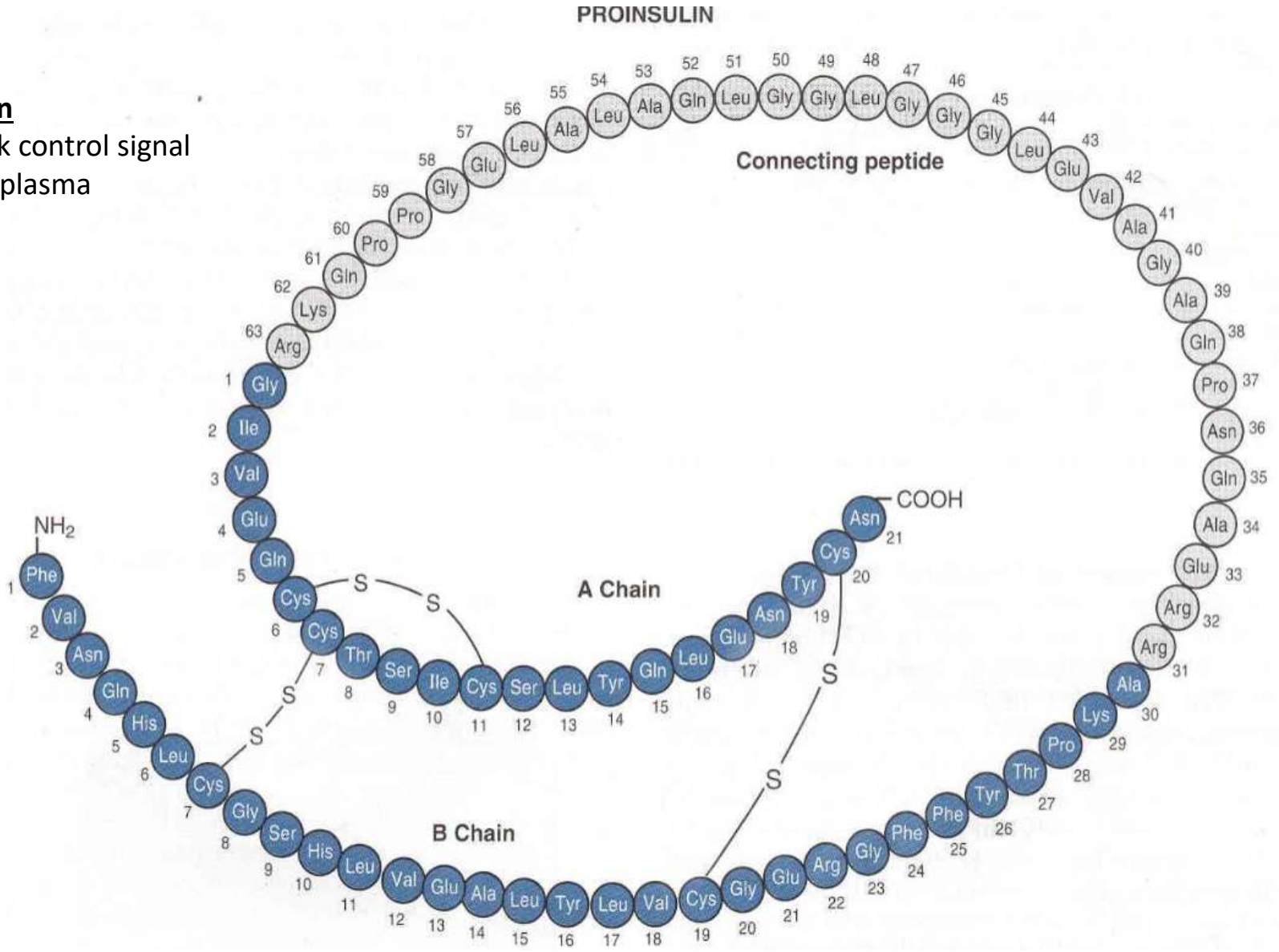

Insulin
Somatostatin
Glucagon
VIP
Insulin enhances glucose uptake and metabolism in the cells
Somatostatin regulates the endocrine system inhibits insulin and glucagon secretion
Glucagon causes the liver to convert stored glycogen into glucose
Vasoactive intestinal peptide stimulates secretion of water, electrolytes, relaxation of enteric smooth muscle, increase motility

Insulin

Regulation of insulin secretion

Mainly regulated by feed back control signal provided by nutrients level in plasma

" Hormone of Abundancy"



Regulators of insulin secretion

Stimulators of insulin secretion	Inhibitors of insulin secretion
↑ Serum glucose	↓ Glucose
↑ Serum amino acids	↓ Amino acids
↑ Serum free fatty acids	↓ Free fatty acids
↑ Serum ketone bodies	
Hormones	Hormones
Gastroinhibitory peptide (GIP)	Somatostatin
Glucagon	Epinephrine (α-receptor)
Gastrin	
Cholecystokinin (CCK)	
Secretin	
Vasoactive intestinal peptide (VIP)	
Epinephrine (β-receptor)	
Parasympathetic nervous system	Sympathetic nervous system stimulation

