ENDOCRINE & PHARMACOLOGY OF DIABETES

Khder Hussein Rasul

Pharmacology II

Spring Semester

Second week

12/02/2025

Outline

- Endocrine system
- Pharmacology of diabetes

Objectives

By the end of this lecture, students should be able to:

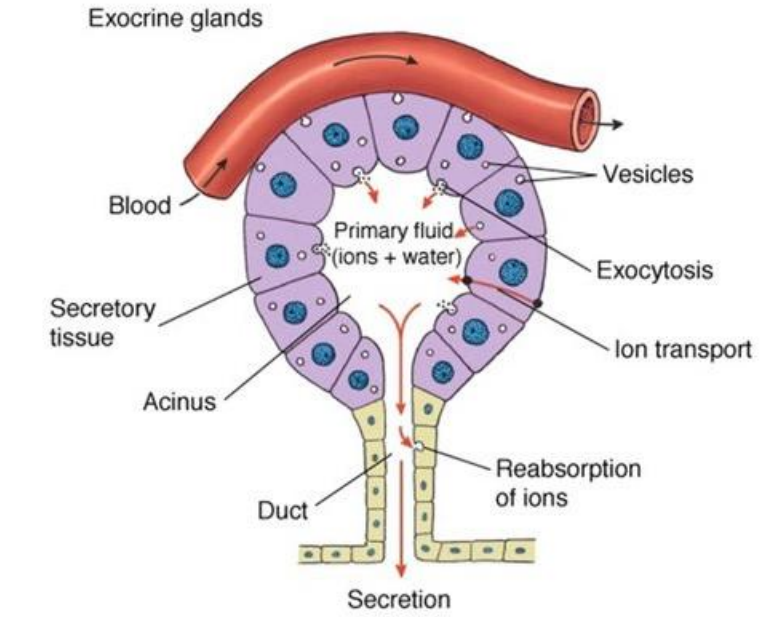
1. Understand endocrine system.
2. Being familiar more with hormone
3. Describe the action of drugs used in diabetes management.
4. Recognize the role of physiotherapists in managing patients receiving diabetes medications

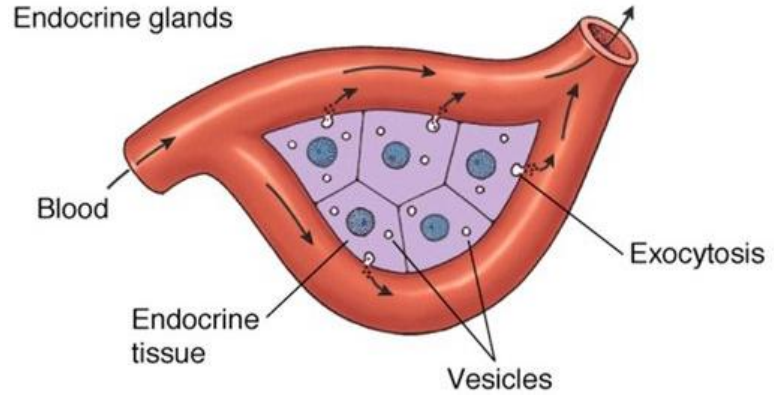
Types of glands

Gland: an organ that makes one or more substances, such as hormones, digestive juices, sweat, tears, saliva, or milk.

1. **Exocrine glands:** release their cellular secretions through a duct which empties to the outside or into the lumen (empty internal space) of an organ. These include sweat glands, salivary and pancreatic glands, and mammary glands. They are not considered a part of the endocrine system.

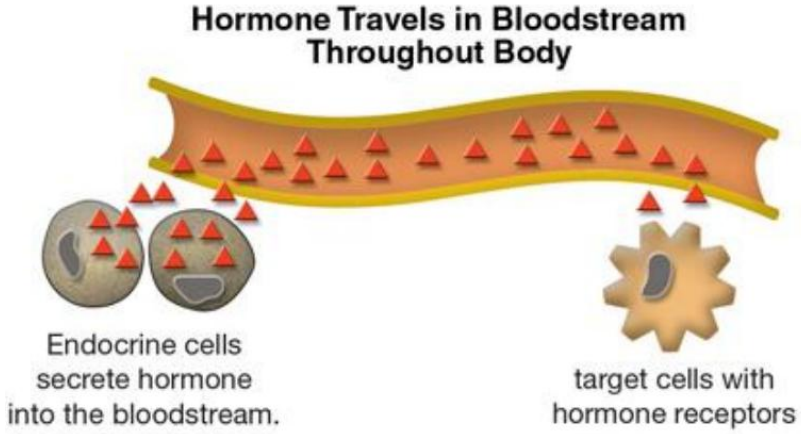
2. **Endocrine glands:** are ductless. This means that they do not have ducts to take their secretions to specific sites. Instead, hormones are secreted directly into capillaries and circulate in the blood throughout the body.





Endocrine system, hormones and target tissues

- **Endocrine system** consists of endocrine glands that secrete chemicals called hormones and produces long-term responses.
- **Hormones** are chemical messengers that stimulate specific cells or tissues into action.
- Each hormone exerts very specific effects on certain organs, called **target organs** or **target tissues**
- **Receptor** is a molecule inside or on the surface of a cell (target cell) that binds to hormone
- Some hormones, such as **insulin** and **thyroxine**, have many target organs. Other hormones, such as **calcitonin** and some **pituitary gland hormones**, have only one or a few target organs.



Endocrine system

- **Endocrine system** is a network of glands that produce and release hormones into the bloodstream to regulate various body functions.

