

The Pancreas

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Exocrine and endocrine cells

- **Acinar** cells (forming most of the pancreas)
 - *Exocrine* function
 - Secrete digestive enzymes
- **Islet** cells (of Langerhans)
 - *Endocrine* function

Pancreatic islet endocrine cells

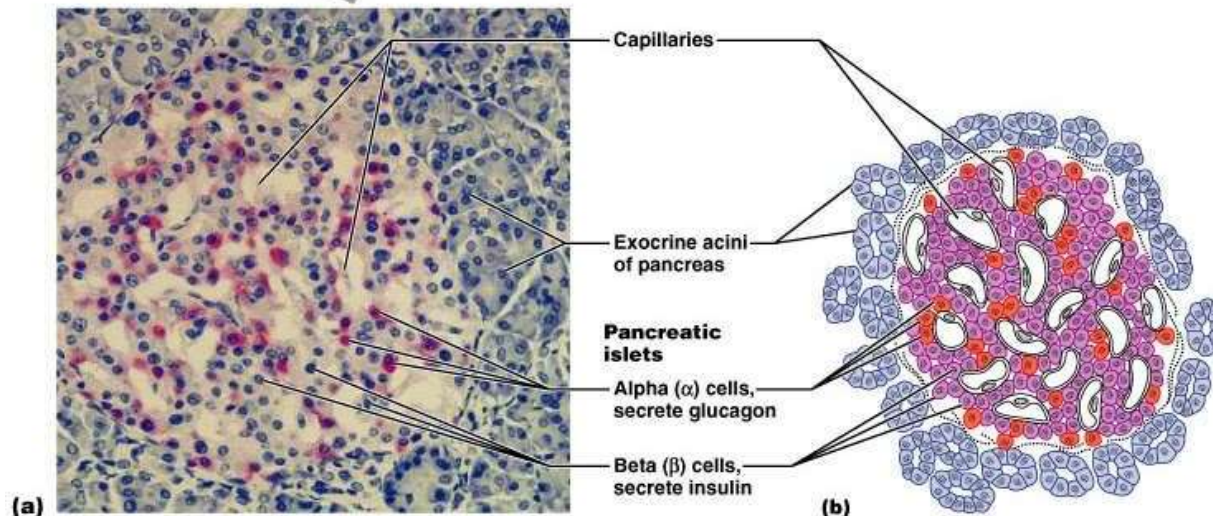
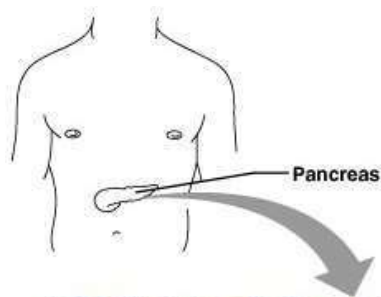
Alpha cells: secrete **glucagon**