INSULIN ACTION ON CARBOHYDRATE METABOLISM

LIVER

- Stimulates glucose oxidation
- Promotes glucose storage as glycogen
- Inhibits glycogenolysis
- Inhibits gluconeogenesis

MUSCLE

- Stimulates glucose uptake (GLUT4)
- Promotes glucose storage as glycogen

ADIPOSE TISSUE

- Stimulates glucose transport into adipocytes
- Promotes the conversion of glucose into triglycerides and fatty acids

"ANTI-DIABETOGENIC"

facilitates amino acids entry into muscle cells

- Facilitates protein synthesis in ribosomes by induction of gene transcription
- Inhibits proteolysis by decreasing lysosomal activity

"**ANABOLIC HORMONE**"

INSULIN ACTION ON FAT METABOLISM

LIVER

- Anti ketogenic & Lipogenic
- Stimulates HMG-CoA reductase

ADIPOSE TISSUE

- Promotes storage of fat
- Inhibits lipolysis by inhibiting Hormone sensitive lipase
- Promotes lipogenesis by stimulating lipoprotein lipase

"ANTI-KETOGENIC"

The absorptive state, or the fed state, occurs after a meal when your body is digesting the food and absorbing the nutrients (catabolism exceeds anabolism). Digestion begins the moment you put food into your mouth, as the food is broken down into its constituent parts to be absorbed through the intestine.

INSULIN ACTION ON PLASMA K+ CONCENTRATION

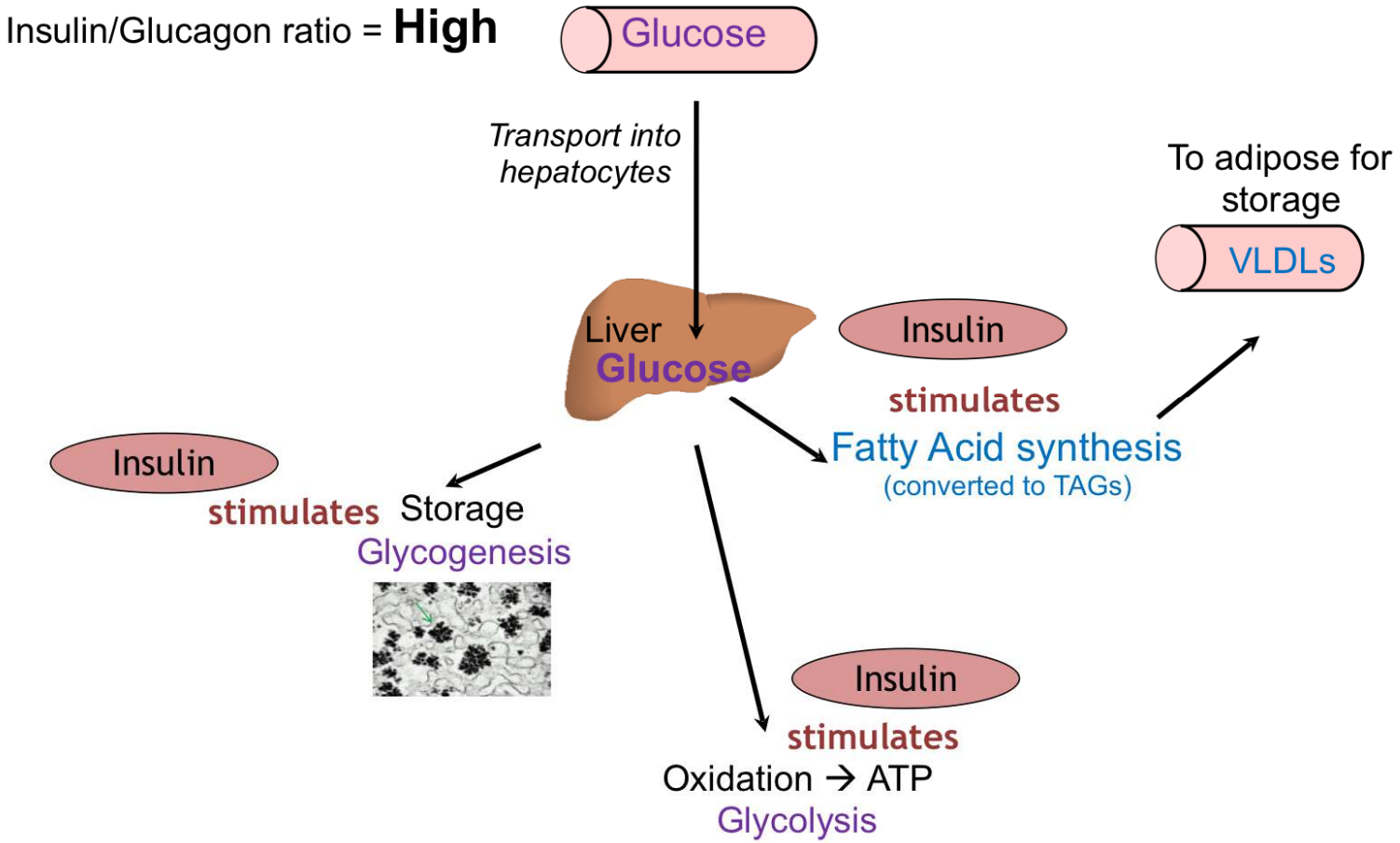
- Facilitates rapid entry of K+ into cell by simulating Na-K ATPase activity
- Thus decreases plasma concentration of K+
- APPLIED: Insulin is given along with glucose in the treatment of Hyperkalemia that occurs in Acute Renal Failure

