Blood sugar regulation

- **It is essential to have continuous supply of glucose to the brain.**
-
- **Brain has an obligatory requirement for glucose**

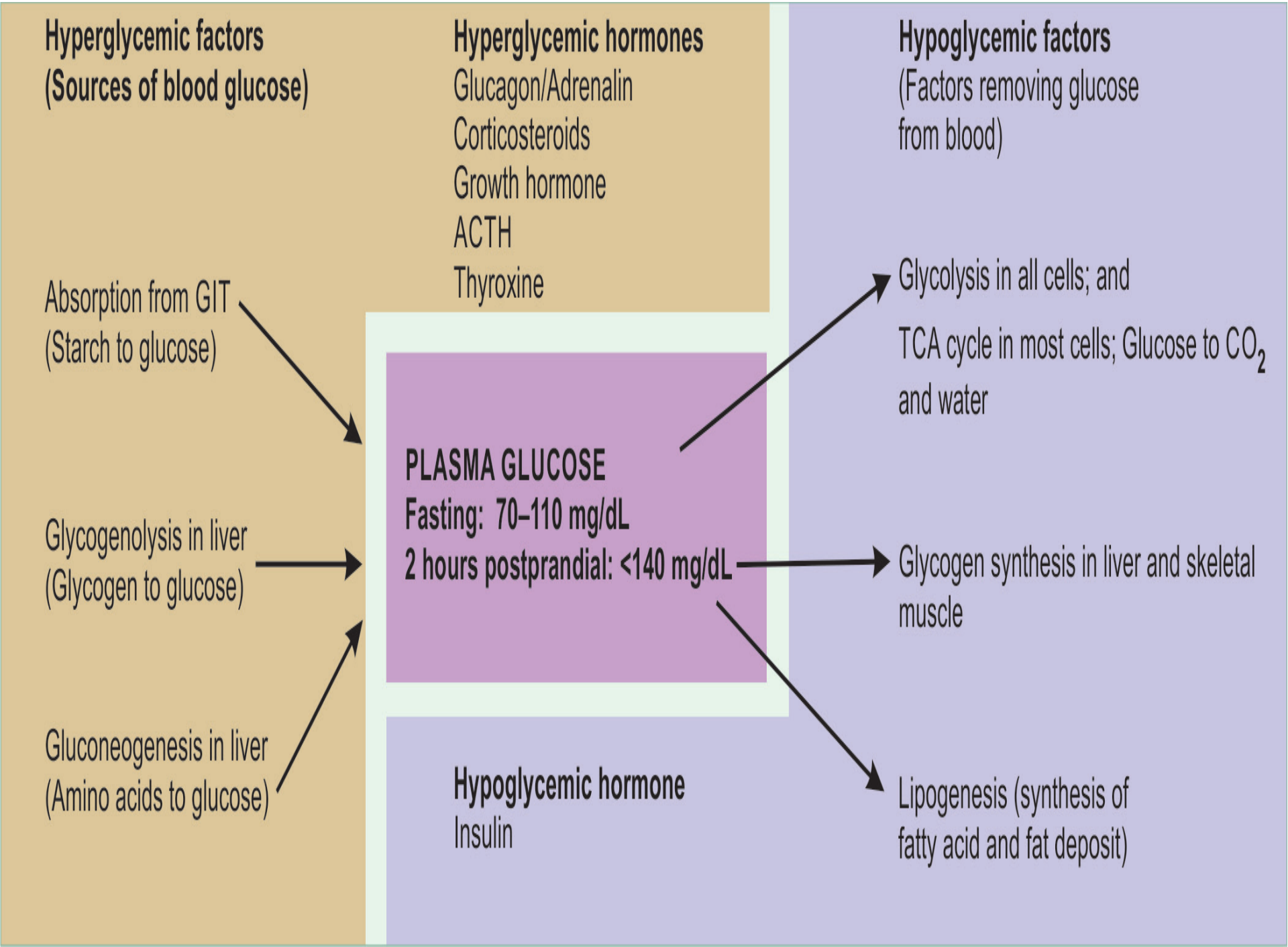
Factors Maintaining Blood sugar

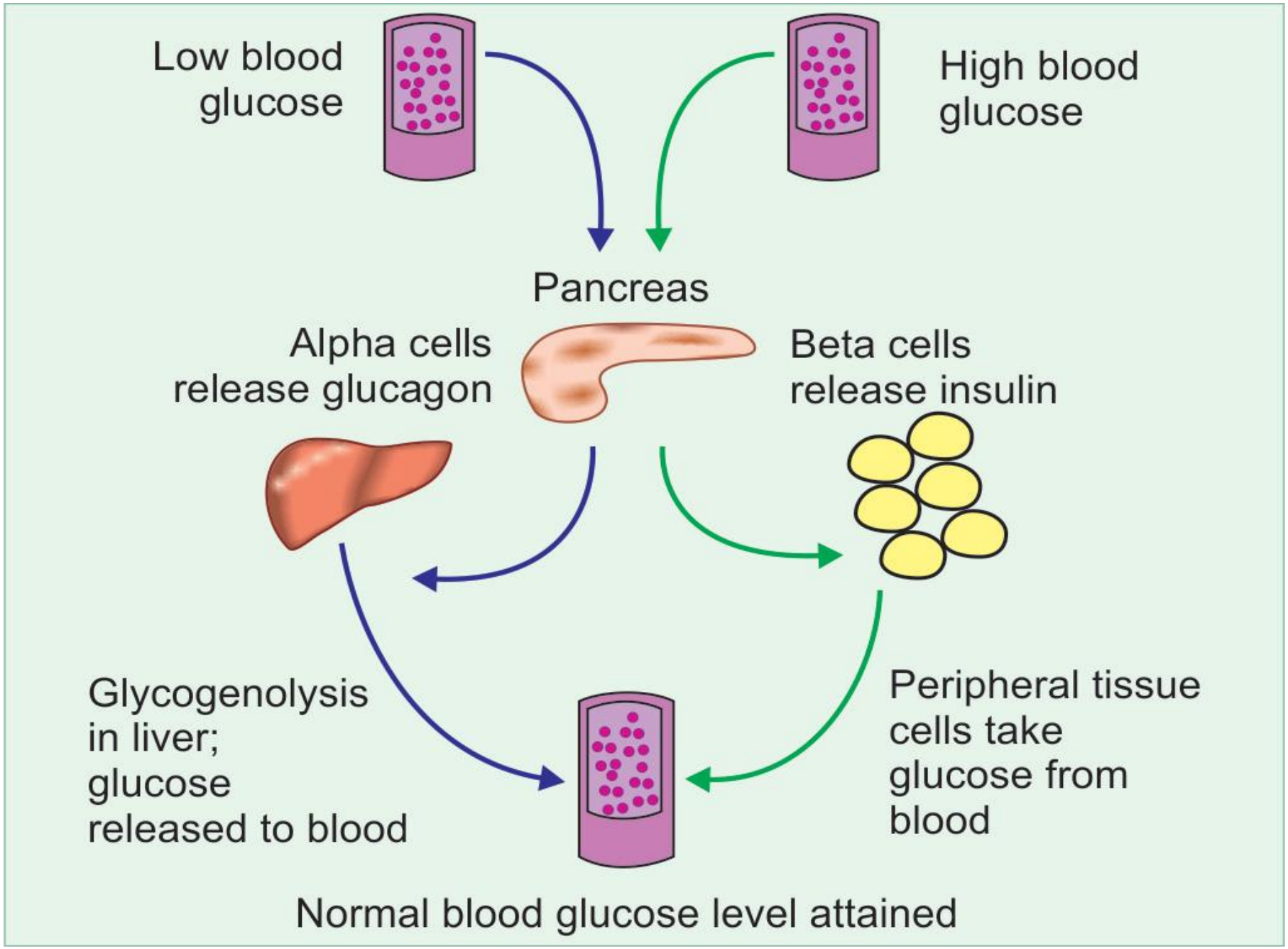
1. Entry of Glucose in to blood