raises blood sugar
mostly in periphery

Beta cells: secrete **insulin**

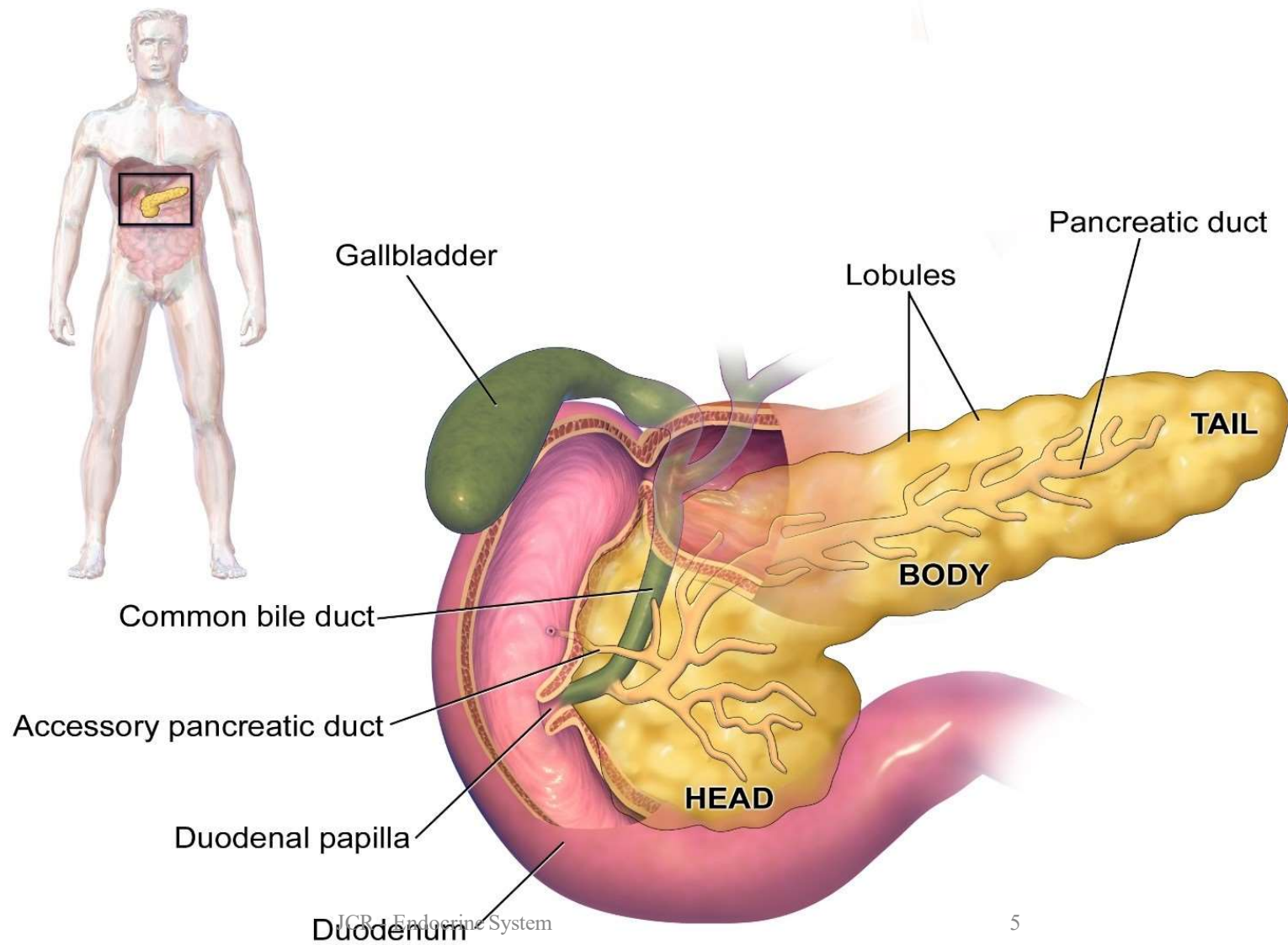
lowers blood sugar
central part (are more abundant)