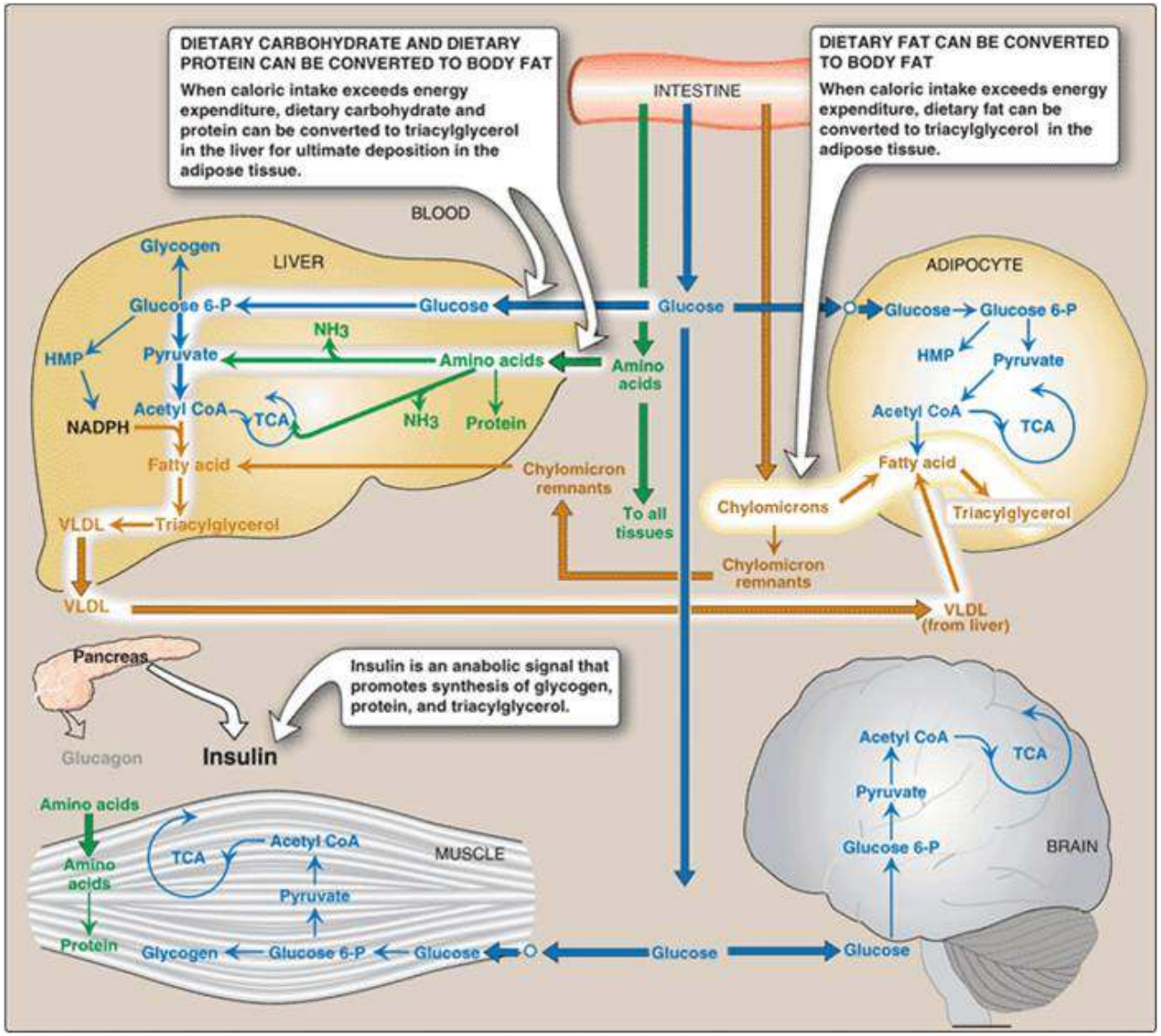
"PHYSIOLGICAL REGULATOR OF PLASMA K+ CONCENTRATION"

Dominates in Fed State Metabolism

- **INCREASE GLUCOSE UPTAKE IN MOST CELLS =➔Anti-Diabetogenic**
- **INCREASE GLUCOSE USE & STORAGE=➔Anabolic**
- **INCREASE PROTEIN SYNTHESIS=➔Anti-ketogenic**
- **INCREASE FAT SYNTHESIS=➔Lipogenic**