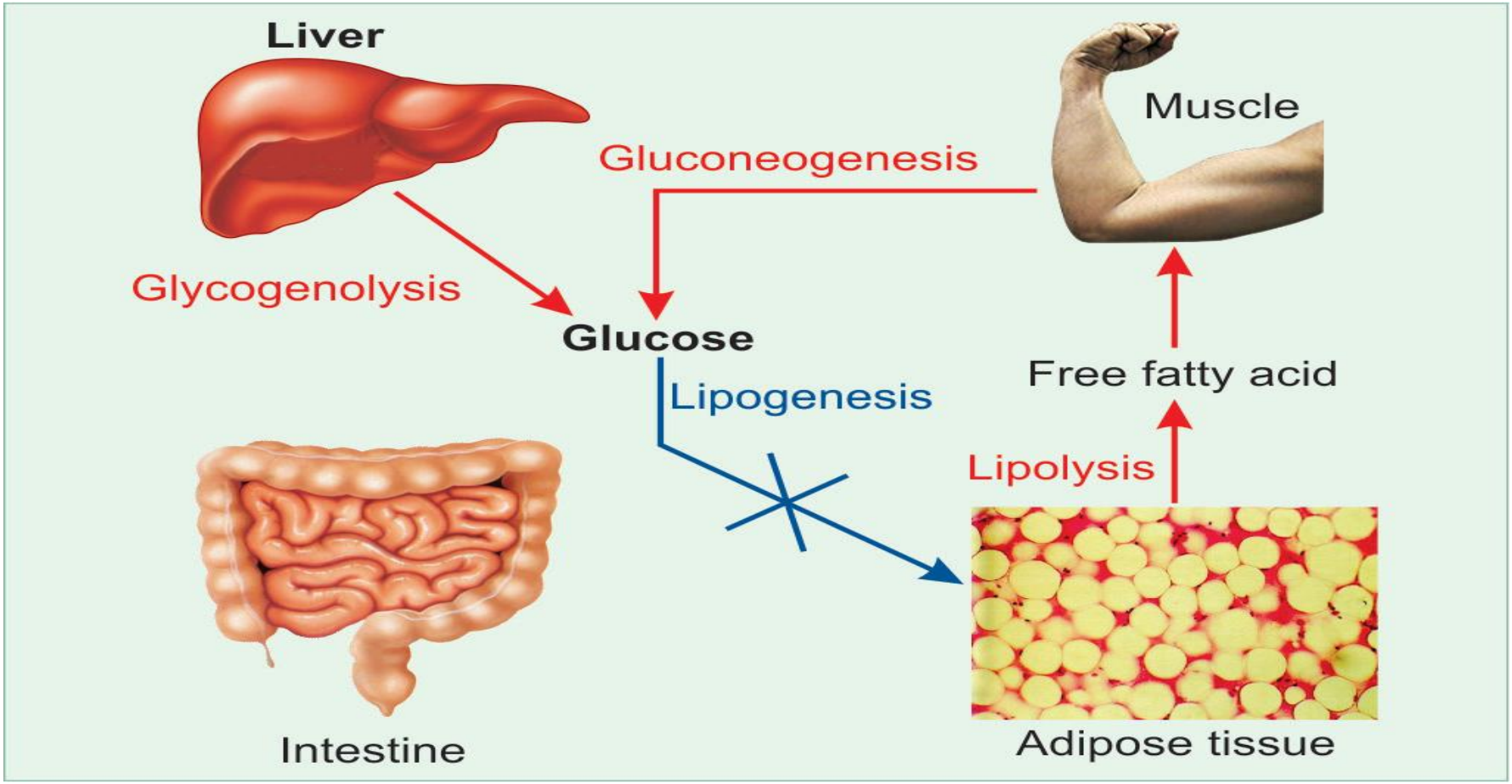
- Absorption from Intestine
- Breakdown of Glucose
- Gluconeogenesis
- Hyperglycemic Hormone