Also rare Delta cells: secrete somatostatin
inhibits glucagon



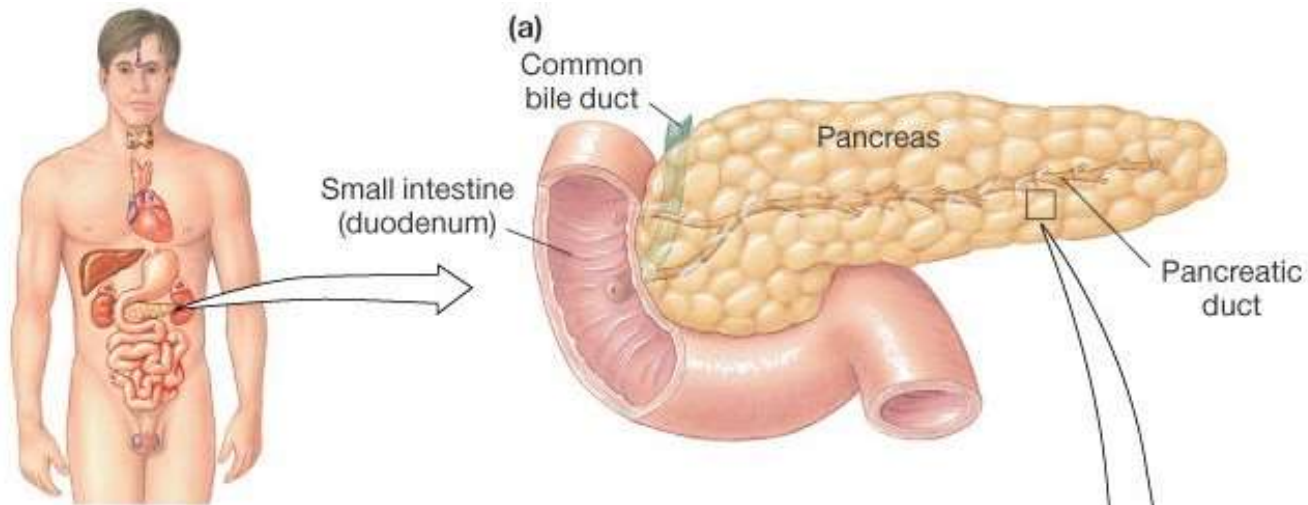
Pancreas

- A triangular gland, which has both exocrine and endocrine cells, located behind the stomach
- Strategic location
- Acinar cells produce an enzyme-rich juice used for digestion (exocrine product)
- Pancreatic islets (**islets of Langerhans**) produce hormones involved in regulating fuel storage and use.



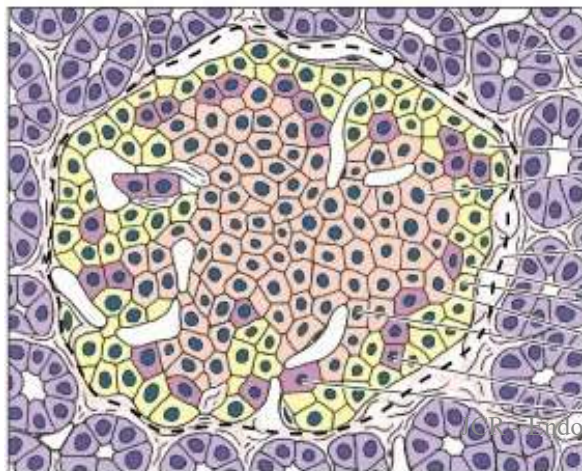
Islets of Langerhans

- 1 Million islets
- 1-2% of the pancreatic mass
- Beta (β) cells produce insulin
- Alpha (α) cells produce glucagon
- Delta (δ) cells produce somatostatin
- F cells produce pancreatic polypeptide



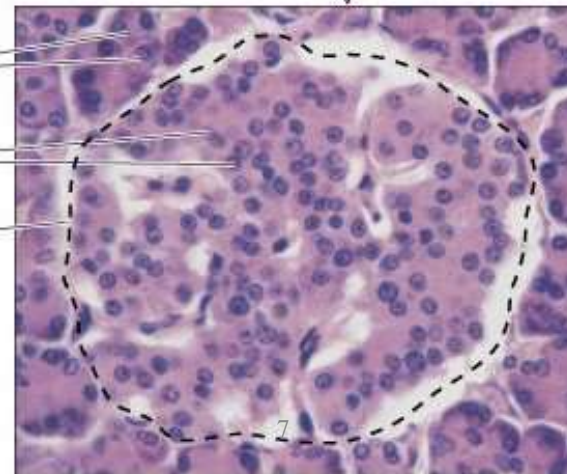
CELL		SECRETES:
Alpha cells		Glucagon
D cells		Somatostatin
Beta cells		Insulin, amylin

(b)



Exocrine cells
Endocrine cells
Islet of Langerhans
Alpha cells
Beta cells
D cells

(c)