Metabolism in Fed State: Liver




DIETARY CARBOHYDRATE AND DIETARY PROTEIN CAN BE CONVERTED TO BODY FAT
When caloric intake exceeds energy expenditure, dietary carbohydrate and protein can be converted to triacylglycerol in the liver for ultimate deposition in the adipose tissue.
DIETARY FAT CAN BE CONVERTED TO BODY FAT
When caloric intake exceeds energy expenditure, dietary fat can be converted to triacylglycerol in the adipose tissue.
INTESTINE
BLOOD
LIVER
Glycogen
Glucose 6-P
Glucose
HMP
Pyruvate
NH3
Amino acids
Acetyl CoA
TCA
NADPH
Protein
Fatty acid
Chylomicron remnants
VLDL
Triacylglycerol
To all tissues
Glucose
Amino acids
ADIPOCYTE
Glucose
Glucose 6-P
HMP
Pyruvate
Acetyl CoA
TCA
Fatty acid
Chylomicrons
Triacylglycerol
Chylomicron remnants
VLDL
VLDL (from liver)
Pancreas
Glucagon
Insulin
Insulin is an anabolic signal that promotes synthesis of glycogen, protein, and triacylglycerol.
Amino acids
Amino acids
TCA
Acetyl CoA
MUSCLE
Pyruvate
Protein
Glycogen
Glucose 6-P
Glucose
Glucose
Glucose
Acetyl CoA
TCA
Pyruvate
Glucose 6-P
BRAIN

GLUCAGON

Produced by alpha cells in the pancreas

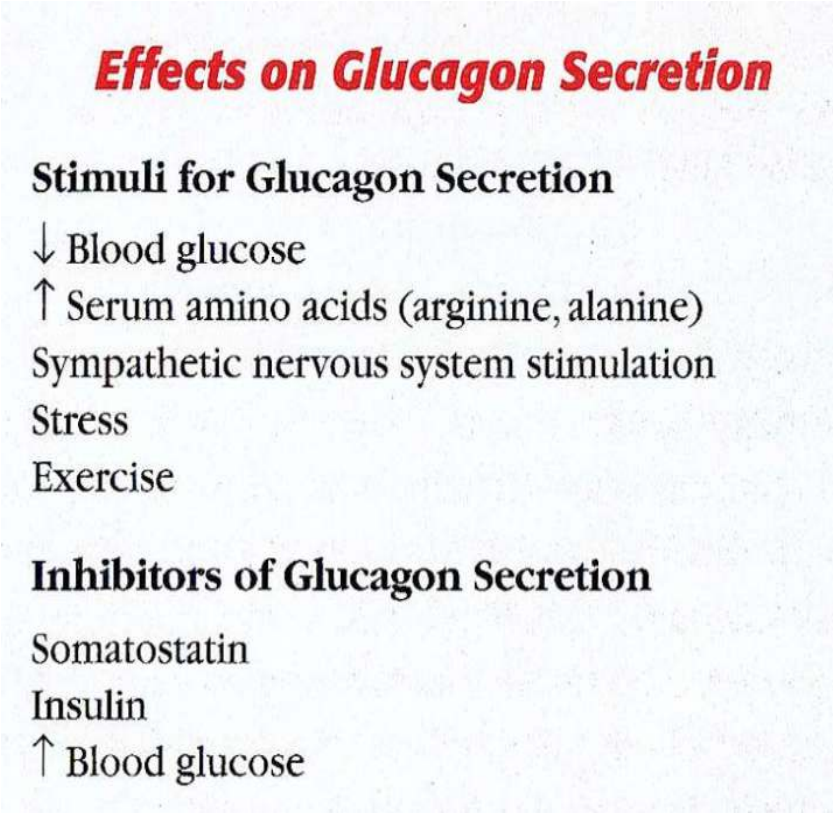
- Its major target is the liver, where it promotes:
  - Glycogenolysis – the breakdown of glycogen to glucose
  - Gluconeogenesis – synthesis of glucose from lactic acid and non carbohydrates
  - Release of glucose to the blood from liver cells

