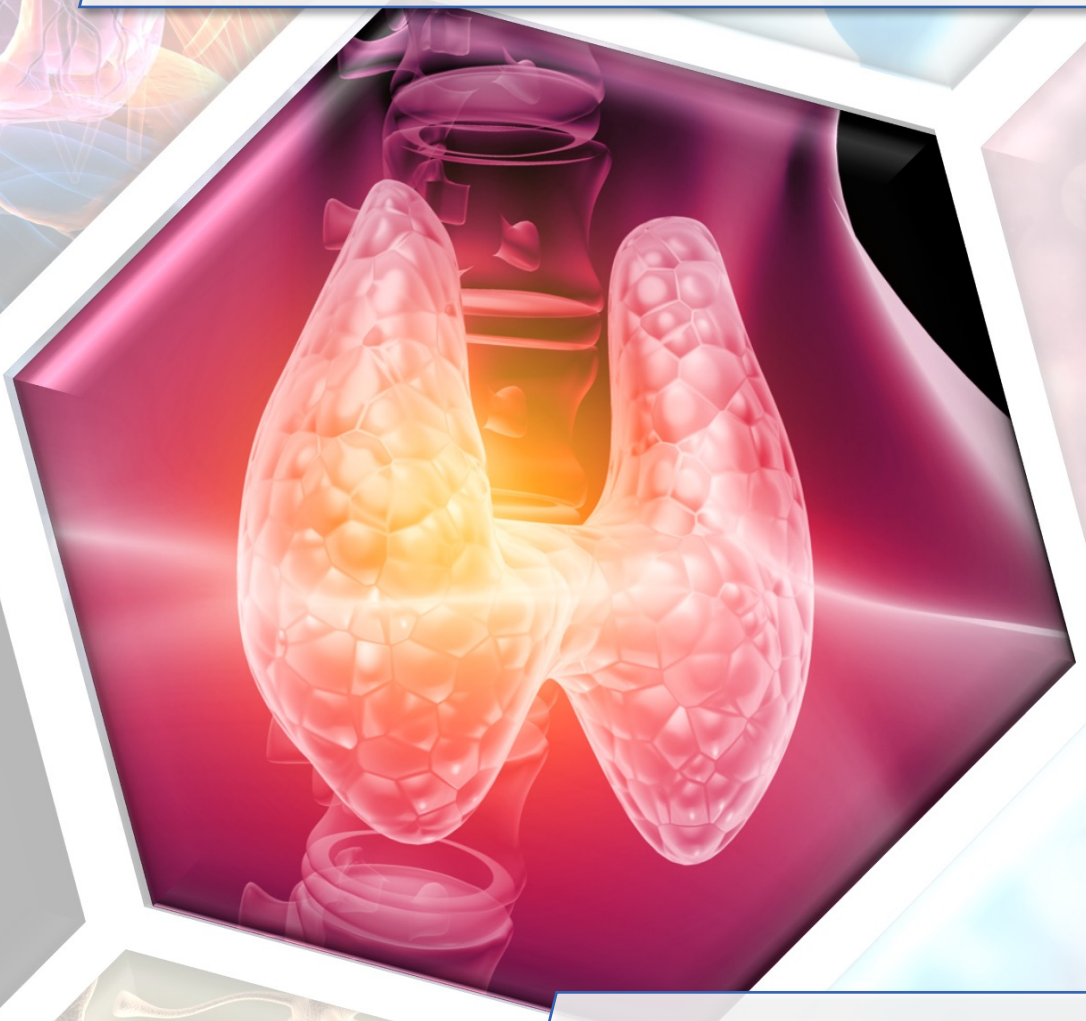
IMPERIAL

# Introduction to diabetes mellitus



21st January 2026

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# Session Plan

## Insulin and its action

## Type 1 diabetes

## Type 2 diabetes

## Management of diabetes

# Overview

## Insulin action:

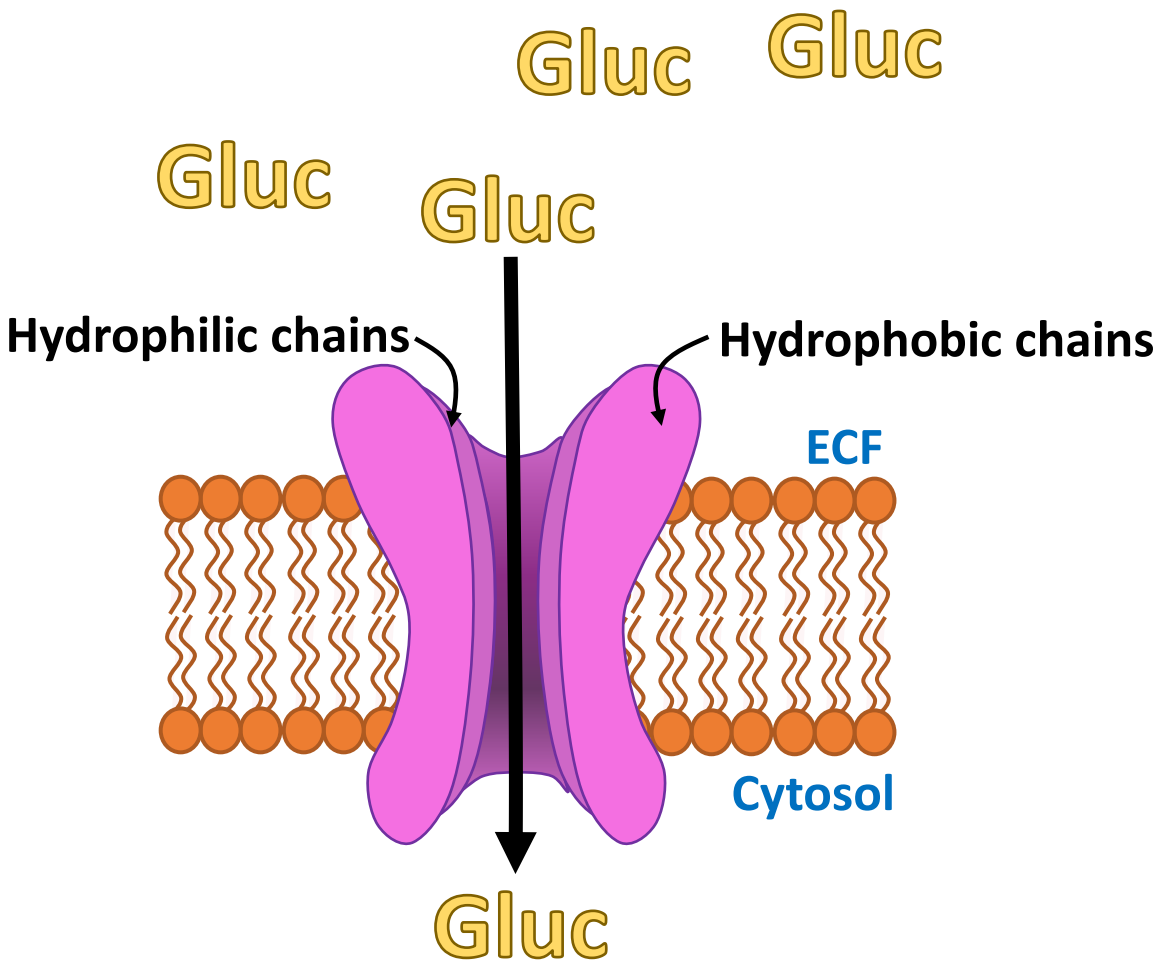
- **Glucose**
  - decrease HGO
  - increase muscle uptake
- **Protein**
  - decrease proteolysis
- **Fat**
  - decrease lipolysis
  - decrease ketogenesis
- In the fasted and fed state

## Clinical implications:

- **Type 1 diabetes**
- **Hypoglycaemia**
- **Insulin Resistance**
- **Type 2 diabetes**
- **Management**