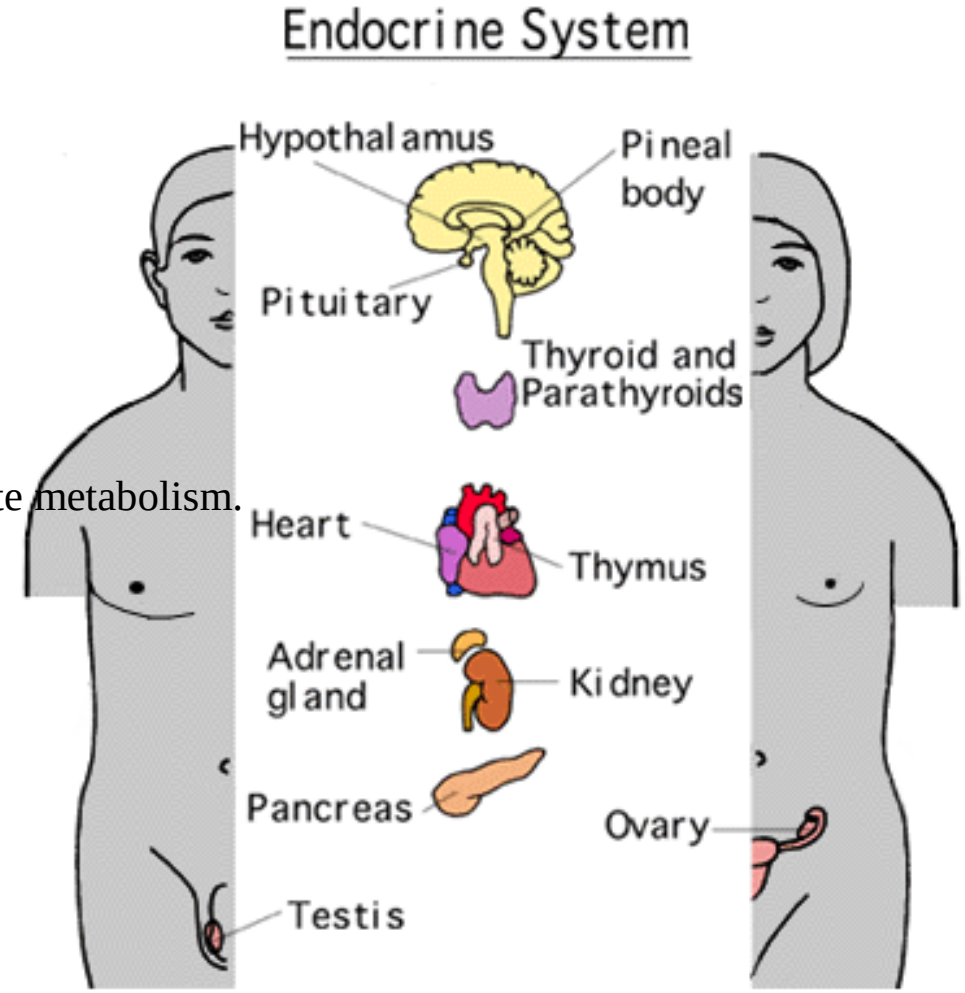
Functions of the endocrine system

1. Regulates growth & development
2. Controls metabolism & energy balance
3. Maintains fluid & electrolyte balance
4. Regulates reproduction & sexual function
5. Helps the body respond to stress & injury