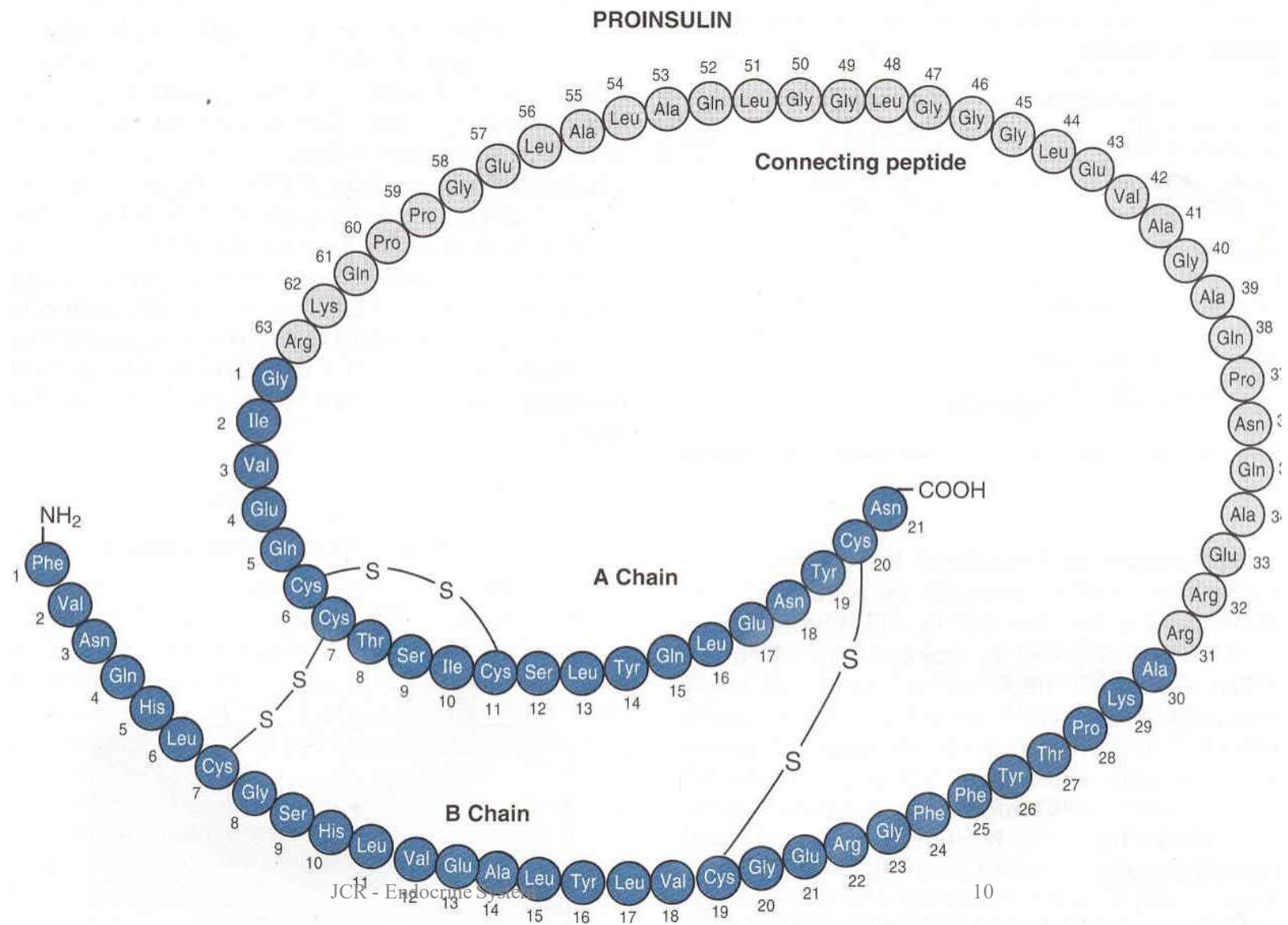


Insulin

- Hormone of nutrient abundance
- A protein hormone consisting of two amino acid chains linked by disulfide bonds
- Synthesized as part of proinsulin (86 AA) and then excised by enzymes, releasing functional insulin (51 AA) and C peptide (29 AA).

Insulin Structure

- 1 Large polypeptide 51 AA (MW 6000)
- 2 Two chains linked by disulfide bonds.
 A chain (21 AA)
 B chain (30 AA)
- 3 Disulfide bonds.