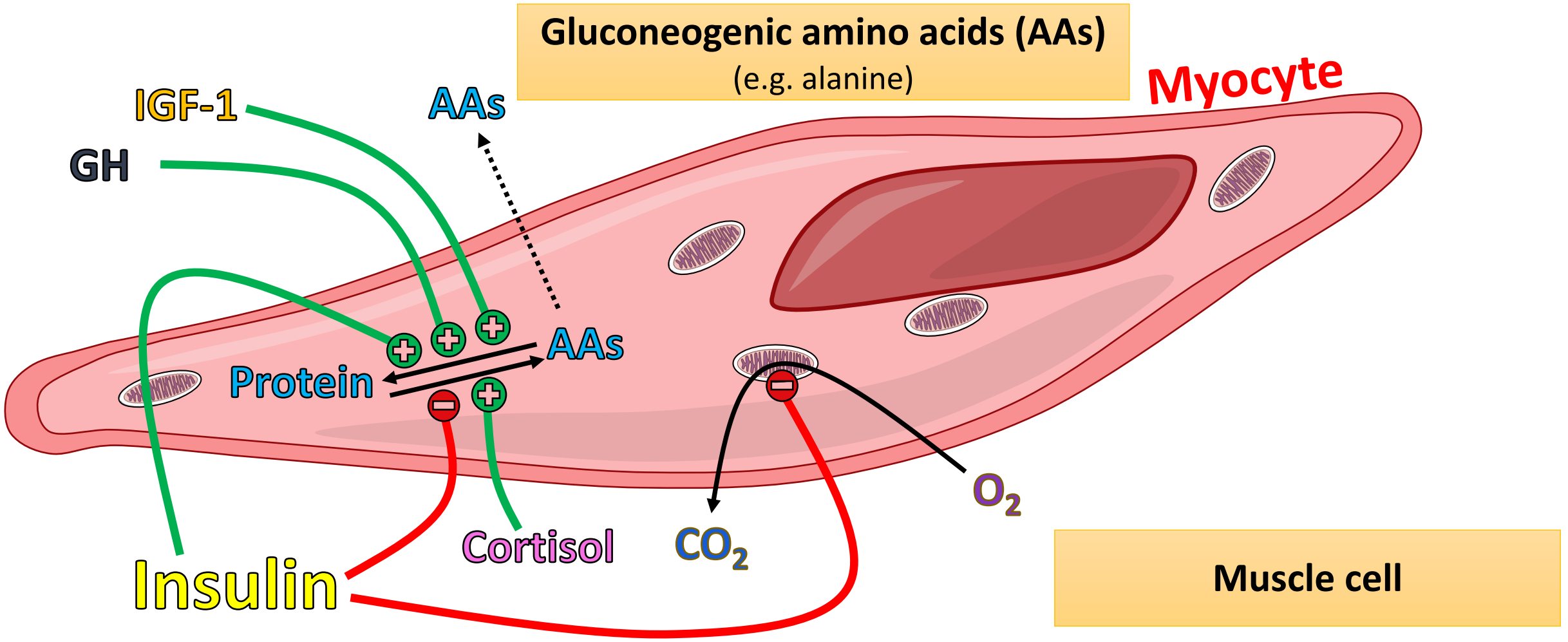
# GLUT-4

- Common in myocytes (muscle) and adipocytes (fat)
- Highly insulin-responsive
- Lies in vesicles
- Recruited and enhanced by insulin
- 7-fold increase glucose uptake



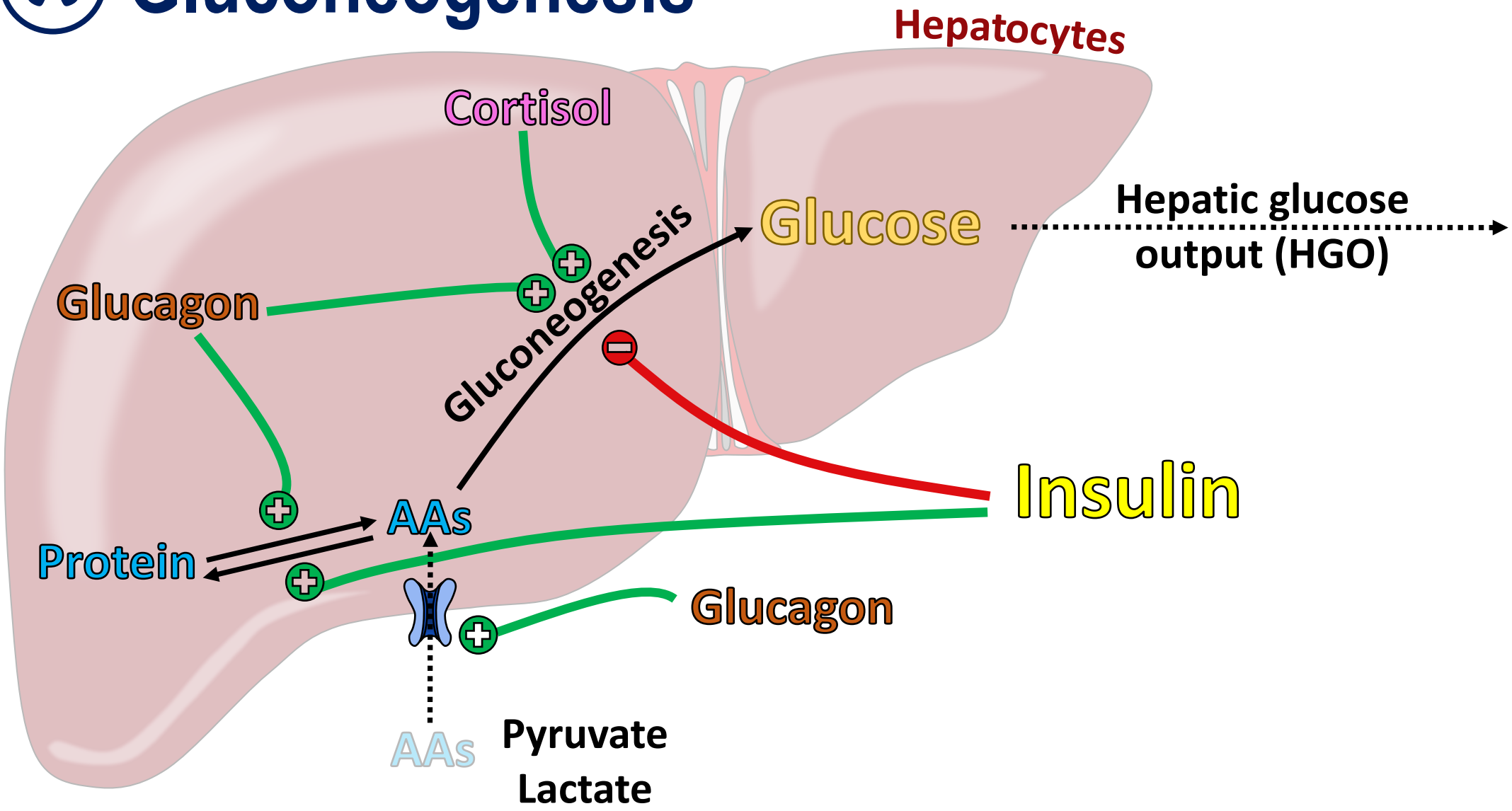

Describe the pathological, physiological and clinical effects of hyper- and hypoglycaemia.
Recall the aetiology, pathophysiology, phenotypic features and clinical presentations of type 1 and type 2 diabetes mellitus.
Describe the management of type 1 and type 2 diabetes, including surveillance and prevention of macrovascular and microvascular complications.

# Effects of insulin on cell metabolism




**Function of endocrine glands:** Summarise the function of the key endocrine glands, including the synthesis, regulation and physiological effects of their hormones

# Gluconeogenesis

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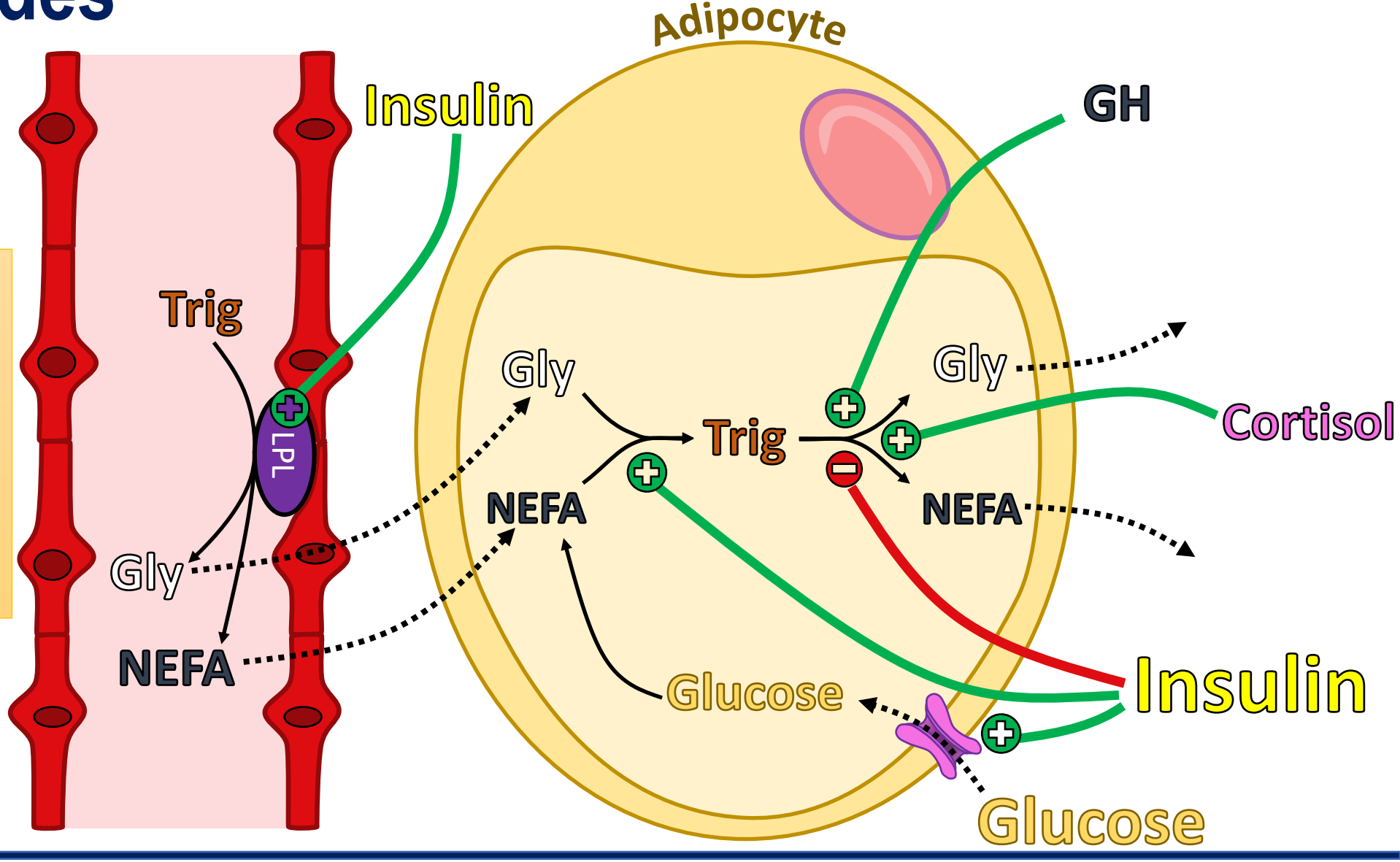
# Fuel stores

| Store | Mass (kg) | Energy (KJ/kg) | Time |
|---|---|---|---|
| **Carbohydrate** (liver & muscle) | 0.5 kg | 16 | 16 hours |
| **Protein** | 8-9 kg | 17 | 15 days |
| **Fat** | 9-10 kg | 37 | 30 to 40 days |