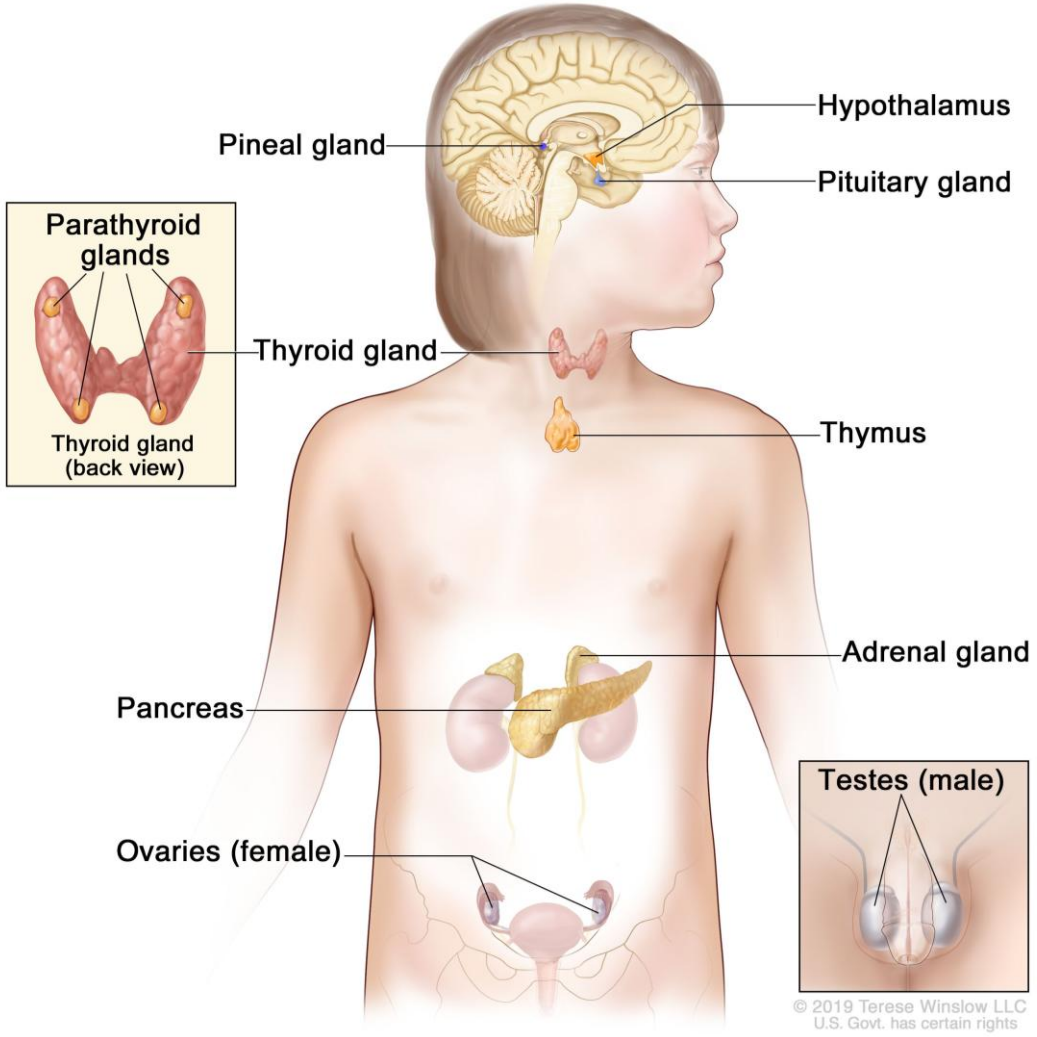
Components of the endocrine system

Key Components of the endocrine system

1. **Hypothalamus:** controls the pituitary gland.
2. **Pituitary gland:** secretes hormones influencing other endocrine glands.
3. **Thyroid gland:** Regulates metabolism, energy production, and growth.
4. **Parathyroid glands:** Maintain calcium balance in the blood.
5. **Adrenal glands:** Produce stress hormones (cortisol, adrenaline) and regulate metabolism.
6. **Pancreas:** Controls blood sugar levels
7. **Gonads (Ovaries & Testes):** Responsible for reproductive hormones



Endocrine glands



Location of endocrine glands

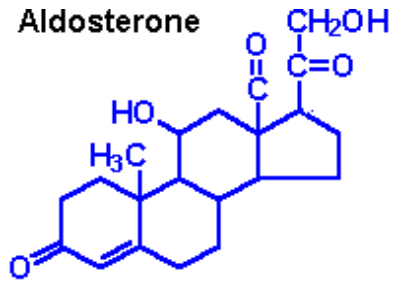
Chemistry of the hormones

Hormones are organized into three main classes based on their chemical structure:

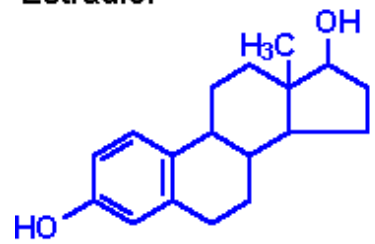
1. Steroid hormones are synthesized from cholesterol

- Steroid hormones are lipid-soluble, so they can pass through cell membranes to reach receptor molecules located inside their target cells.
- Example of steroid hormones: aldosterone, estrogen, and testosterone.

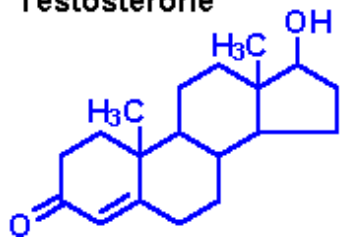
Aldosterone



Estradiol



Testosterone

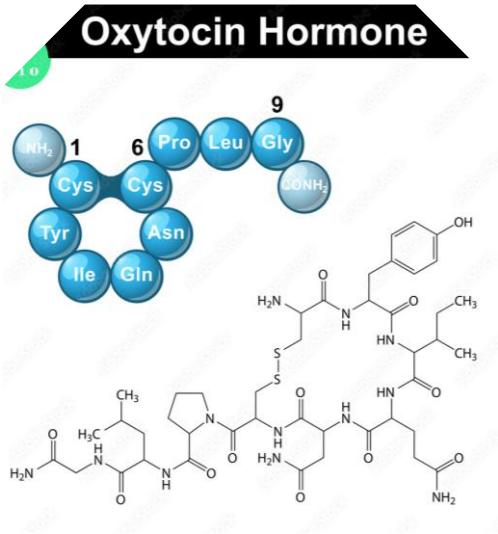


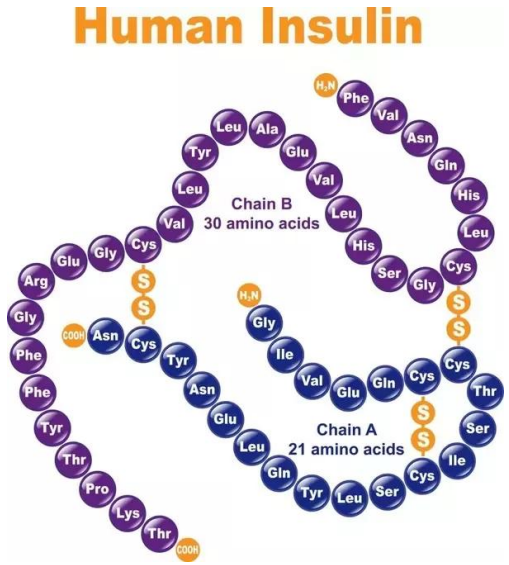
Chemistry of the hormones

2. Peptide and protein hormones are structured from chains of amino acids

These hormones are chains of amino acids

- Short chains of amino acids called peptides
- Oxytocin is peptide hormone
- Long chains of amino acids called proteins.
- Insulin is protein hormone.