Insulin Action on Cells

- Insulin is the hormone of abundance.
- The major targets for insulin are:
 - liver
 - Skeletal muscle
 - adipose tissue
- The net result is fuel storage

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

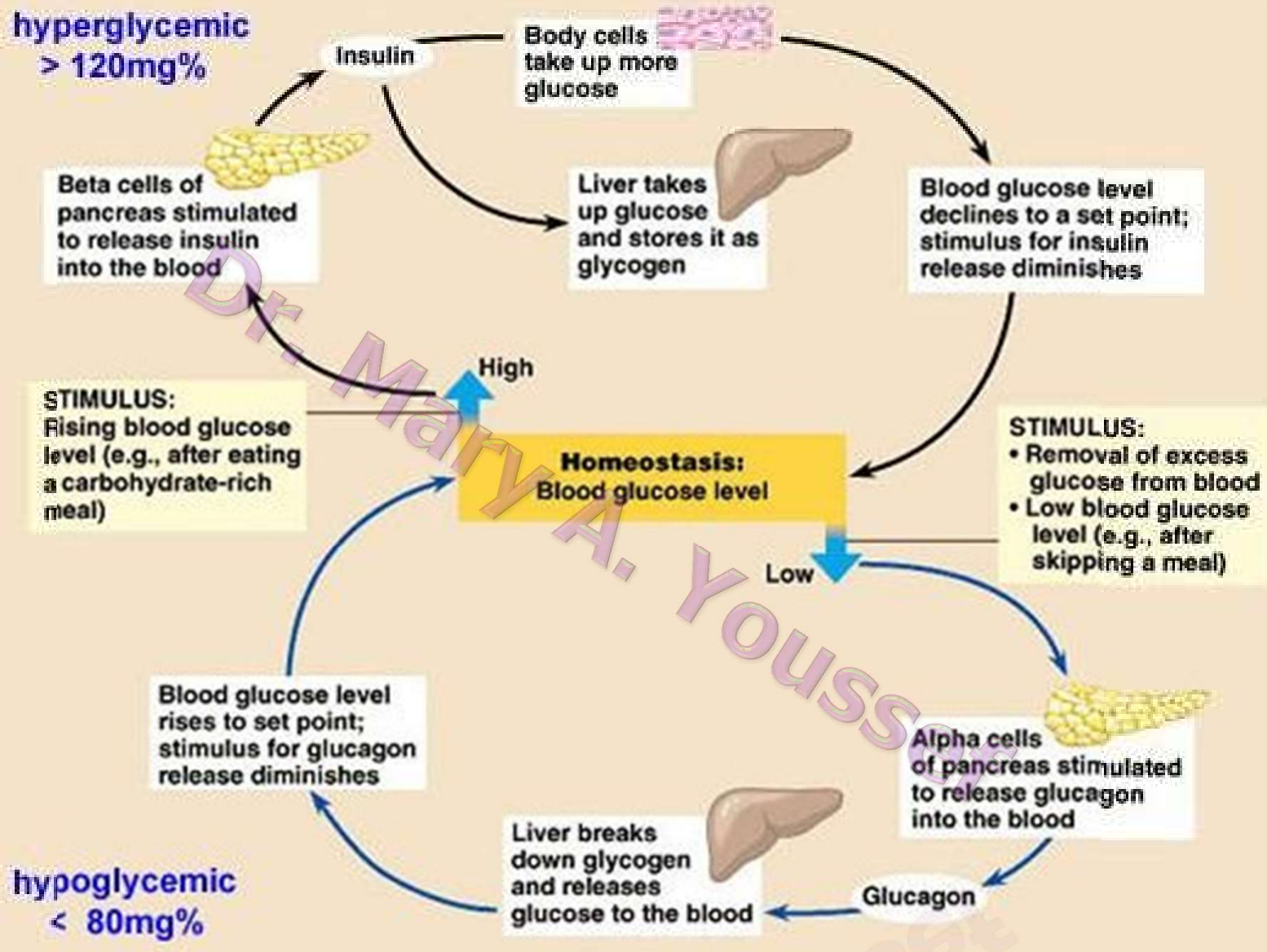
Glucagon

- A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent
- Produced by α 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 noncarbohydrates
 - Release of glucose to the blood from liver cells