**Depletable within a one day fast**

# Triglycerides

**Lipoprotein lipase** (LPL) enzyme breaks down triglycerides that would otherwise be unable to leave the circulation

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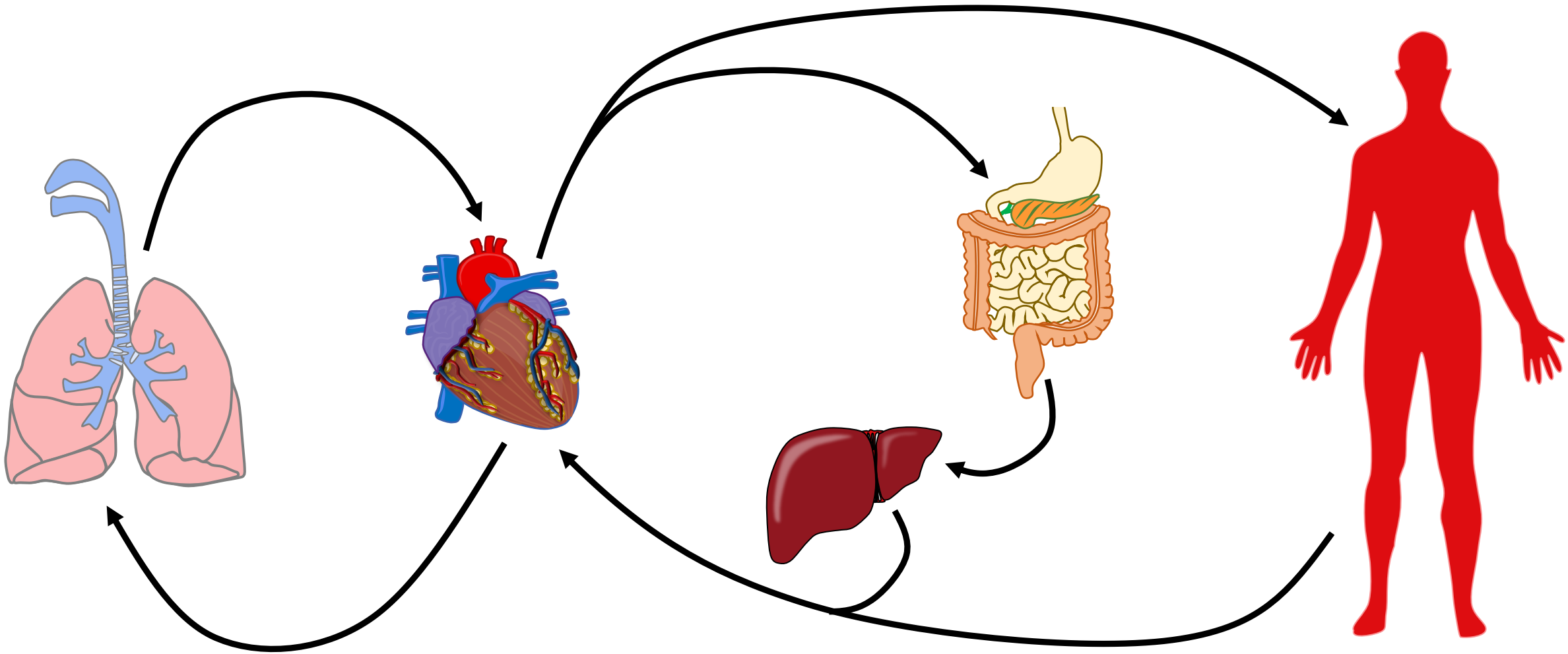
# Circulation



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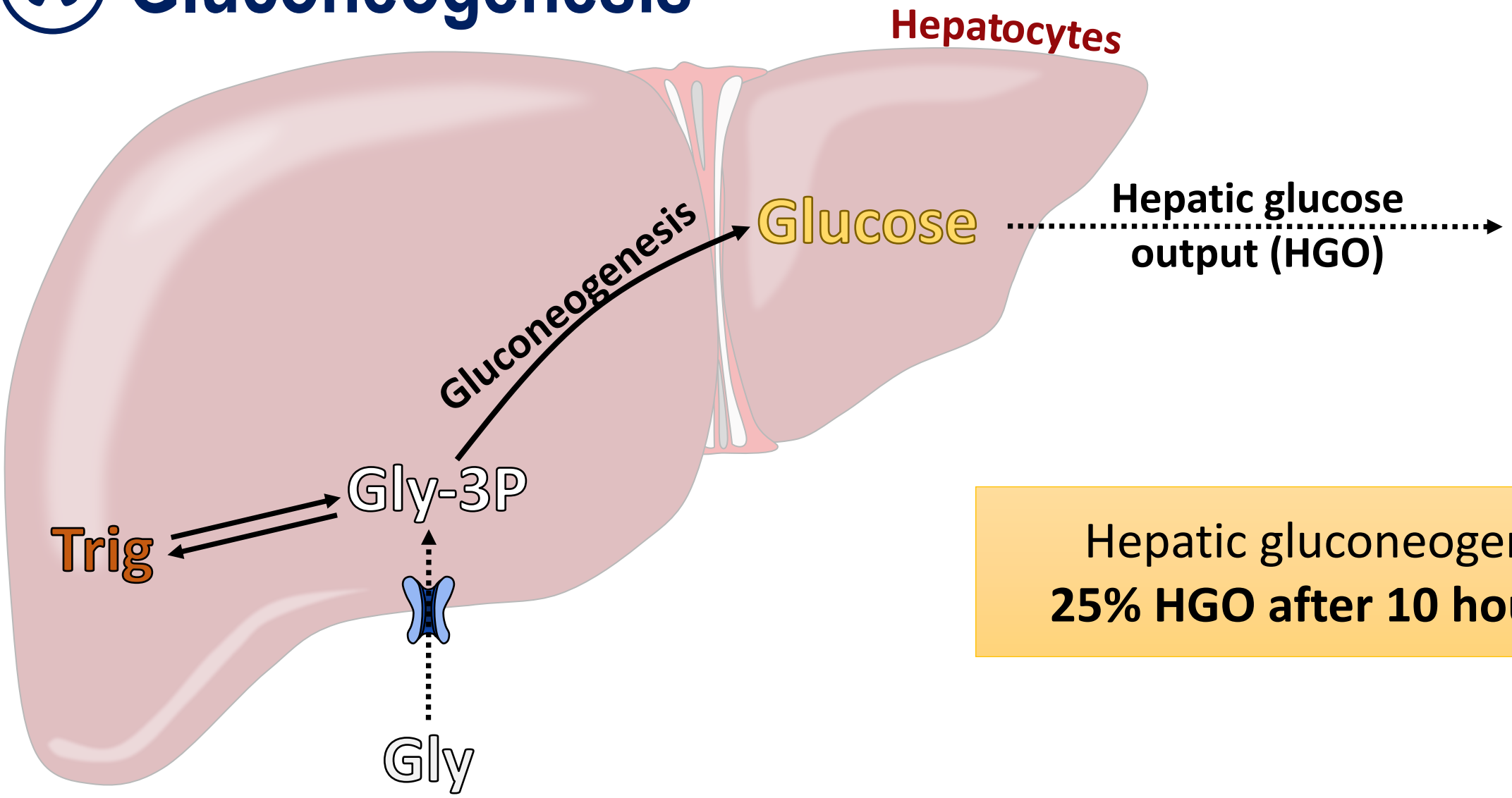
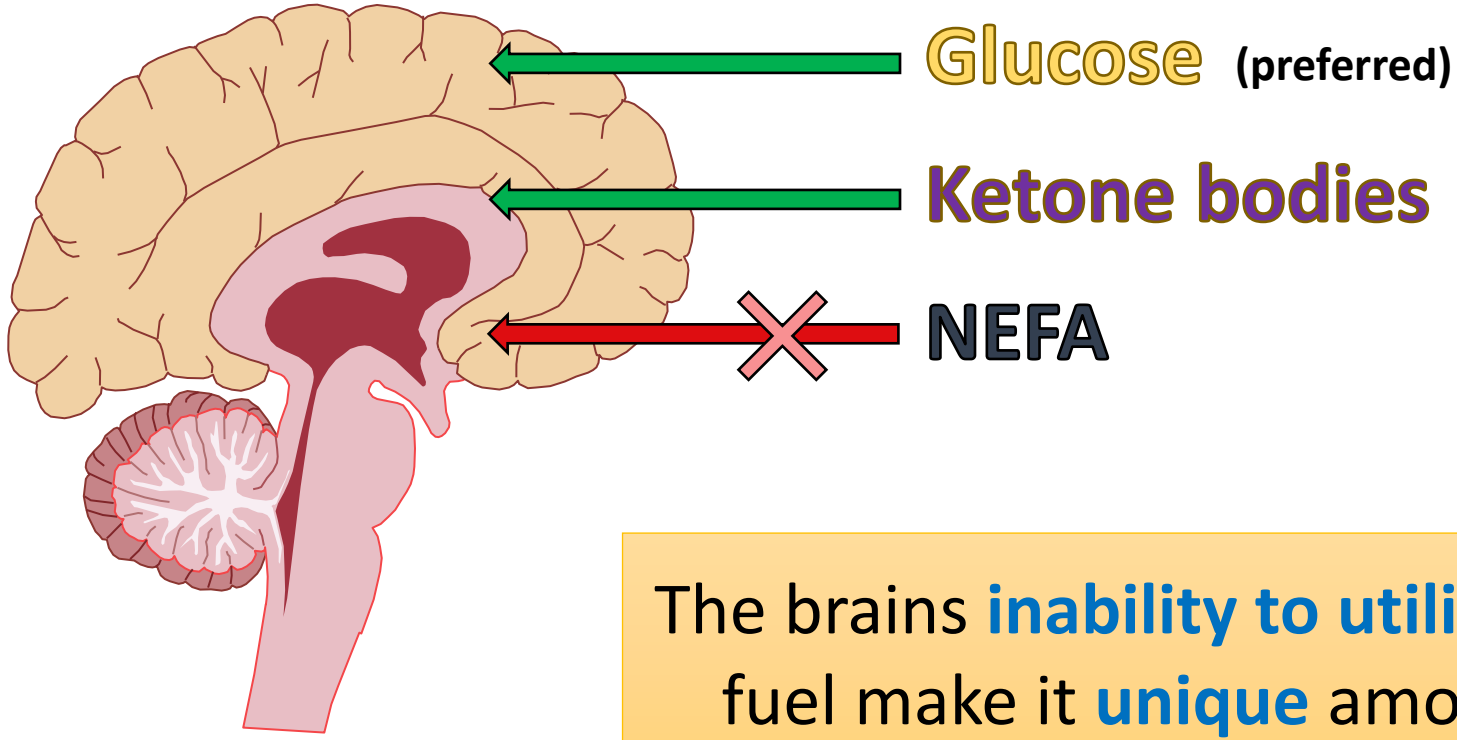
# Gluconeogenesis