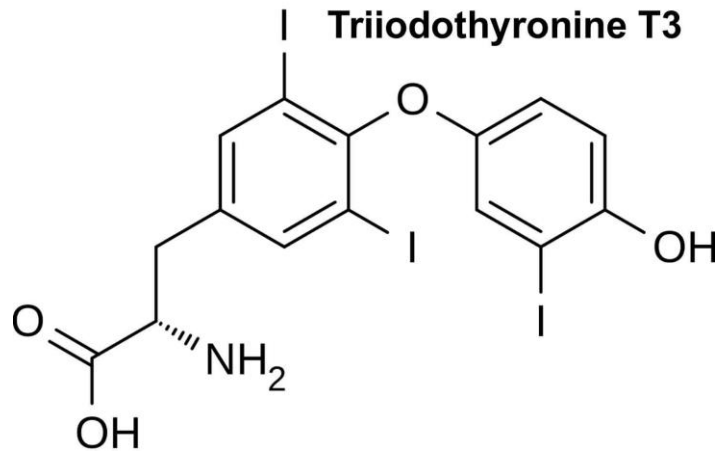


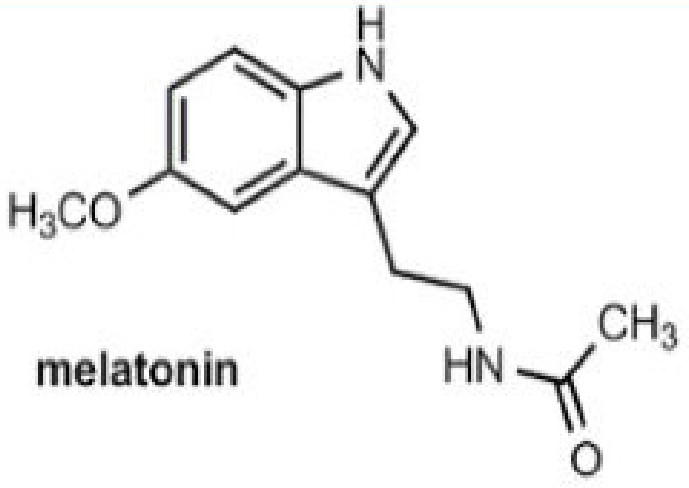


Chemistry of the hormones

3. Amine hormones are modified amino acids (Amino acid derivatives)

- These simple hormones are structural variations of the amino acids.
- The derivatives of tyrosine, such as the thyroid hormones released by the thyroid gland.
- Melatonin, secreted by the pineal gland, is derived from tryptophan.





Pharmacology of Diabetes Mellitus

Diabetes is a chronic metabolic disorder characterized by high blood sugar levels (hyperglycemia) due to defects in insulin production, insulin action, or both.

Types of Diabetes Mellitus

1. Type 1 Diabetes Mellitus (T1DM) – Insulin-dependent diabetes
2. Type 2 Diabetes Mellitus (T2DM) – Insulin resistance diabetes

Type 1 Diabetes Mellitus (T1DM) – Insulin-Dependent Diabetes

Type 1 Diabetes Mellitus (T1DM) – Insulin-Dependent Diabetes

An autoimmune disorder where the body's immune system attacks pancreatic β-cells, leading to little or no insulin production.

Causes: Autoimmune destruction of insulin-producing β-cells in the pancreas.

Onset: Usually in childhood or adolescence but can occur at any age.

Treatment: Requires lifelong insulin therapy.

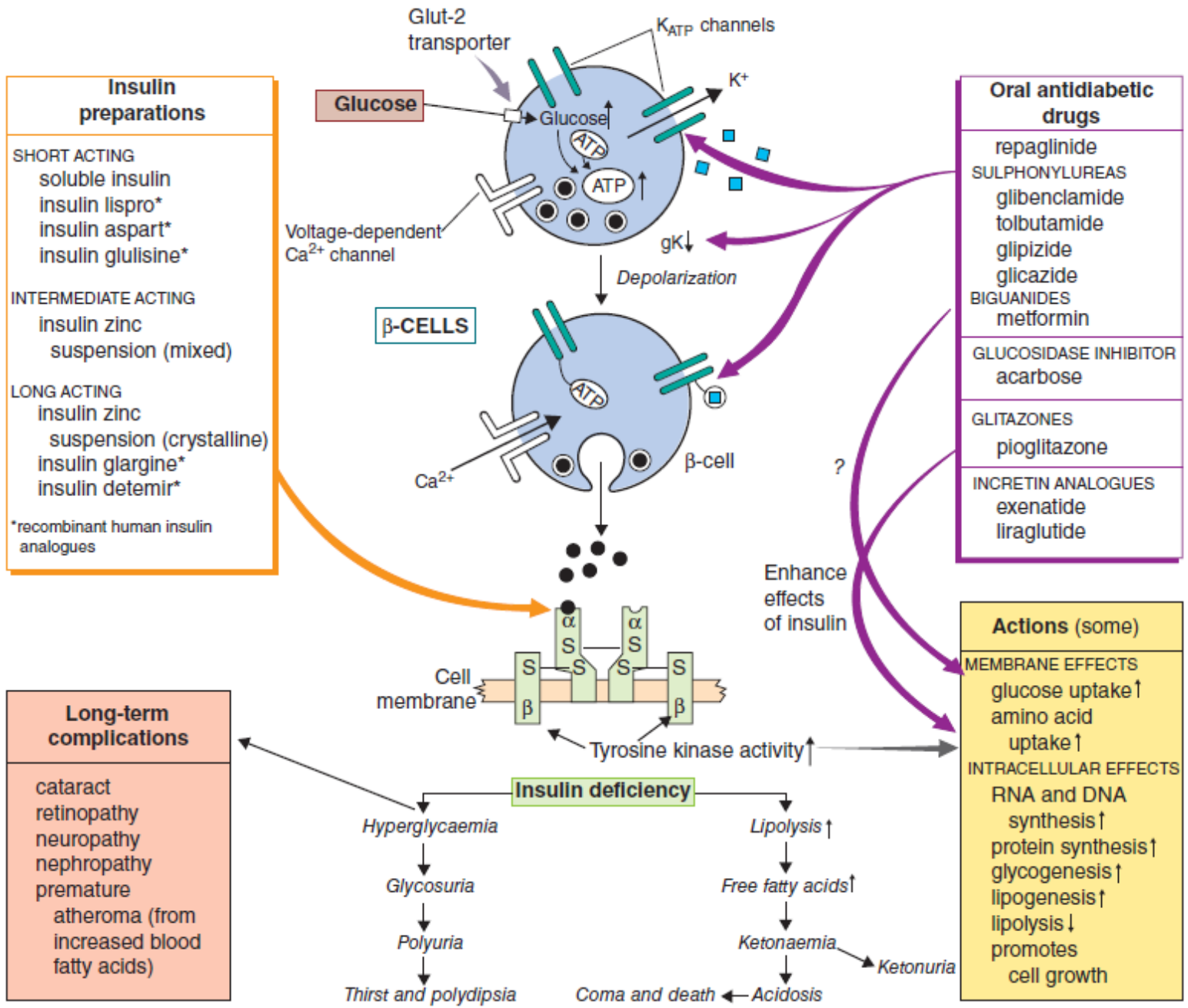
Symptoms: Rapid weight loss, excessive thirst (polydipsia), frequent urination (polyuria), and fatigue.