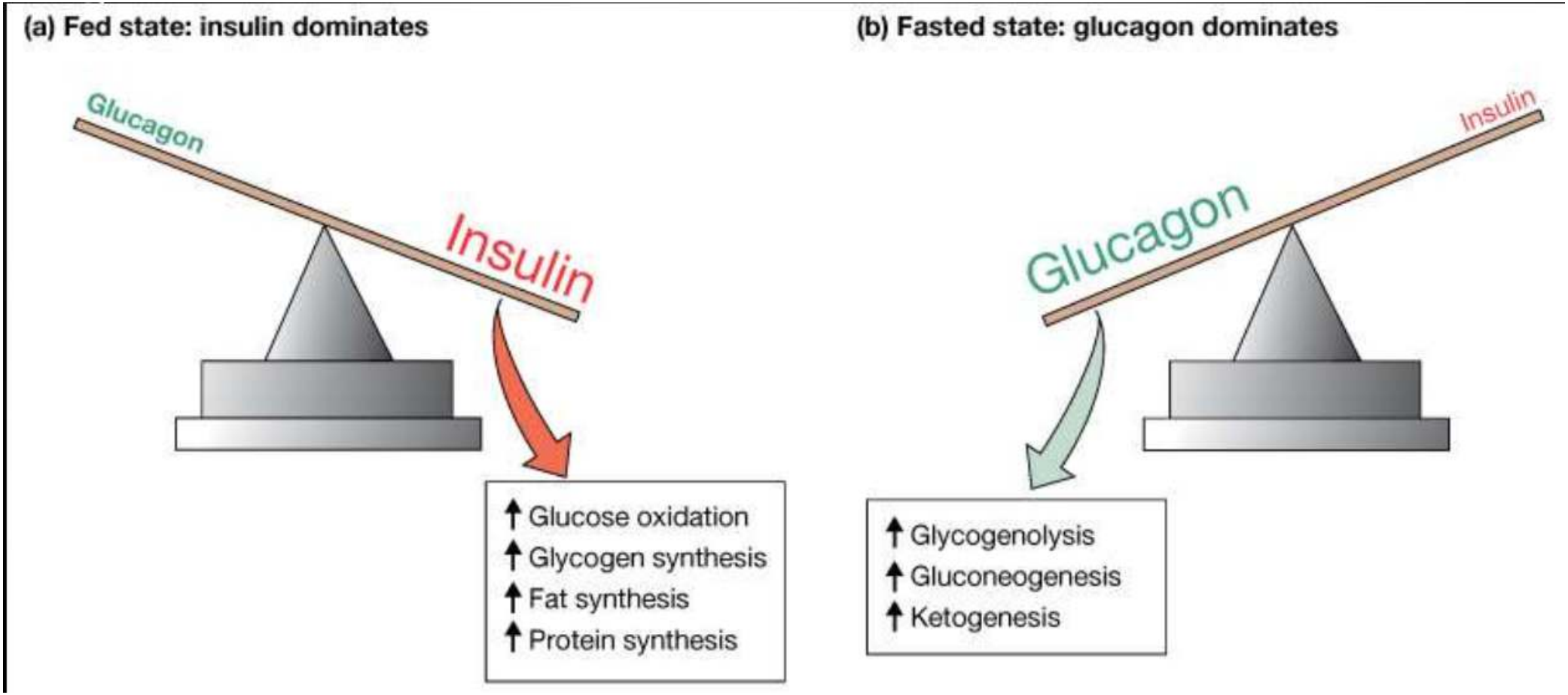
Stimulates glycogenolysis, gluconeogenesis & inhibits glycogenesis
- Promotes lipolysis & ketogenesis
- Increases calorigenesis

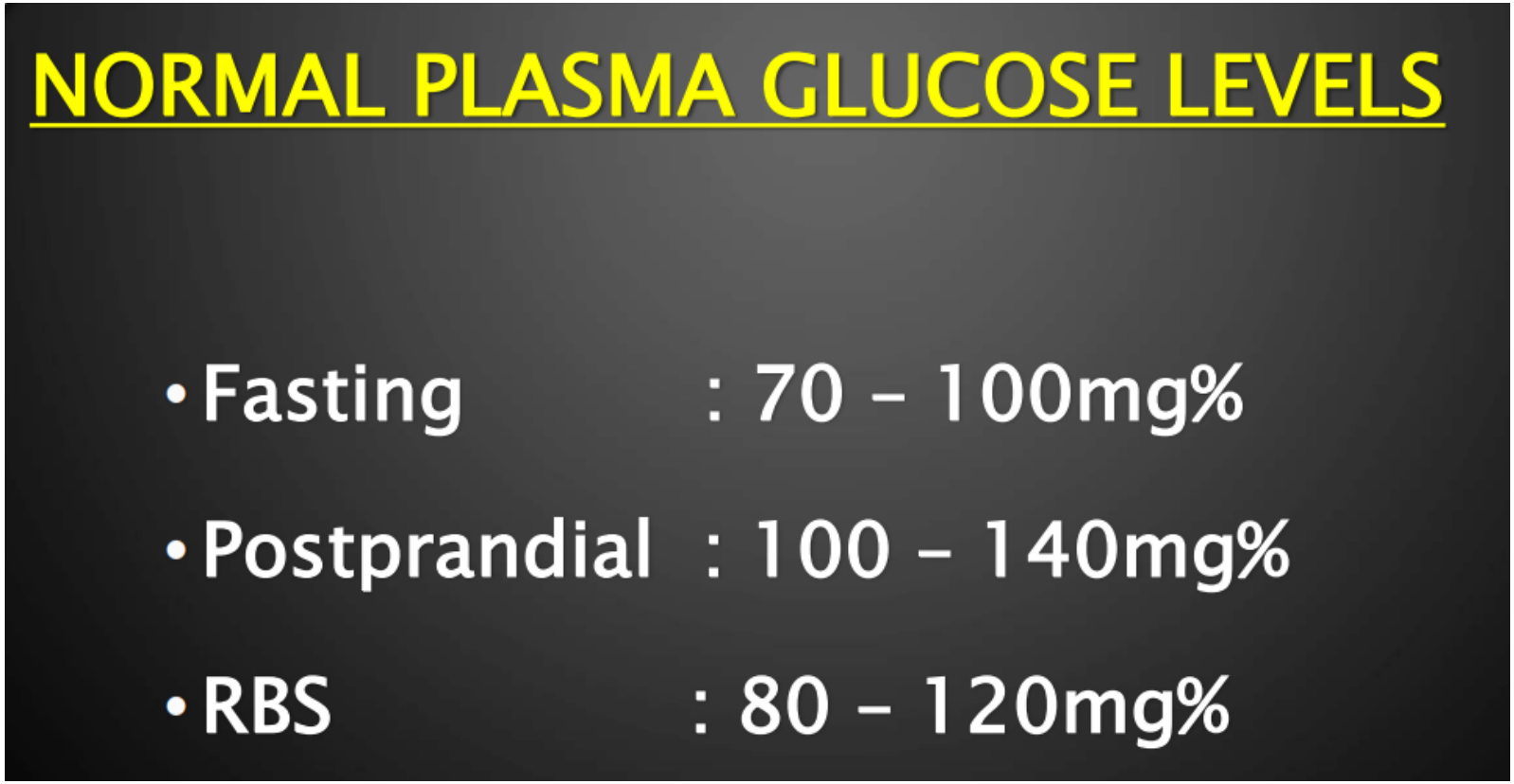
"Prodiabetogenic and Ketogenic"