2. Depletion of Glucose

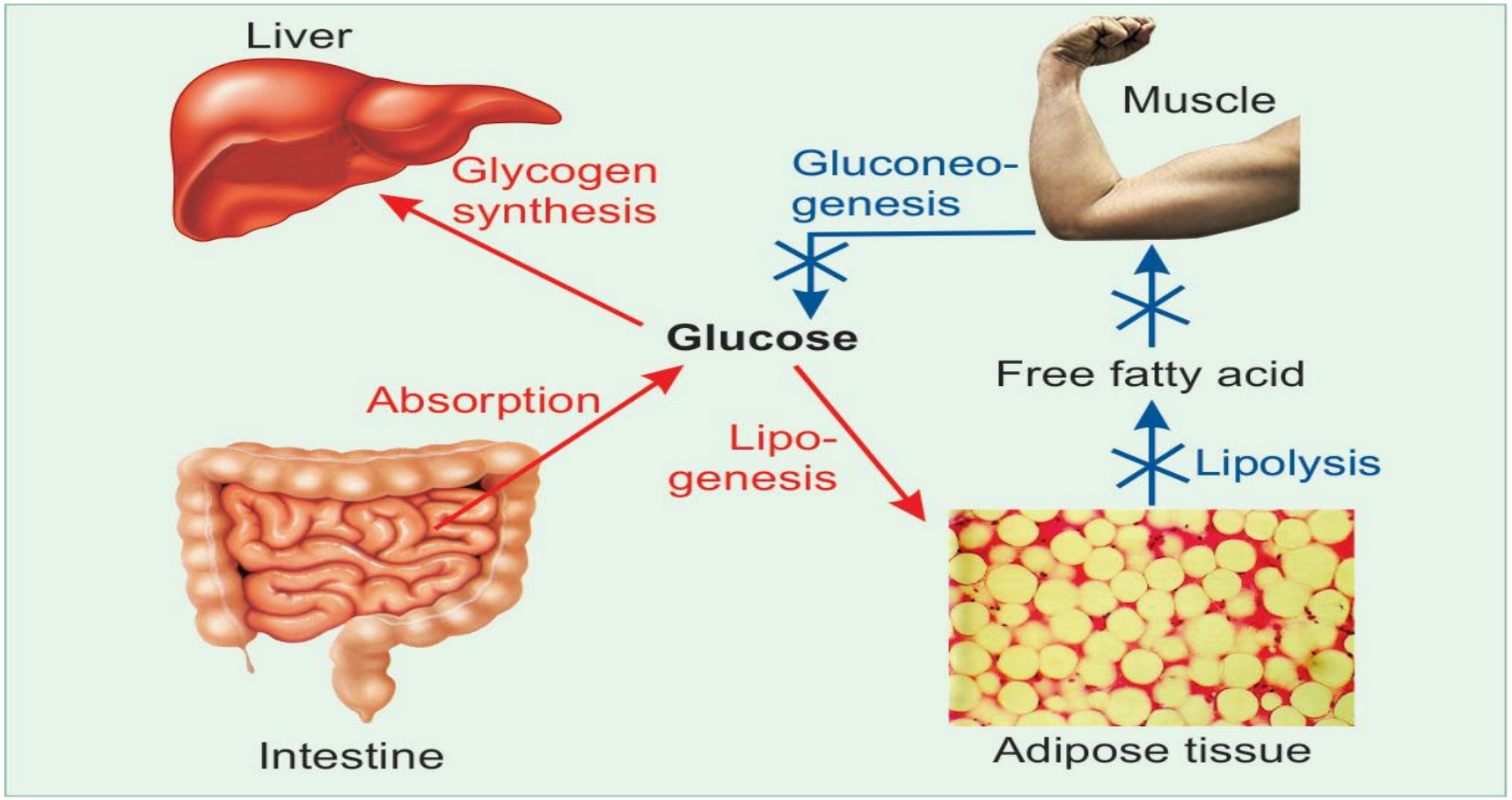
- Utilization by tissues for energy
- Glycogen synthesis
- Conversion of glucose in to fat(Lipogenesis)
- Hypoglycaemic Hormone


Hyperglycemic factors
(Sources of blood glucose)
Hyperglycemic hormones
Glucagon/Adrenalin
Corticosteroids
Growth hormone
ACTH
Thyroxine
Hypoglycemic factors
(Factors removing glucose from blood)
Absorption from GIT
(Starch to glucose)
Glycogenolysis in liver
(Glycogen to glucose)
Gluconeogenesis in liver
(Amino acids to glucose)
PLASMA GLUCOSE
Fasting: 70–110 mg/dL
2 hours postprandial: <140 mg/dL
Glycolysis in all cells; and
TCA cycle in most cells; Glucose to CO_2 and water
Glycogen synthesis in liver and skeletal muscle
Lipogenesis (synthesis of fatty acid and fat deposit)
Hypoglycemic hormone
Insulin


Low blood glucose
High blood glucose
Pancreas
Alpha cells release glucagon
Beta cells release insulin
Glycogenolysis in liver; glucose released to blood
Peripheral tissue cells take glucose from blood
Normal blood glucose level attained



Blood glucose regulation during **fasting state (high glucagon).** Red arrows indicate activation; blue arrow indicates inhibition.



Blood glucose regulation during postprandial state (high insulin). Red arrows indicate activation; blue arrow indicates inhibition.