Hepatic gluconeogenesis

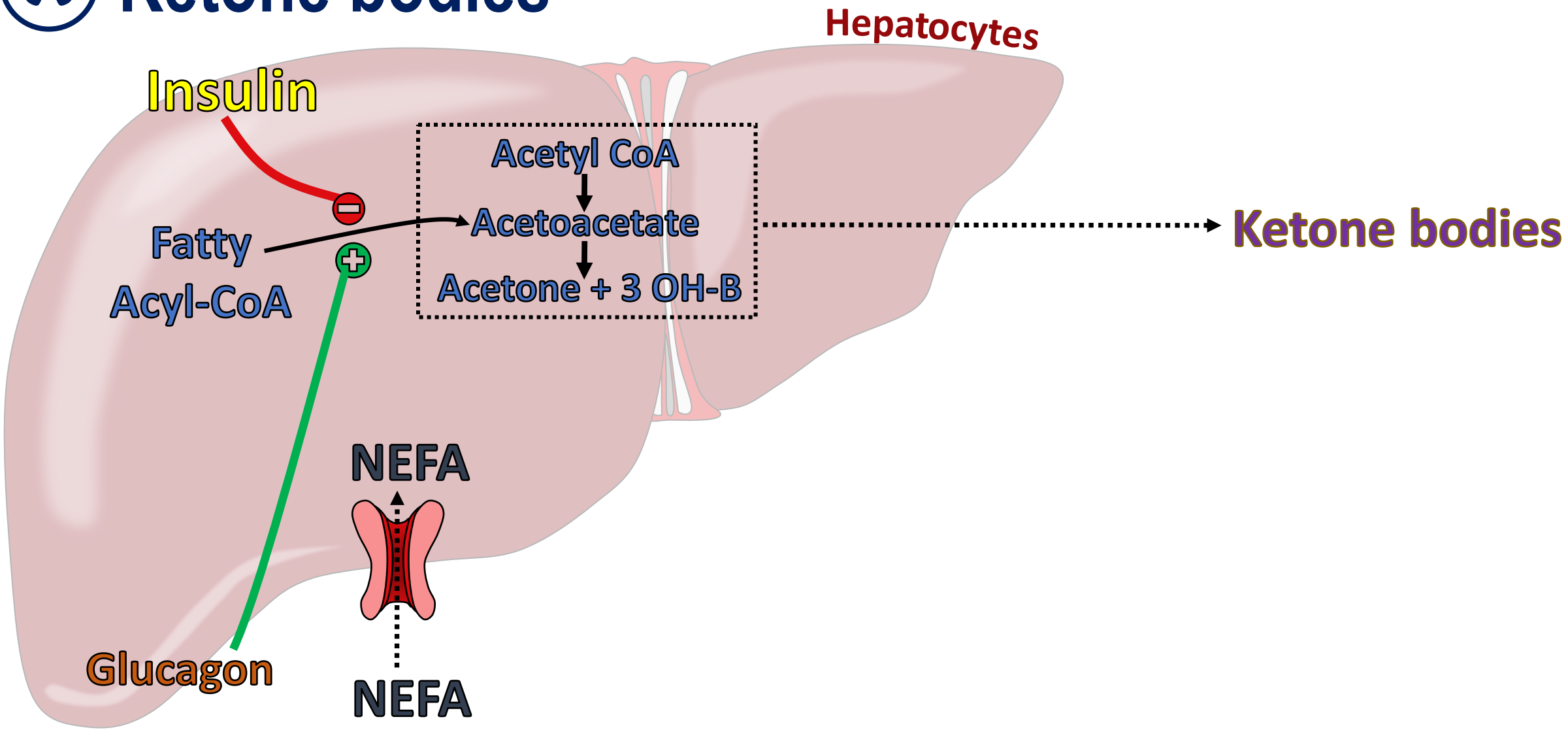
**25% HGO after 10 hour fast**

# Cerebral energy requirement




The brains **inability to utilise fatty acids** as a fuel make it **unique** among body tissues

# Ketone bodies

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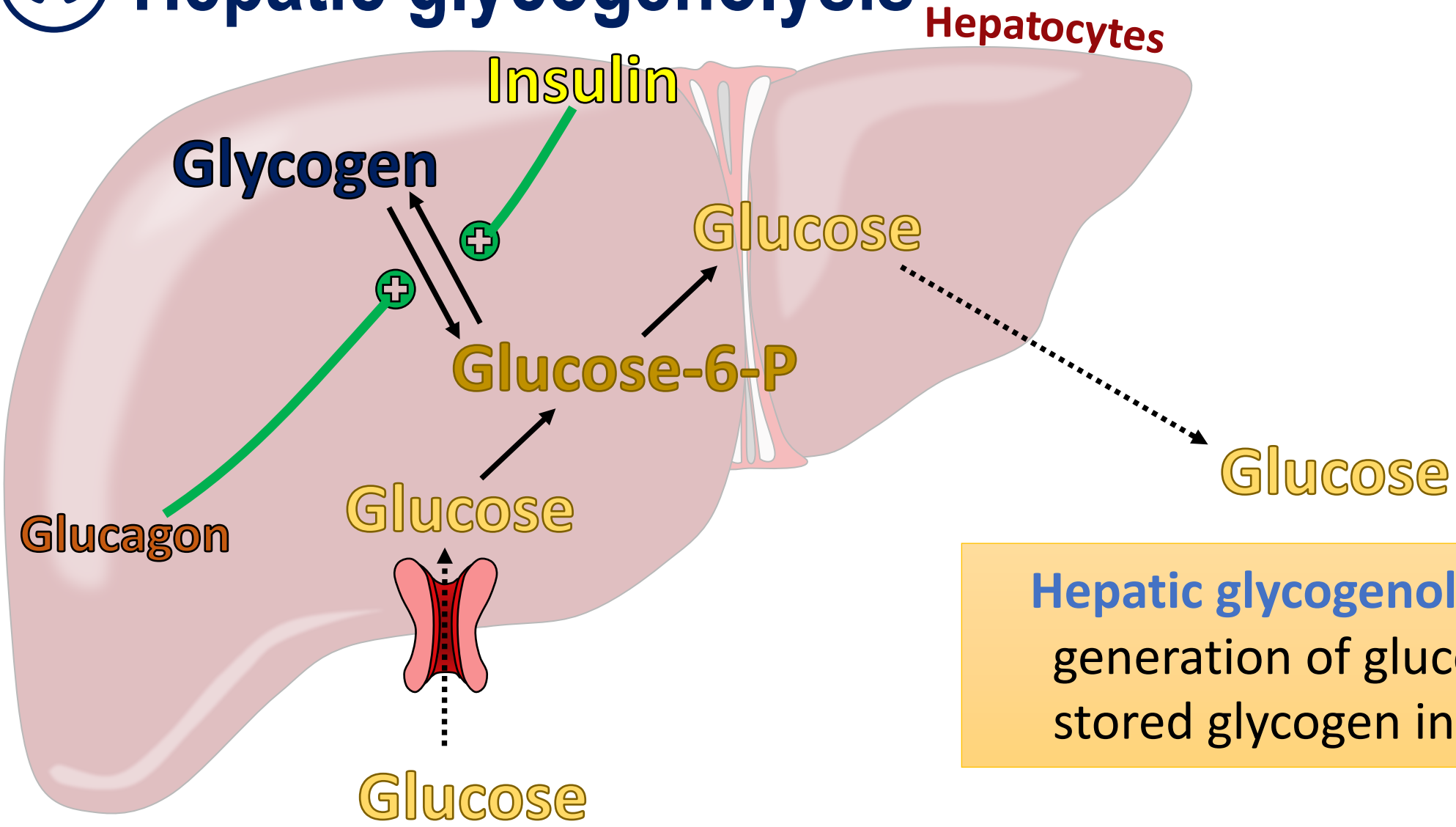
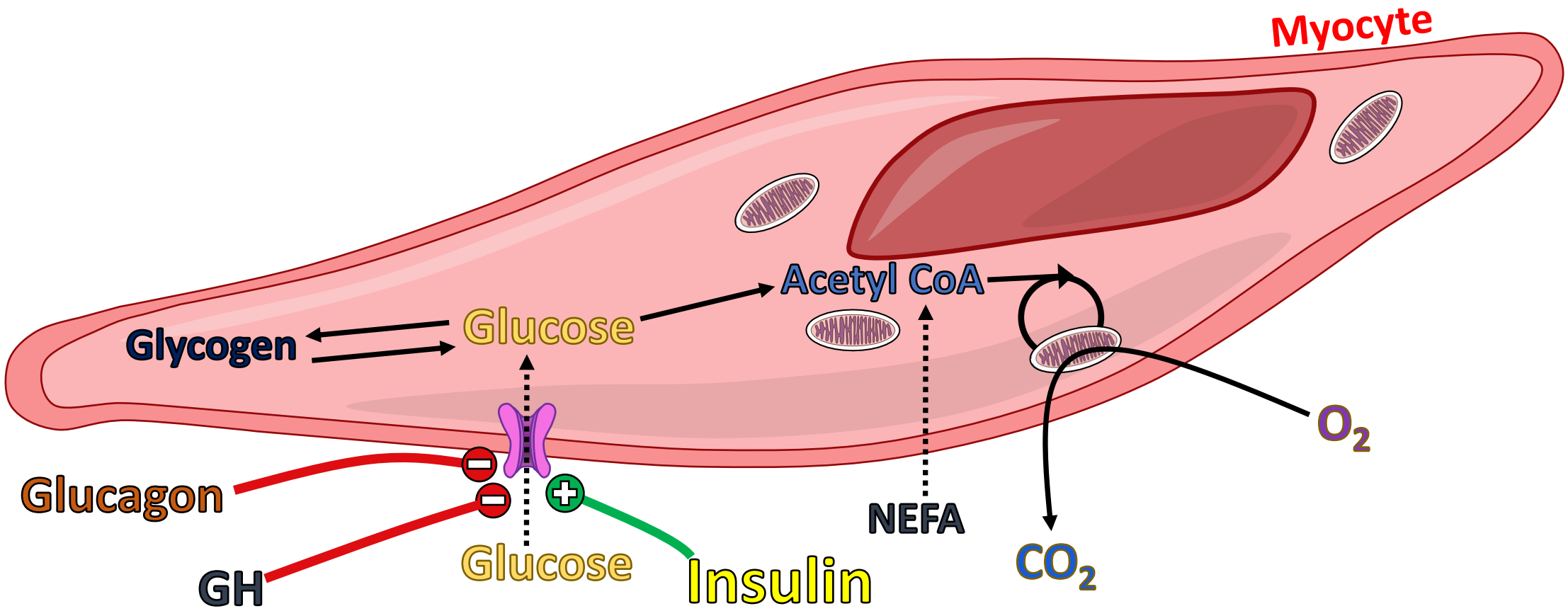
# Hepatic glycogenolysis