Physiological Action of Glucagon

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

hyperglycemic
> 120mg%



Actions of Glucagon

	Insulin	Glucagon
On CHO metabolism	↓ glycogenolysis ↓ gluconeogenesis	↑ glycogenolysis ↑ gluconeogenesis
On lipid metabolism	Lipogenesis	Lipolysis
On protein metabolism	Anabolic	Catabolic
Stimulus	hyperglycemia	hypoglycemia

Somatostatin

- Secreted from D cells of pancreas
- Also secreted from hypothalamus & GIT
- A peptide hormones with 2 forms, one with 14 AAs & the other with 28 AAs

Functions

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

Diabetes Mellitus (DM)

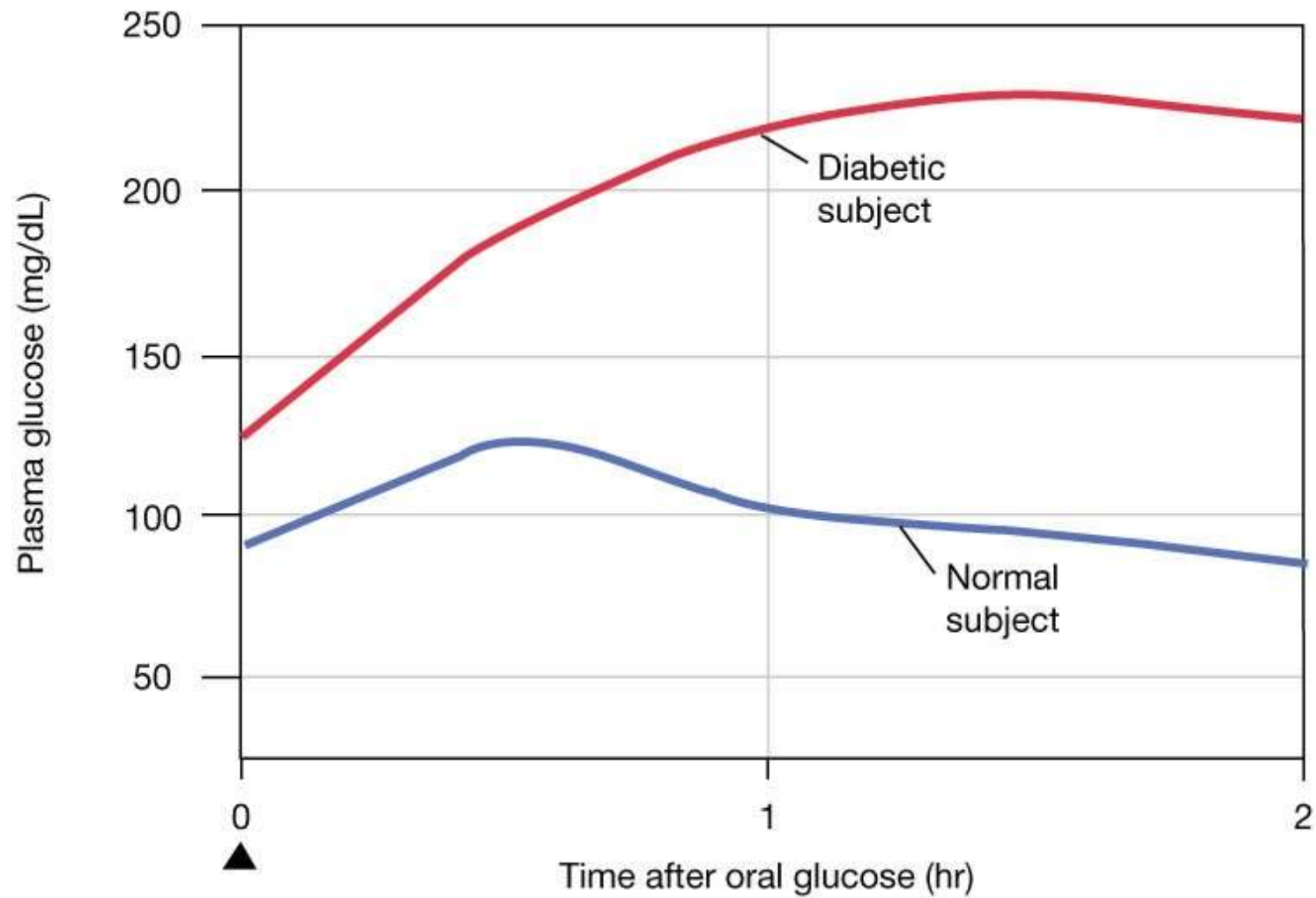
- A serious disorder of carbohydrate metabolism
- Results from hyposecretion or hypoactivity of insulin
- The three cardinal signs of DM are:
 - Polyuria – huge urine output
 - Polydipsia – excessive thirst
 - Polyphagia – excessive hunger and food consumption