Type 2 Diabetes Mellitus (T2DM) – Insulin Resistance Diabetes

- A metabolic disorder where cells become resistant to insulin, and the pancreas cannot produce enough insulin to compensate.
- **Causes:** Obesity, sedentary lifestyle and genetics.
- **Onset:** More common in adults over 40.
- **Treatment:** Lifestyle changes, oral medications (Metformin), and sometimes insulin.
- **Symptoms:** Often mild at first—fatigue, slow wound healing, frequent infections.

Insulin

- Insulin is a hormone secreted by the β-cells of the islets of Langerhans in the pancreas.
- Blood glucose stimulates insulin release.
- Insulin binds to specific receptors in the cell membranes, initiating a number of actions, including an increase in glucose uptake by the muscle, liver and adipose tissue.
- In diabetes mellitus, there is a relative or total absence of insulin, which causes reduced glucose uptake by insulin-sensitive tissues and has serious consequences.
- Lipolysis and muscle proteolysis result in weight loss and weakness.
- In the blood, causing an acidosis (ketoacidosis).

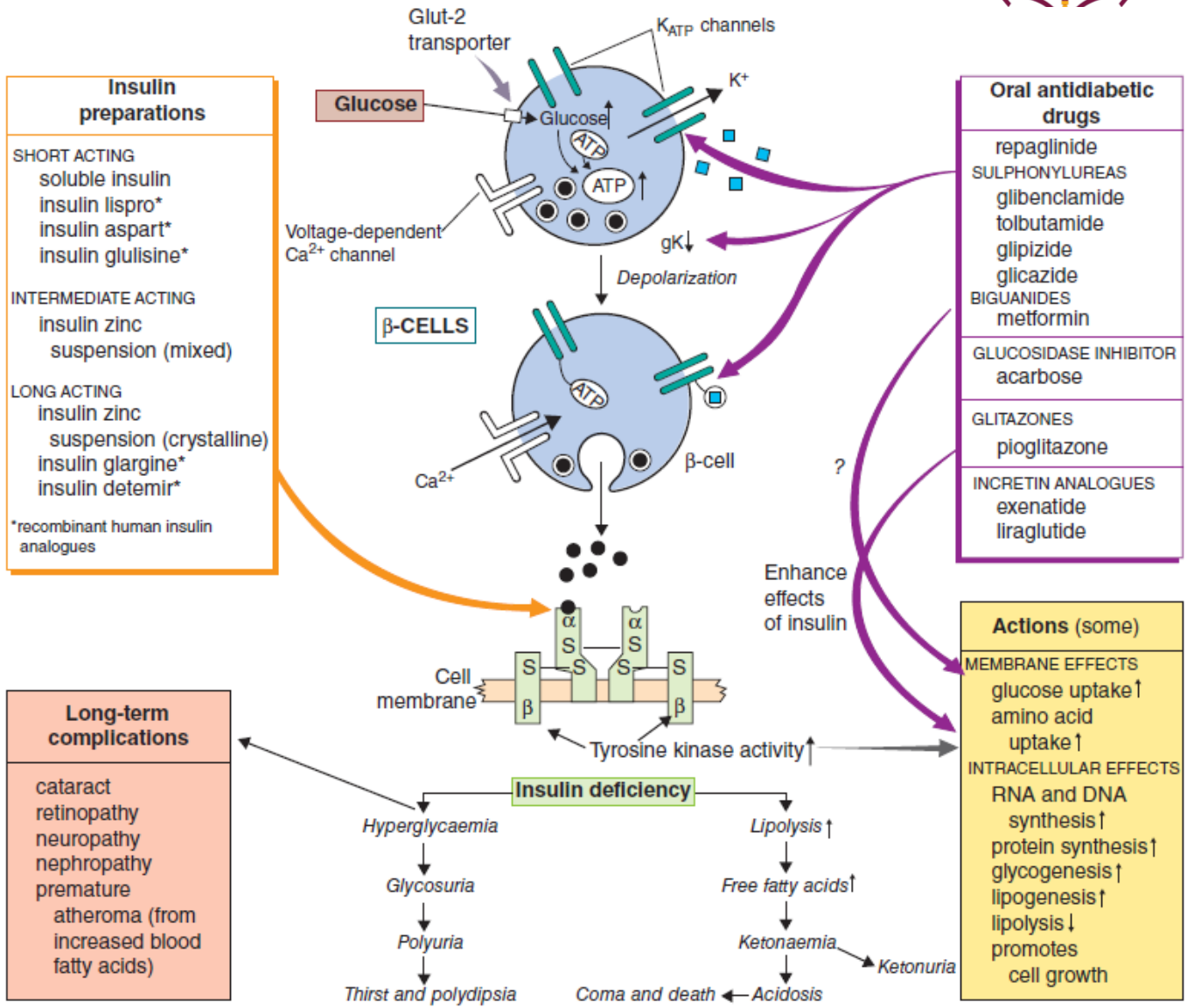

Insulin preparations
SHORT ACTING
soluble insulin
insulin lispro*
insulin aspart*
insulin glulisine*
INTERMEDIATE ACTING
insulin zinc suspension (mixed)
LONG ACTING
insulin zinc suspension (crystalline)
insulin glargine*
insulin detemir*
*recombinant human insulin analogues
Glut-2 transporter
K_{ATP} channels
Glucose
K^+
Glucose
ATP
ATP
Voltage-dependent Ca^{2+} channel
gK↓
Depolarization
β-CELLS
ATP
Ca^{2+}
β-cell
Oral antidiabetic drugs
repaglinide
SULPHONYLUREAS
glibenclamide
tolbutamide
glipizide
glicazide
BIGUANIDES
metformin
GLUCOSIDASE INHIBITOR
acarbose
GLITAZONES
pioglitazone
INCRETIN ANALOGUES
exenatide
liraglutide
?
Enhance effects of insulin
Cell membrane
Tyrosine kinase activity↑
Actions (some)
MEMBRANE EFFECTS
glucose uptake↑
amino acid uptake↑
INTRACELLULAR EFFECTS
RNA and DNA synthesis↑
protein synthesis↑
glycogenesis↑
lipogenesis↑
lipolysis↓
promotes cell growth
Long-term complications
cataract
retinopathy
neuropathy
nephropathy
premature atheroma (from increased blood fatty acids)
Insulin deficiency
Hyperglycaemia
Glycosuria
Polyuria
Thirst and polydipsia
Lipolysis↑
Free fatty acids↑
Ketonaemia
Ketonuria
Acidosis
Coma and death