**Hepatic glycogenolysis** is the generation of glucose from stored glycogen in the liver

# Muscle cells

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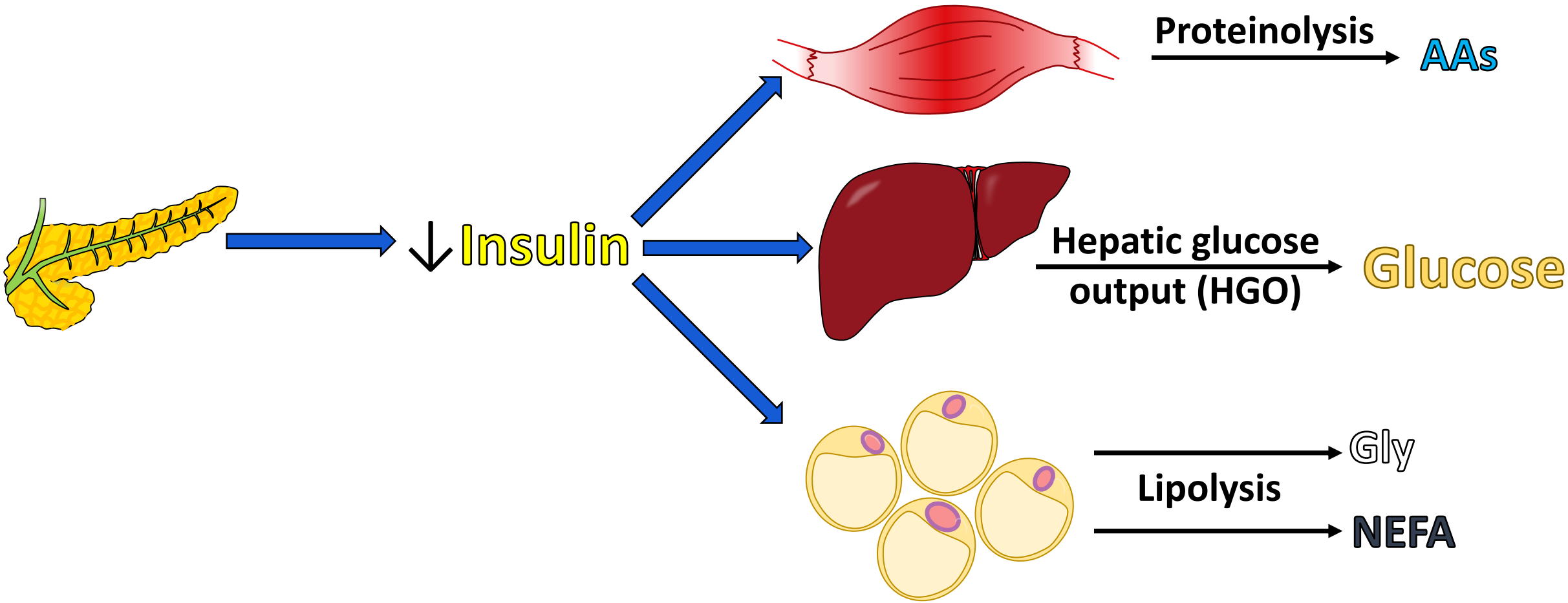
# Fasted state

- Low insulin-to-glucagon ratio
- [Glucose] 3.0-5.5mmol/l
- ↑ [NEFA]
- ↓ [amino acid] when prolonged

- ↑ Proteolysis
- ↑ Lipolysis
- ↑ HGO from glycogen and gluconeogenesis
- Muscle to use lipid
- Brain to use glucose, later ketones
- ↑ Ketogenesis when prolonged

# Response to fasting

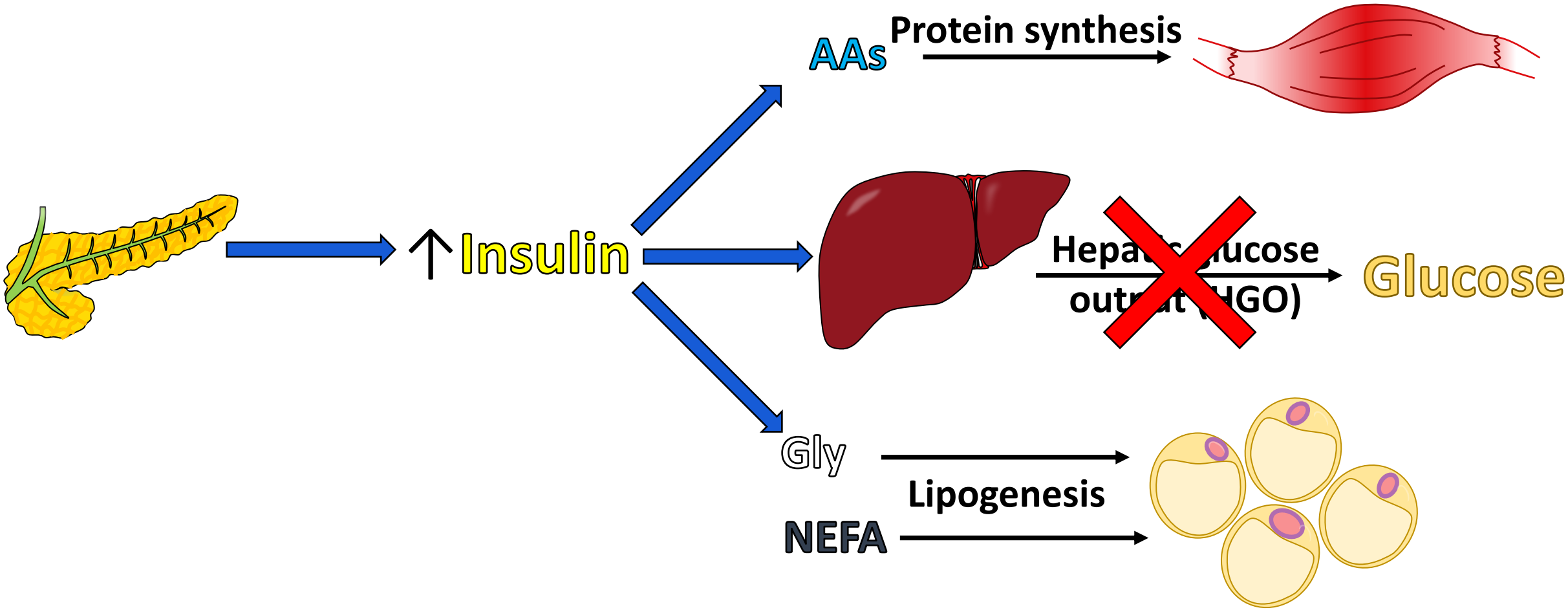


# Fed state

- Stored insulin released then 2nd phase
- High [insulin] to [glucagon] ratio

- Stop HGO
- ↑ Glycogen
- ↓ gluconeogenesis
- ↑ protein synthesis
- ↓ proteolysis
- ↑ Lipogenesis