Diabetes Mellitus Type I

Type 1: beta cells destroyed- no insulin produced chronic fasted state, "melting flesh", ketosis, acidosis, glucosuria, diuresis & coma

Diabetes Mellitus Type II

- Over 15 million diabetics in USA- 10% type I, 90% type II
- More common in some ethnic groups
- Insulin resistance keeps blood glucose too high
- Chronic complications: atherosclerosis, renal failure & blindness



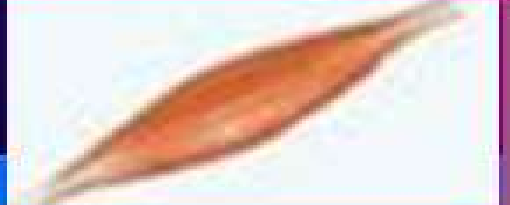


Fasting plasma
glucose
concentration

Symptoms of Diabetes Mellitus

- Hyperglycemia
- Polyuria
- Polydipsia
- Polyphagia
- Ketoacidosis
- Hyperlipidemia
- Muscle wasting
- Electrolyte depletion

Diabetes mellitus

Organ/tissue	Response	Blood	urine	Signs & symptoms
	Decreased glucose uptake	Hyperglycemia	glucosuria	Polyuria dehydration
	Glycogenolysis Gluconeogenesis	Hyperglycemia	Osmotic diuresis	Polydipsia
	Protein catabolism			Weight loss Polyphagia (Hyperphagia)

Diagnosis

- Demonstrating persistence hyperglycemia & glycosuria
- Glucose Tolerance Test (GTT) – oral is preferred
- Estimation of Fasting Blood Glucose (FBG)
- FBS more than 126 mg% in more than two occasions confirms DM

Treatment

- Insulin therapy
- Oral hypoglycemic agents
- Life style modifications

The Pineal Gland

- At the end of a short stalk on the roof of the diencephalon
- Pinealocytes with dense calcium particles
- Can be seen on x-ray (because of Ca^{++})
- Melatonin helps regulate the circadian rhythm
 - The biological clock of the diurnal (night/day) rhythm
 - Complicated feedback via retina's visual input

The Gonads (testes and ovaries)

main source of the steroid sex hormones

- Testes
 - Interstitial cells secrete androgens
 - Primary androgen is testosterone
 - Maintains secondary sex characteristics
 - Helps promote sperm formation
- Ovaries
 - Androgens secreted by thecal folliculi
 - Directly converted to estrogens by follicular granulosa cells
 - Granulosa cells also produce progesterone
 - Corpus luteum also secretes estrogen and progesterone

Endocrine cells in various organs

- The heart: atrial natriuretic peptide (ANP)
 - Stimulates kidney to secrete more salt
 - Thereby decreases excess blood volume, high BP and high blood sodium concentration
- GI tract & derivatives: Diffuse neuroendocrine system (DNES)

Endocrine cells in various organs continued

- The heart: atrial natriuretic peptide (ANP)
 - Stimulates kidney to secrete more salt
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- GI tract & derivatives: Diffuse neuroendocrine system (DNES)
- The placenta secretes steroid and protein hormones
 - Estrogens, progesterone
 - CRH
 - HCG
- The kidneys
 - Juxtaglomerular cells secrete renin
 - Renin indirectly signals adrenal cortex to secrete aldosterone
 - Erythropoietin: signals bone marrow to increase RBC production
- The skin
 - Modified cholesterol with uv exposure becomes Vitamin D precursor
 - Vitamin D necessary for calcium metabolism: signals intestine to absorb Ca^{++}