INSULIN–GLUCAGON RATIO

- **Insulin** is hormone of **energy storage**
- **Glucagon** is hormone of **energy release**
- A balance should be maintained for normal metabolic functions
- After a normal balance diet is 3
- After overnight fasting decreases to 1, may decrease to as low as 0.4 after prolonged fasting
- Physiological significance – during neonatal period a low I/G ratio is critical for survival

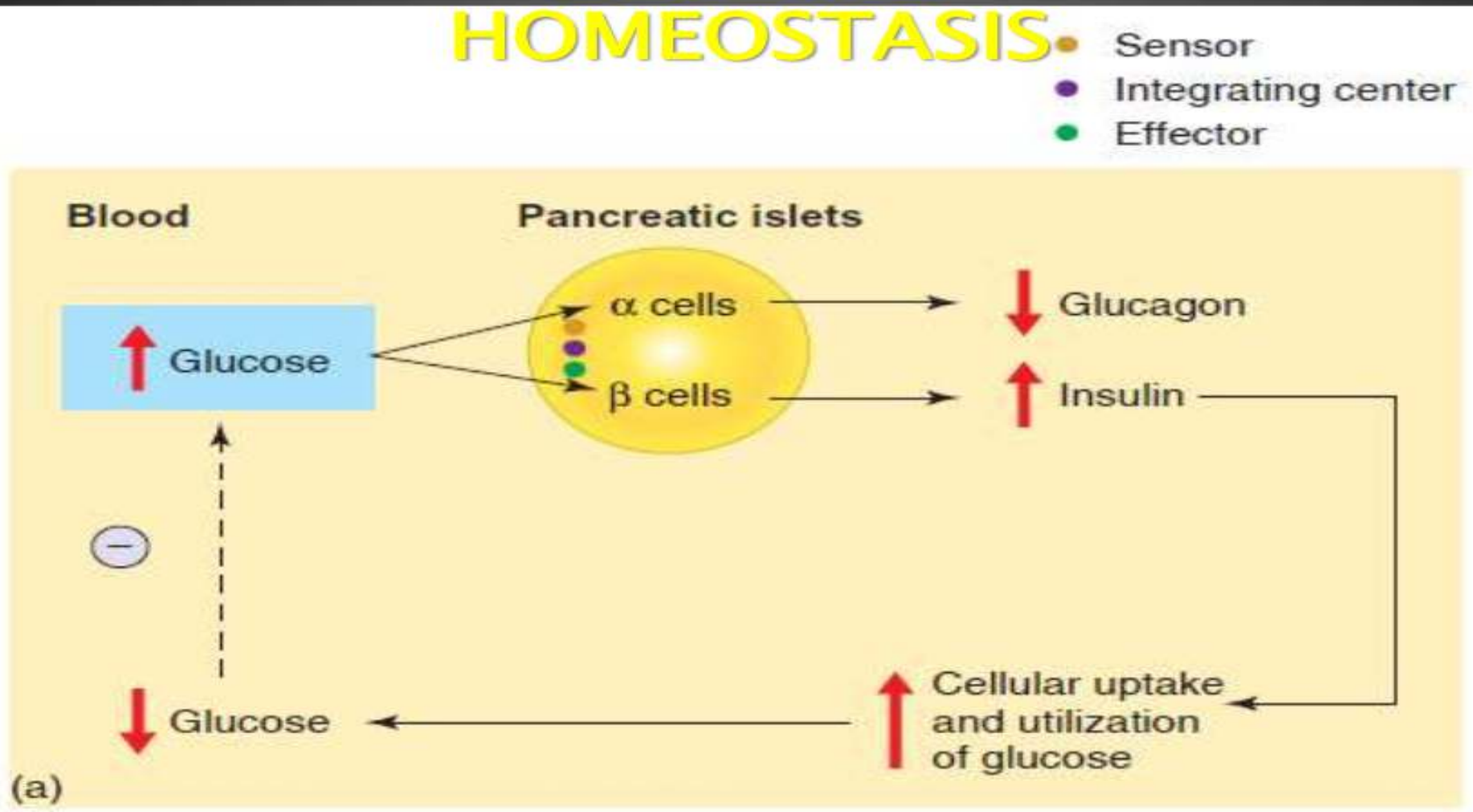