# Response to feeding

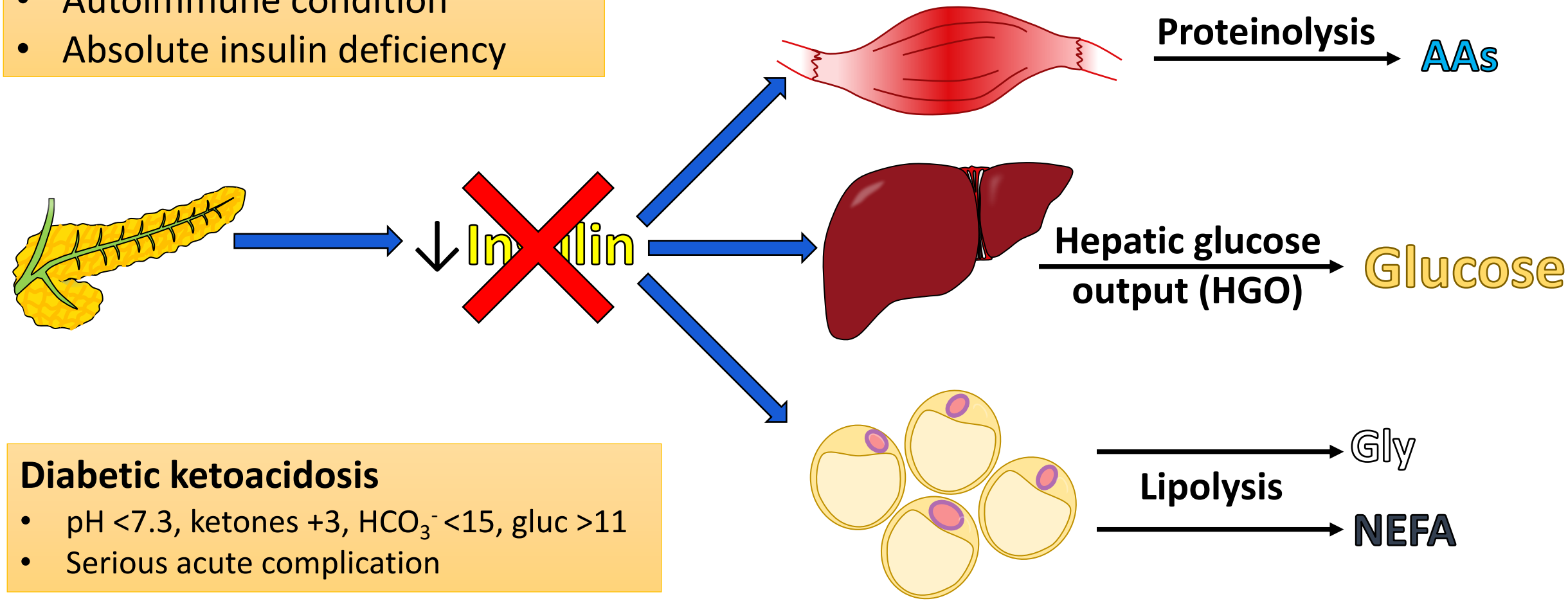


# Diagnosis of Diabetes Mellitus

- Fasting glucose >7.0 mmol/L
- Random glucose >11.1 mmol/L
- Oral glucose tolerance test
  - Fasting glucose
  - 75g glucose load
  - 2-hour glucose
- HbA1c (>48mmol/mol)
- **A diagnosis requires 2 positive tests or 1 positive test + symptoms**

# Pathophysiology in type 1 diabetes

- Autoimmune condition
- Absolute insulin deficiency




**Diabetic ketoacidosis**

- pH <7.3, ketones +3, $HCO_3^-$ <15, gluc >11
- Serious acute complication

# Presentation of T1DM

- Weight loss
- Hyperglycaemia
- Glycosuria with osmotic symptoms (polyuria, nocturia, polydipsia)
- Ketones in blood and urine

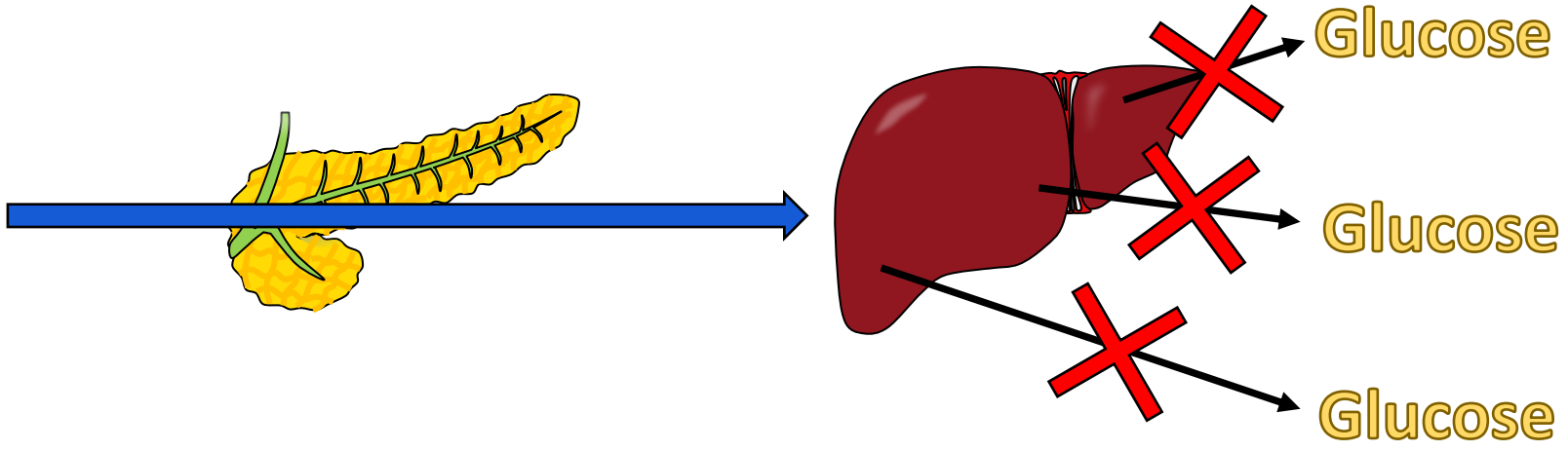
- Useful diagnostic tests:
  - Antibodies: GAD, IA2
  - C-peptide
  - Presence of ketones

The melting of flesh to produce urine

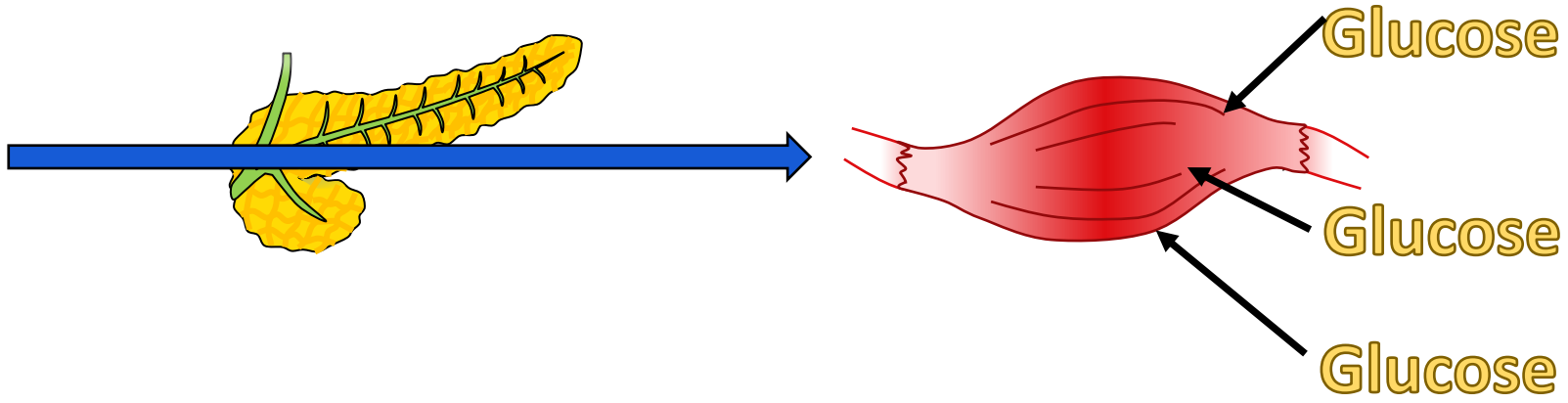
Arateus 150AD

# Insulin induced hypoglycaemia

**Too much insulin administered**




**Too much insulin administered**



# Counterregulatory response to hypoglycaemia

↑ Glucagon
↑ Catecholamines
↑ Cortisol
↑ Growth hormone

→

↑ Hepatic glucose output with glycogenolysis and gluconeogenesis
↑ Lipolysis

**Impaired awareness of hypoglycaemia**

- Reduced ability to recognise symptoms of hypoglycaemia
- Due to loss of counterregulatory response
- Recurrent hypoglycaemia

# Symptoms and signs of hypoglycaemia

| Autonomic | Neuroglycopenic |
| --- | --- |
| • Sweating<br>• Pallor<br>• Palpitations<br>• Shaking | • Slurred speech<br>• Poor vision<br>• Confusion<br>• Seizures<br>• Loss of consciousness |