Pharmacology of Diabetes Mellitus

Short-acting insulins

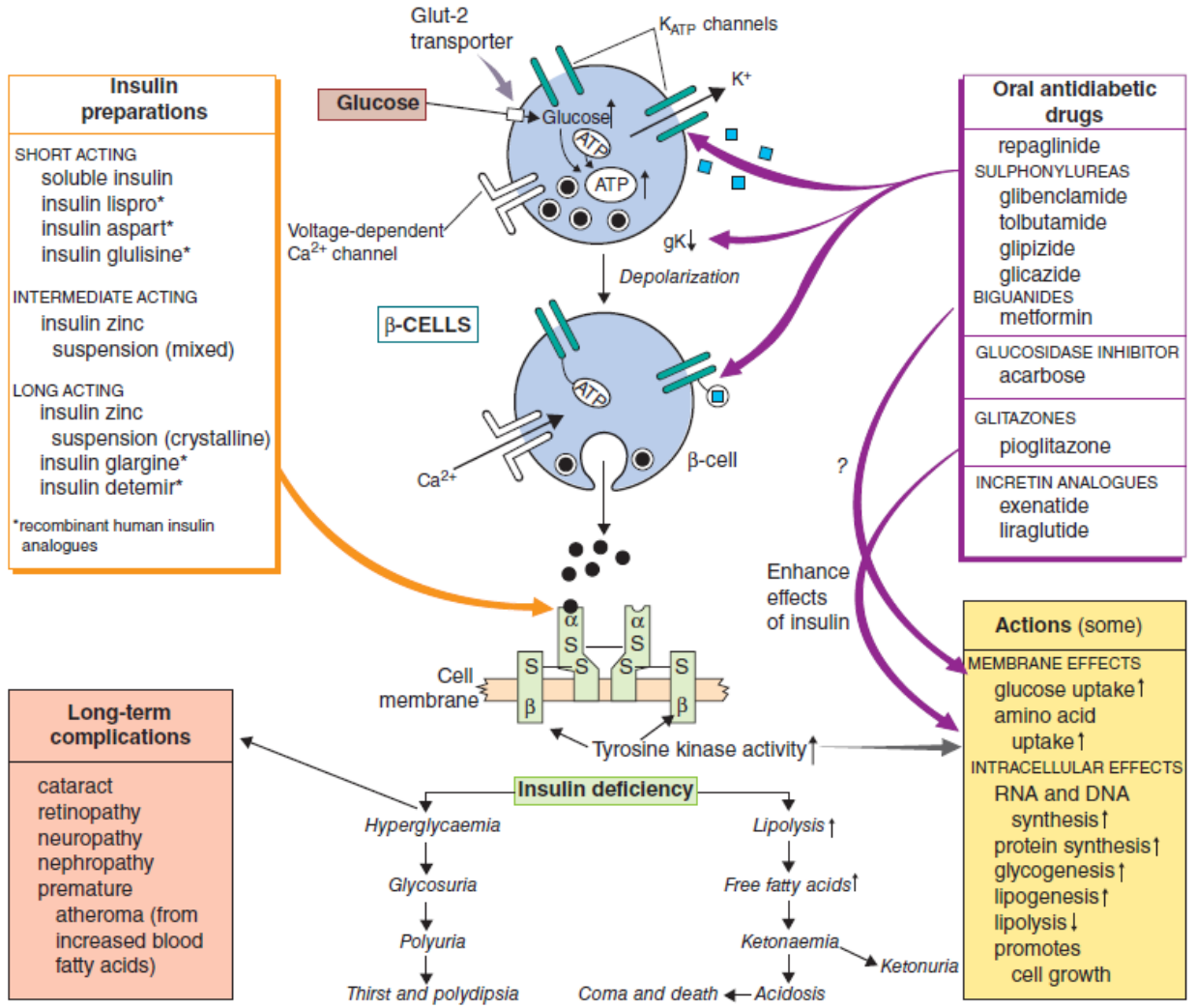
For example Insulin lispro

1. Rapid-acting insulin analog
2. Onset of action 10-15 minutes
3. Peak action 30-90 minutes
4. Duration of action 3-5 hours
5. Route of administration Subcutaneous (SC) injection, IV (in hospital settings)
6. Half-Life ~1 hour
7. Time to administer 5-15 minutes before meals