(a) Fed state: insulin dominates
Glucagon
Insulin
↑ Glucose oxidation
↑ Glycogen synthesis
↑ Fat synthesis
↑ Protein synthesis
(b) Fasted state: glucagon dominates
Insulin
Glucagon
↑ Glycogenolysis
↑ Gluconeogenesis
↑ Ketogenesis



Rbs = random blood sugar

GLUCOSE HOMEOSTASIS



GLUCOSE HOMEOSTASIS

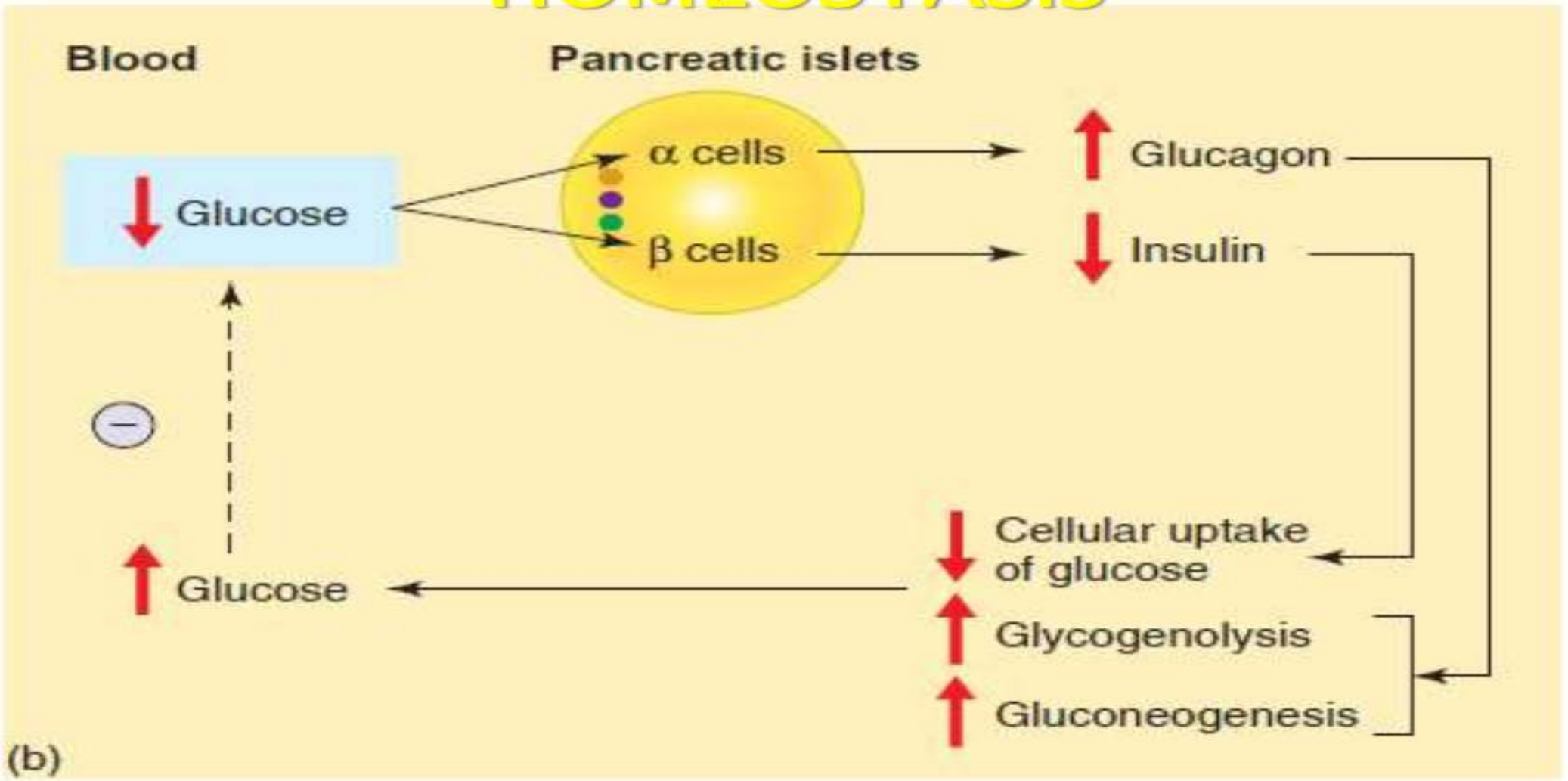


Table: 49.4 Major differences between Type 1 and Type 2 diabetes mellitus.