**Severe hypoglycaemia**

Defined as an episode where a person needs third party assistance to treat

# Questions

**Q1. A 32 year old woman with T1DM feels sweaty and unwell at 11am whilst at work. Her CBG is 3.2mmol/L. Which of of the following is a potential cause of her low glucose?**

**Q2. A 24 year old man with T1DM feels a bit shaky after running. His CBG is 3.0mmol/L.**
**Which of the following would be the most appropriate hypoglycaemia treatment?**

**Q3. A 50 year old woman is found unconscious. A CBG is done and is 1.5mmol/L. Select the most appropriate treatment from the following available options.**

# Pathophysiology in type 2 diabetes - Insulin resistance

**Insulin resistance resides in liver, muscle and adipose tissue**

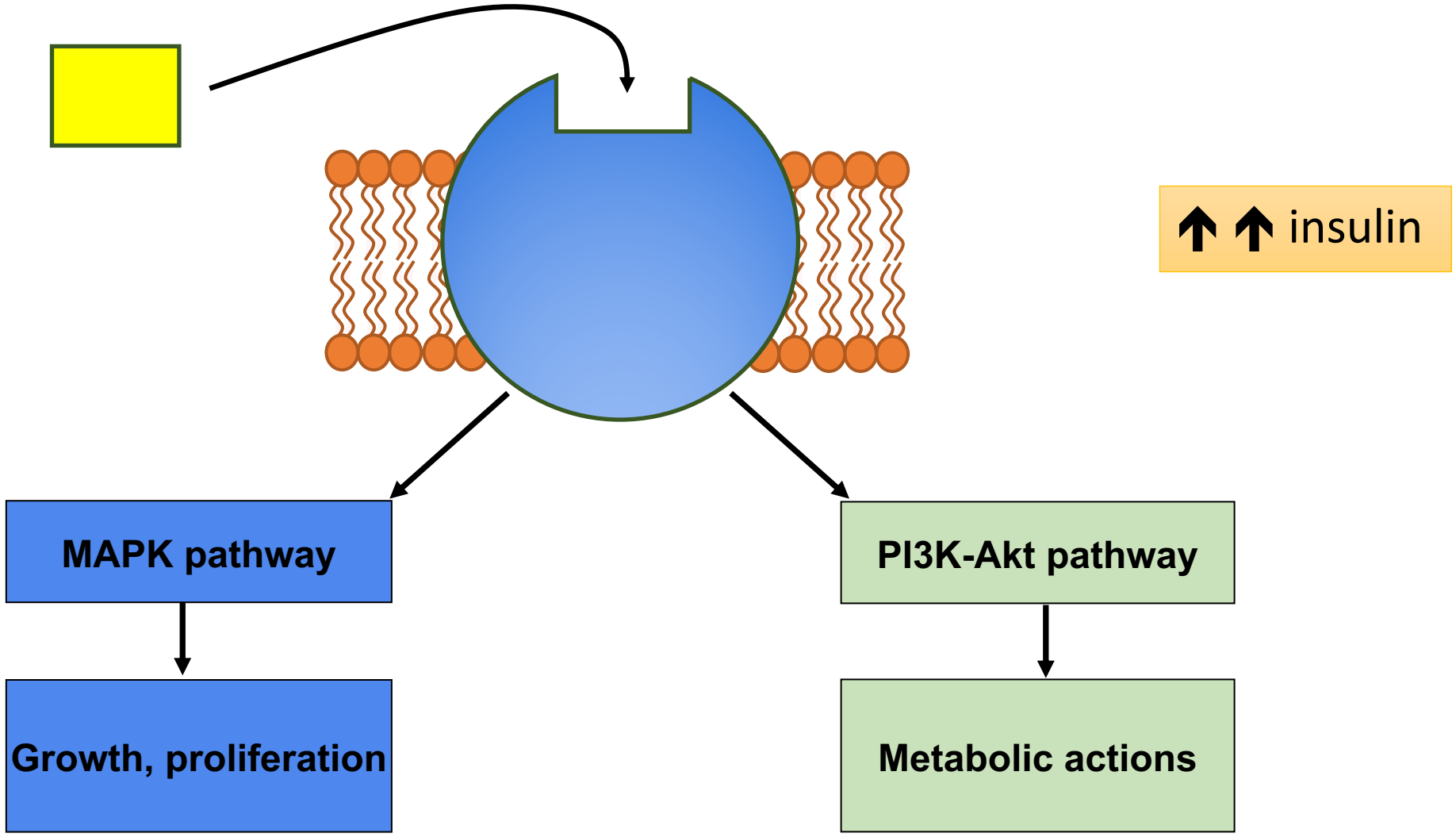
All metabolic sites and all arms of intermediary metabolism