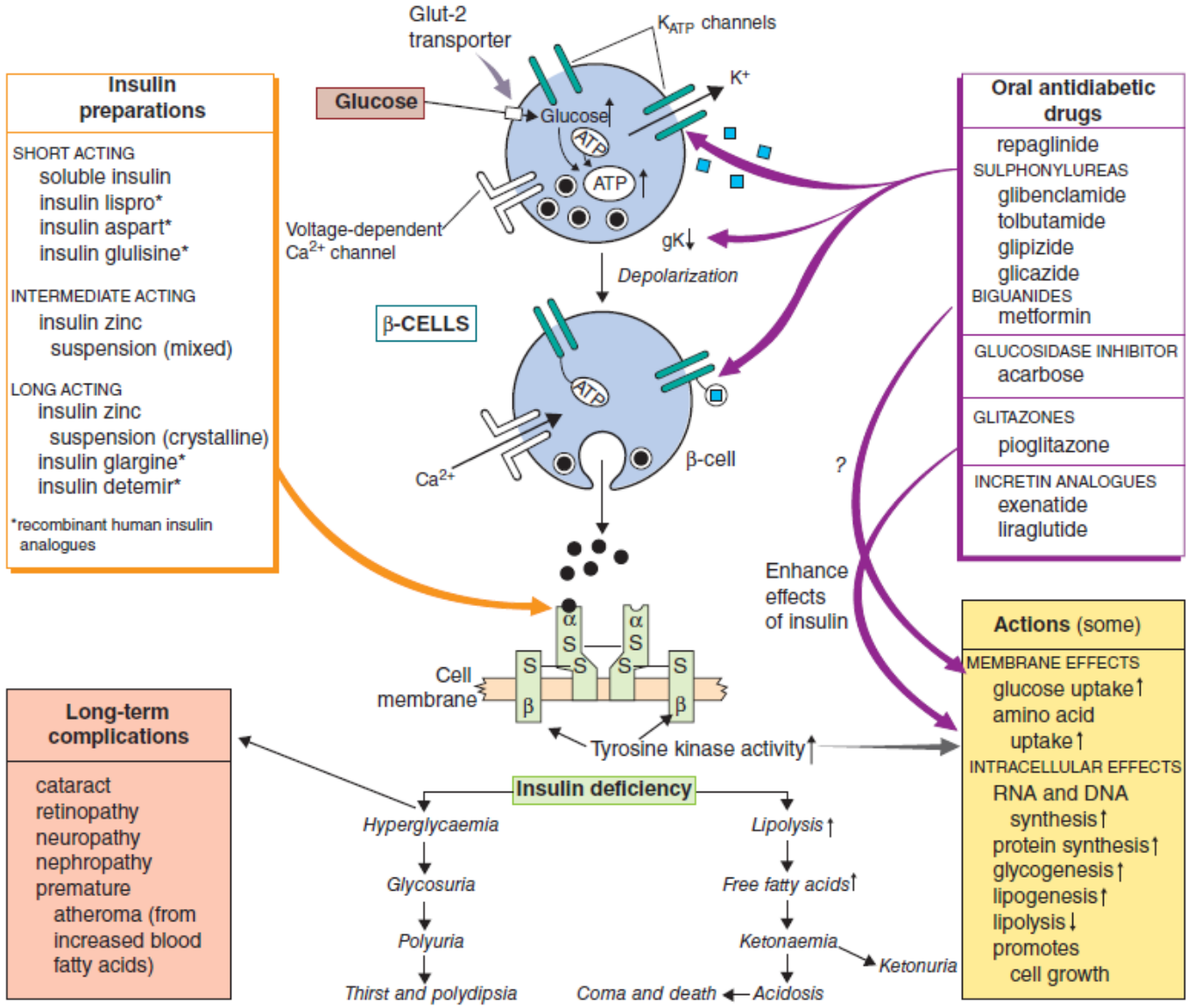


Mechanism of action Insulin lispro

1. Binds to insulin receptors on target cells (liver, muscle, adipose tissue) → stimulates glucose uptake and inhibits glucose production.
2. Promotes glycogenesis
3. Inhibits lipolysis
4. Enhances protein synthesis