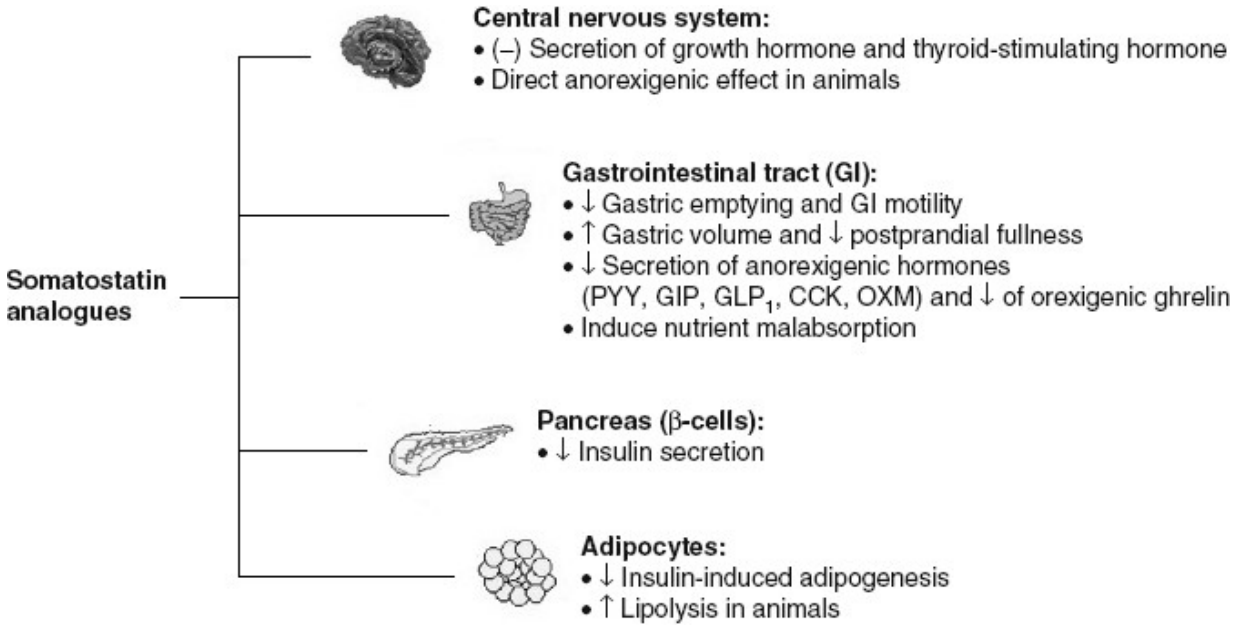
	Type I	Type II
1. Age of onset	Before the age of 40 (Juvenile onset diabetes)	After the age of 40 (Maturity onset diabetes)
2. Body fat mass	Not obese	Obese
3. Incidence	10% of the total diabetes	90% of the total diabetes
4. Genetic susceptibility	Concordance rate is < 50%	Concordance rate is > 50%
5. Incidence of ketoacidosis	High	Low
6. B cell mass of pancreas	B cells destroyed	B cells morphology is normal.
7. Nature of onset	Rapid	Gradual
8. Usual complication	Ketoacidotic coma	Hyperosmolal coma

SOMATOSTATIN

Secreted from D cells of pancreas
- Also secreted in SOMATOSTATIN hypothalamus & GIT

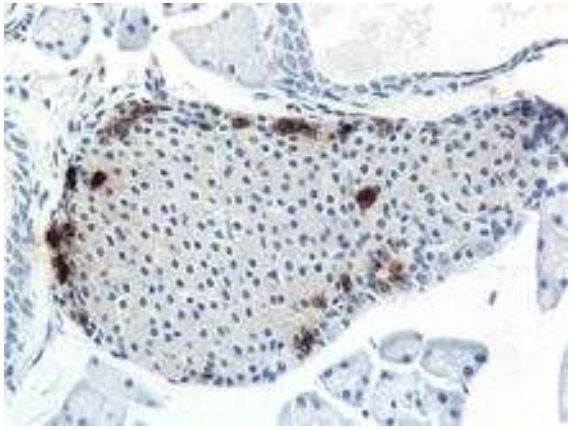
SOMATOSTATIN

- Inhibits secretion of insulin & glucagon
- Inhibits GI motility* & GI secretions
- Regulates feedback control of gastric emptying



PANCREATIC POLYPEPTIDE

•Pancreatic polypeptide (PP) is a polypeptide secreted Secreted from F cells of pancreas or PP Cells = predominantly in the head of the pancreas.



- Structurally similar to Neuropeptide Y secreted from hypothalamus
- •Secreted in response to food intake
- Inhibits exocrine pancreatic secretion
- Slows the absorption of food from the GI tract

- The function of PP is to self-regulate pancreatic secretion activities (endocrine and exocrine).
- It also has effects on hepatic glycogen levels and gastrointestinal secretions.
- Its secretion in humans is increased after a protein meal, fasting, exercise, and acute hypoglycemia, and is decreased by somatostatin and intravenous glucose.
- Plasma PP has been shown to be reduced in conditions associated with increased food intake and elevated in anorexia nervosa. In addition, peripheral administration of PP has been shown to decrease food intake