- Glucose
- Fatty acids

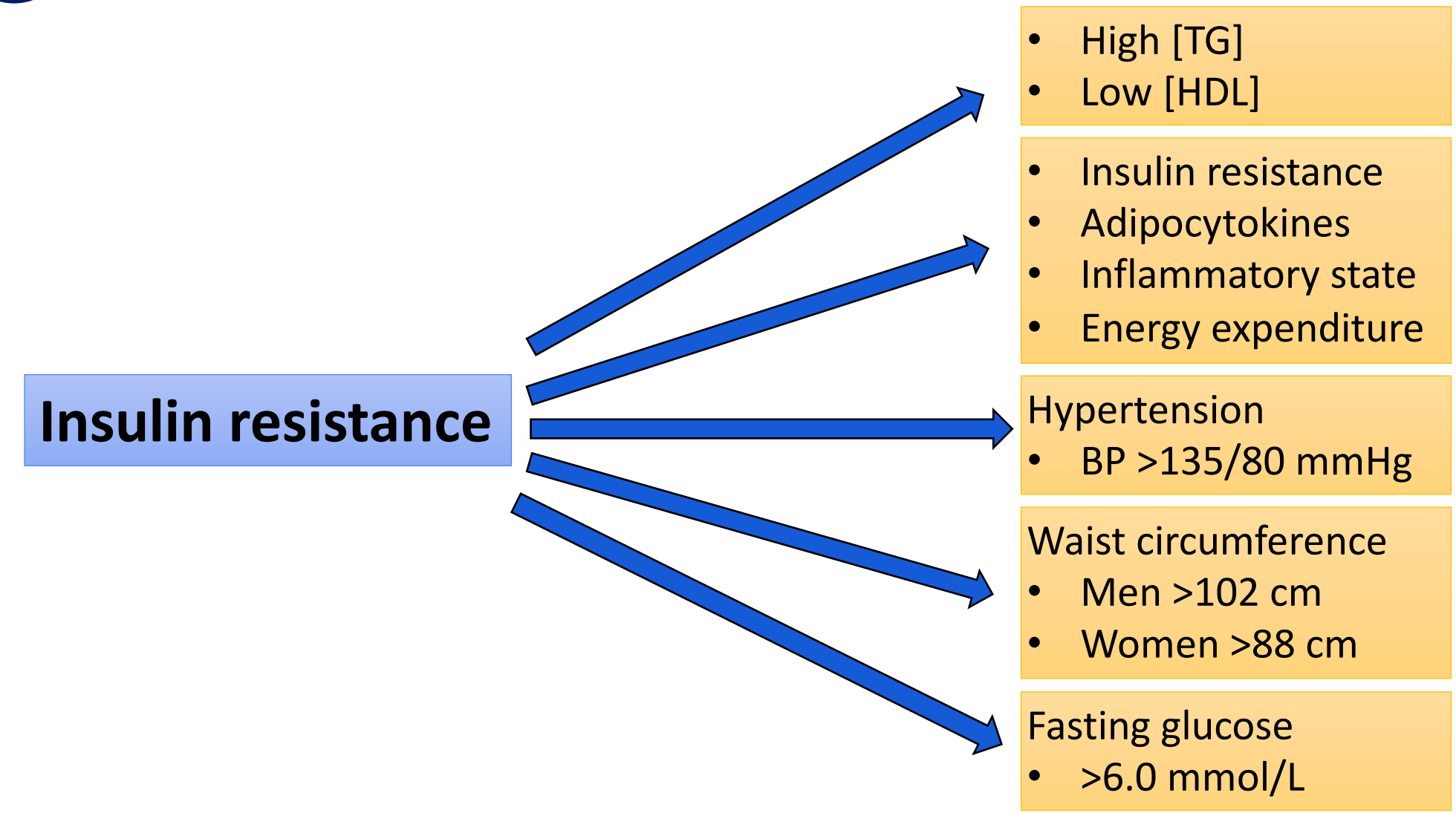
Enough insulin to suppress

- Ketogenesis
- Proteolysis

# Insulin resistance



# Insulin resistance

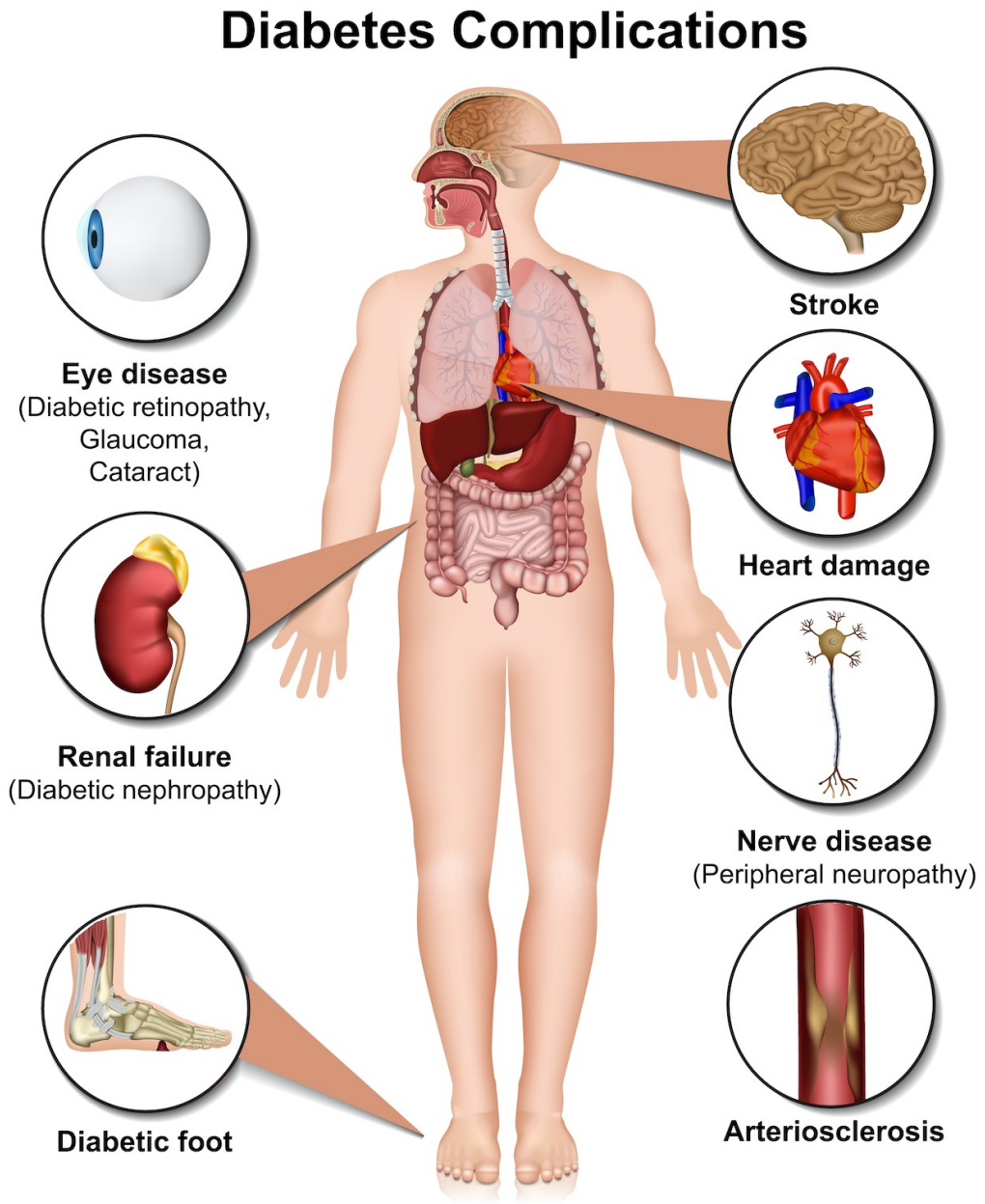


# Presentation of T2DM

- Hyperglycaemia
- Overweight
- Dyslipidaemia
- Less osmotic symptoms
- With complications
- Insulin resistance
- Later insulin deficiency

**Risk factors:**

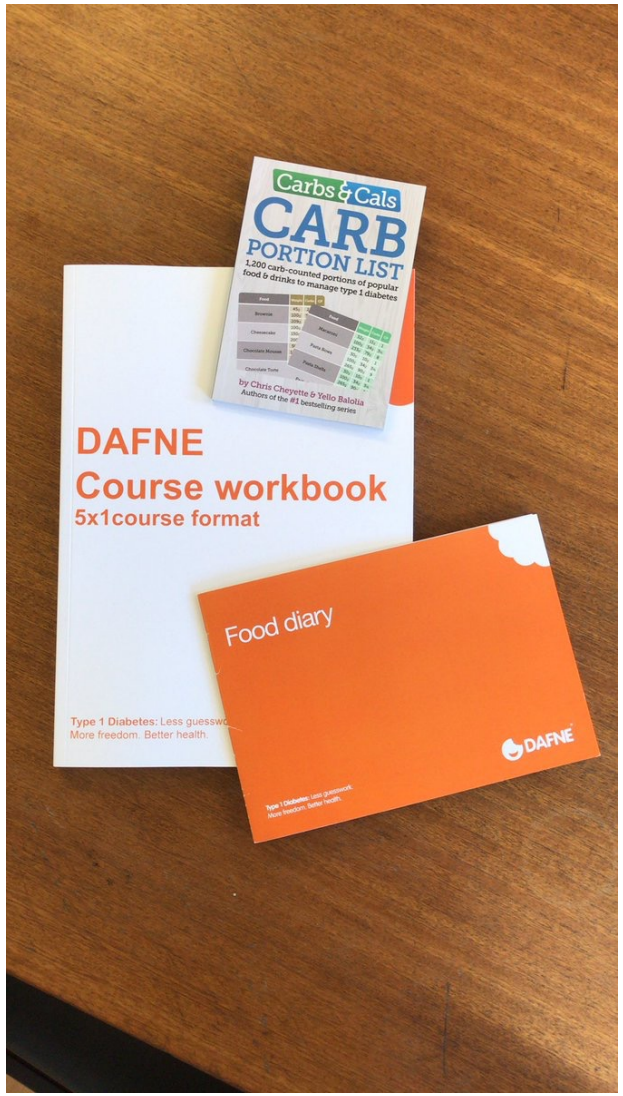
| | |
|---|---|
| Age | PCOS |
| ↑BMI | Family Hx |
| Ethnicity | Inactivity |

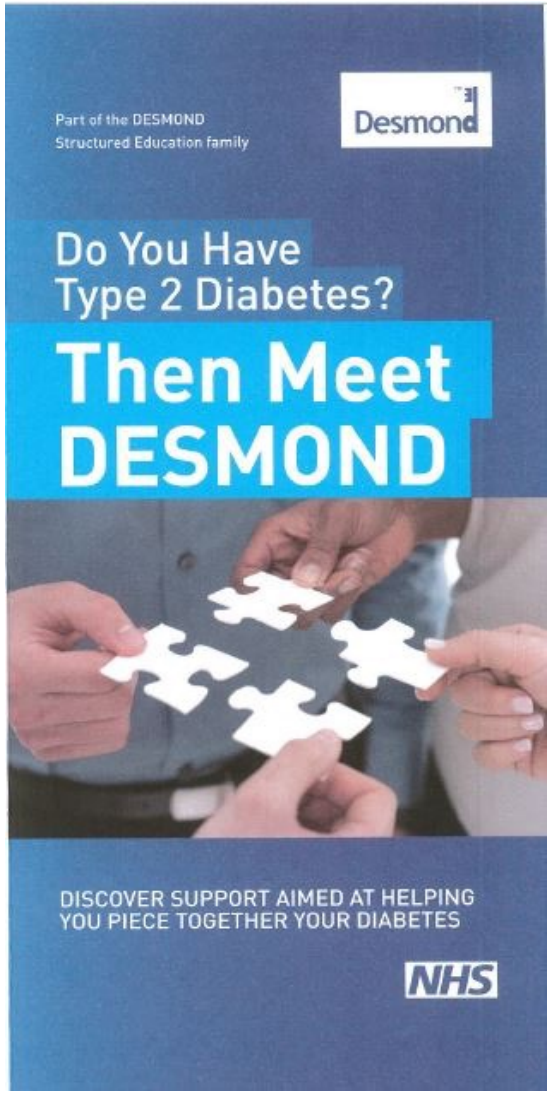


# Dietary Recommendations and Education

**Healthy eating or diet**

- Total calories control
- Reduce calories as fat
- Reduce calories as refined carbohydrate
- Increase calories as complex carbohydrate
- Increase soluble fibre
- Decrease sodium




**Endocrine disorders:** Describe the clinical features and treatment options of endocrine disorders.

# Management of diabetes mellitus

## Type 1 diabetes

- Exogenous insulin (basal-bolus regime)
- Self-monitoring of glucose
- Structured education
- Technology

## Type 2 diabetes

- Diet
- Oral medication
- Structured education
- May need insulin later

- Monitoring and prevention of long-term diabetes-related complications:
  - Retinopathy
  - Neuropathy
  - Nephropathy
  - Cardiovascular

# Session Review

## Insulin and its action

Insulin release results in:

- Uptake of glucose by the adipose and muscle cells through GLUT4 receptors
- Stimulation of glycogen synthesis
- Stimulates conversion of glucose to fatty acids and protein
- Inhibition of glycogenolysis and gluconeogenesis, and glucagon release.

**Insufficient insulin results in:**

- Glucose accumulation in the blood
- Reduced glucose uptake into skeletal, cardiac and smooth muscle, and adipose tissue.
- Increases glycogenolysis and gluconeogenesis, and glucagon release.
- Increases fat breakdown >> ketone bodies
- Increases protein breakdown

## Type 1 diabetes

- Autoimmune condition causing absolute insulin deficiency
- Clinical presentation: weightloss, osmotic symptoms, hyperglycaemia, ketonaemia
- Diabetic ketoacidosis (DKA) is a serious acute complication
- Hypoglycaemia is caused by too much insulin administration
- Counter-regulatory hormones in hypoglycaemia include glucagon, cortisol, catecholamines, GH

## Type 2 diabetes

- Often presents later in life compared to type 1
- Insulin resistance is important part of pathogenesis
- Risk factors include high BMI, family Hx, ethnicity

## Management of diabetes

- Management pathway in type 1 and type 2 diabetes are different
- Exogenous insulin administration is crucial in type 1
- Optimal glucose control reduces risk of complications