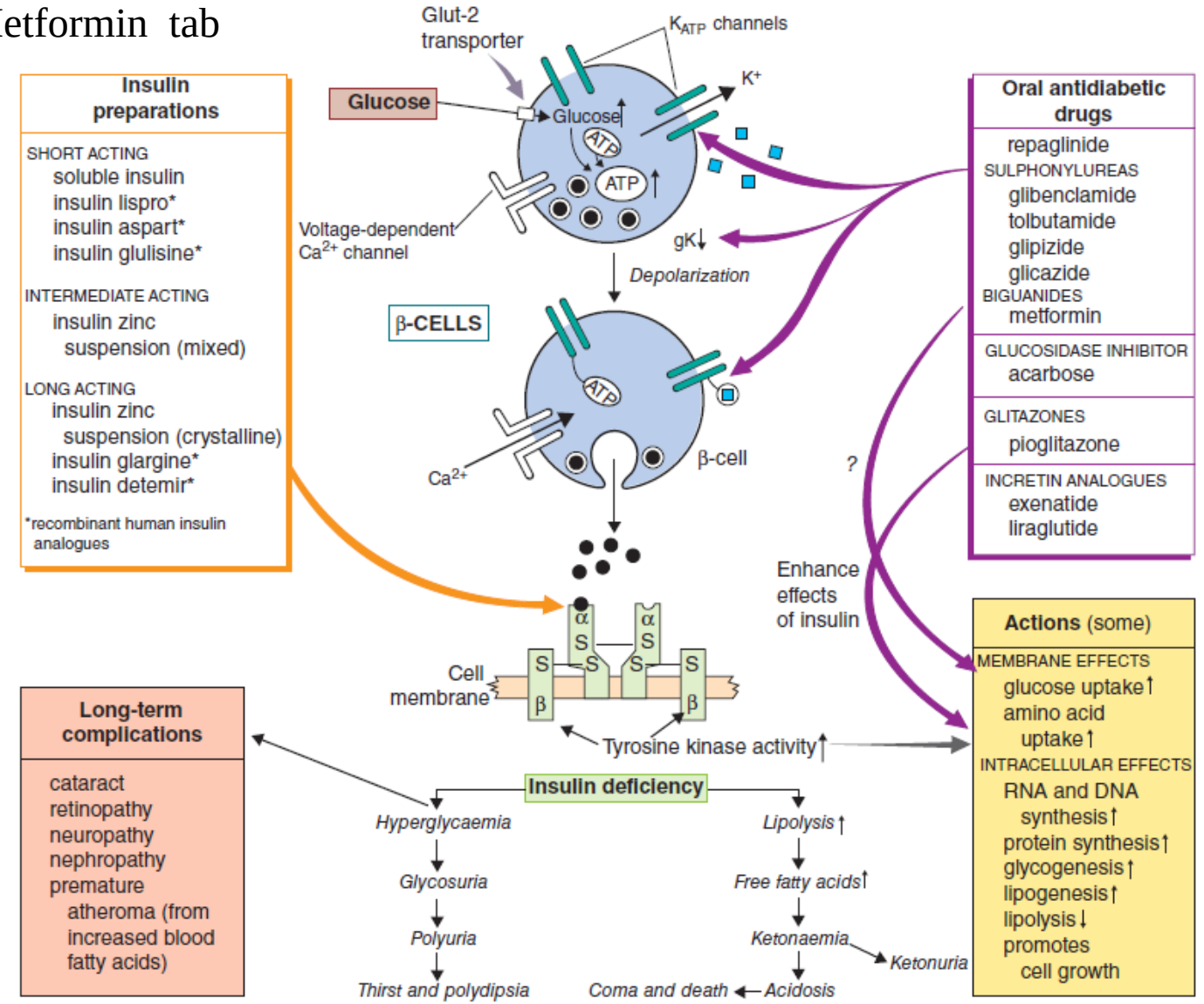
Intermediate and long acting



Oral antidiabetic drugs

Glibinclamide tab, Glicazide tab, Pioglitzon tab and Metformin tab

1. Sulphonylureas and rapaglinide stimulate insulin release from the pancreatic islets and so the patient must have partially functional β-cells for these drugs to be of use.
2. Hypoglycaemia and hypoglycaemic coma may be induced by longer-acting drugs, especially in elderly patients.

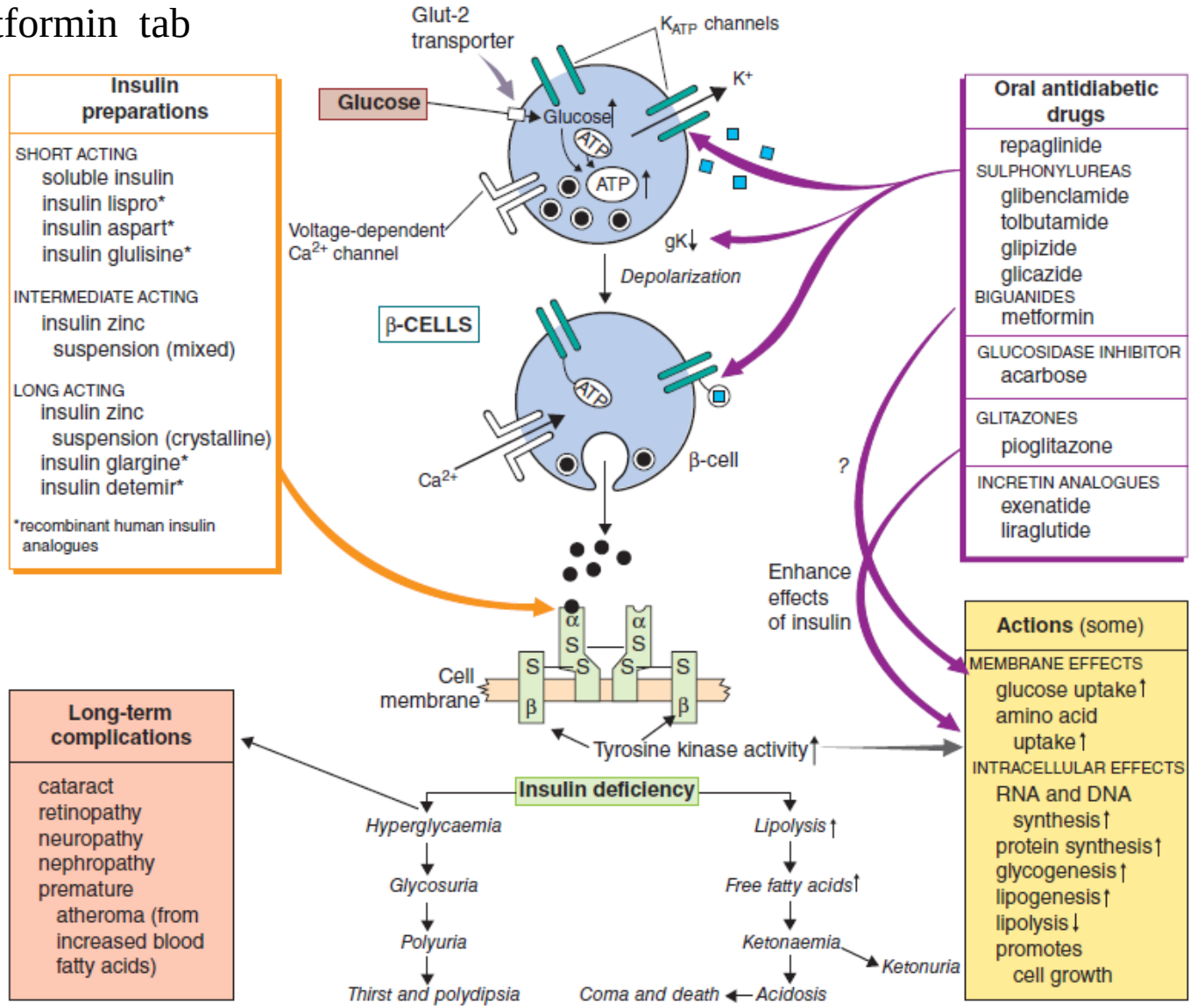


Oral antidiabetic drugs

Glibinclamid tab, Glicazide tab, Pioglitzon tab and Metformin tab

Metformin

1. Metformin is the first-line drug for patients with type 2 diabetes
2. Metformin reduces hepatic glucose production and acts peripherally to increase glucose uptake.
3. it does not increase insulin release, it rarely causes hypoglycaemia.
4. **Adverse effects** include nausea, vomiting, diarrhoea and, very occasionally, potentially fatal lactic acidosis.



Physiotherapy consideration

- Patients on SGLT2 inhibitors have a risk of dehydration and ketoacidosis.
- Patients using insulin or sulfonylureas should monitor hypoglycemia risk during exercise.

Physiotherapists play a crucial role in managing patients receiving diabetic medications. Their contributions include:

1. **Enhancing glycemic control through exercise**
2. **Preventing and managing diabetic complications**
3. **Patient Education & Lifestyle Modifications**