Pathway increases blood Sugar

1. Gluconeogenesis
2. Glycogenolysis

Pathway decreases blood Sugar

- Glycogenesis
- Glycolysis

Effect of hormone

A. Effect of insulin (hypoglycemic hormone)
   1. Lowers blood glucose
   2. Favors glycogen synthesis
   3. Promotes glycolysis
   4. Inhibits gluconeogenesis

B. Glucagon (hyperglycemic hormone)
   1. Increases blood glucose
   2. Promotes glycogenolysis
   3. Enhances gluconeogenesis
   4. Depresses glycogen synthesis
   5. Inhibits glycolysis

- Cortisol (hyperglycemic hormone)
  - 1. Increases blood glucose level
  - 2. Increases gluconeogenesis
  - 3. Releases amino acids from the muscle
- D. Epinephrine or adrenaline (hyperglycemic)
  - 1. Increases blood glucose level
  - 2. Promotes glycogenolysis
  - 3. Increases gluconeogenesis
  - 4. Favors uptake of amino acids
- E. Growth hormone (hyperglycemic)
  - 1. Increases blood glucose level
  - 2. Decreases glycolysis
  - 3. Mobilizes fatty acids from adipose tissue

- **Normal persons, fasting plasma glucose value is 70–110 mg/dl**
- **Fasting (post-absorptive) state means, glucose is estimated after an overnight fast of 12 hours. Following a meal, the glucose level does not rise above 140 mg/dl due to prompt secretion of insulin.**

- **Normoglycemia = blood glucose level is within normal limits.**

- **Hyperglycemia = values are above the normal range (Greek, hyper = above). Hyperglycemia is harmful.**

- **Hypoglycemia = the value falls below normal levels. (Greek, hypo = below). If it is below 50 mg/dl, it may be fatal.**

- **Estimation of glucose is the commonest analysis done in clinical laboratories.**

- **Blood is collected using an anticoagulant (potassium oxalate) and an inhibitor of glycolysis (sodium fluoride). Fluoride inhibits the enzyme, enolase.**

- **If fluoride is not added, cells will utilise glucose at the rate of about 10 mg per hour, and false low values may be obtained.**

GLUCOSE TOLERANCE TEST

OBJECTIVES:

1. To determine the blood glucose concentrations following an oral glucose load.

2. To be able to discuss the physiological mechanisms by which blood glucose concentrations are controlled.

3. To recognize the importance of Glucose Tolerance Tests (GTTs) in diagnosis, particularly of diabetes mellitus.

WHAT IS A GLUCOSE TOLERANCE TEST?

- It is a laboratory method to check how the body breaks down (metabolizes) blood sugar, and how quickly it is cleared from the blood.

- It is one of the tools used to initial diagnosis of prediabetes, diabetes, insulin resistance.

** ***2 types of GTT:***

a. Oral Glucose Tolerance Test ***(OGTT)***
   - ingestion of glucose solution in 5 minutes.
   - most common form of GTT.
   - fasting blood sugar (FBS) is measured before ingestion of glucose .

b. Intravenous Glucose Tolerance Test ***(IGTT)***
   - glucose is injected into the vein for three(3) minutes.
   - blood insulin levels are measured before the injection.

Indication -

Most commonly done to check diabetes in:

* obese patients
* pregnancy (as a screening test during the 24th – 28th weeks of pregnancy)
* patients with non-healing skin infections or recurrent attacks of skin infections
* patients with family history of diabetes

Contraindication

1. There is no indication for doing OGTT in a person with DM.

2. It has no role in follow up of diabetes. It is only for initial diagnosis.

PREPARATION AND PRECAUTIONS:

1. Patient instructed to take carbohydrate intake at least three (3) days prior to the test. balanced diet containing at least 150 – 200 gm
CHO/ day for three (3) days

2. Do not eat, drink, smoke or exercise strenuously for at least **8 hours before** the first blood sugar is taken.

3. All medications taken by the subject must be noted and stopped, if possible, at least three(3) days prior to the test.

PROCEDURE for OGTT:

1. The subject fasts for 10-14 hours or overnight.

2. Blood and urine samples are taken for analysis at zero time (baseline).

3. The subject is then given a glucose solution to drink. He / She ingests 1 g/kg BW in 300 ml. It should be drunk within 5 minutes.

4. Blood and urine samples are taken every 30 min (after taking glucose solution) for three hours.

Causes of Abnormal GTT

1. Impaired Glucose Tolerance

Here Blood glucose level are above the normal range but below the diabetic levels

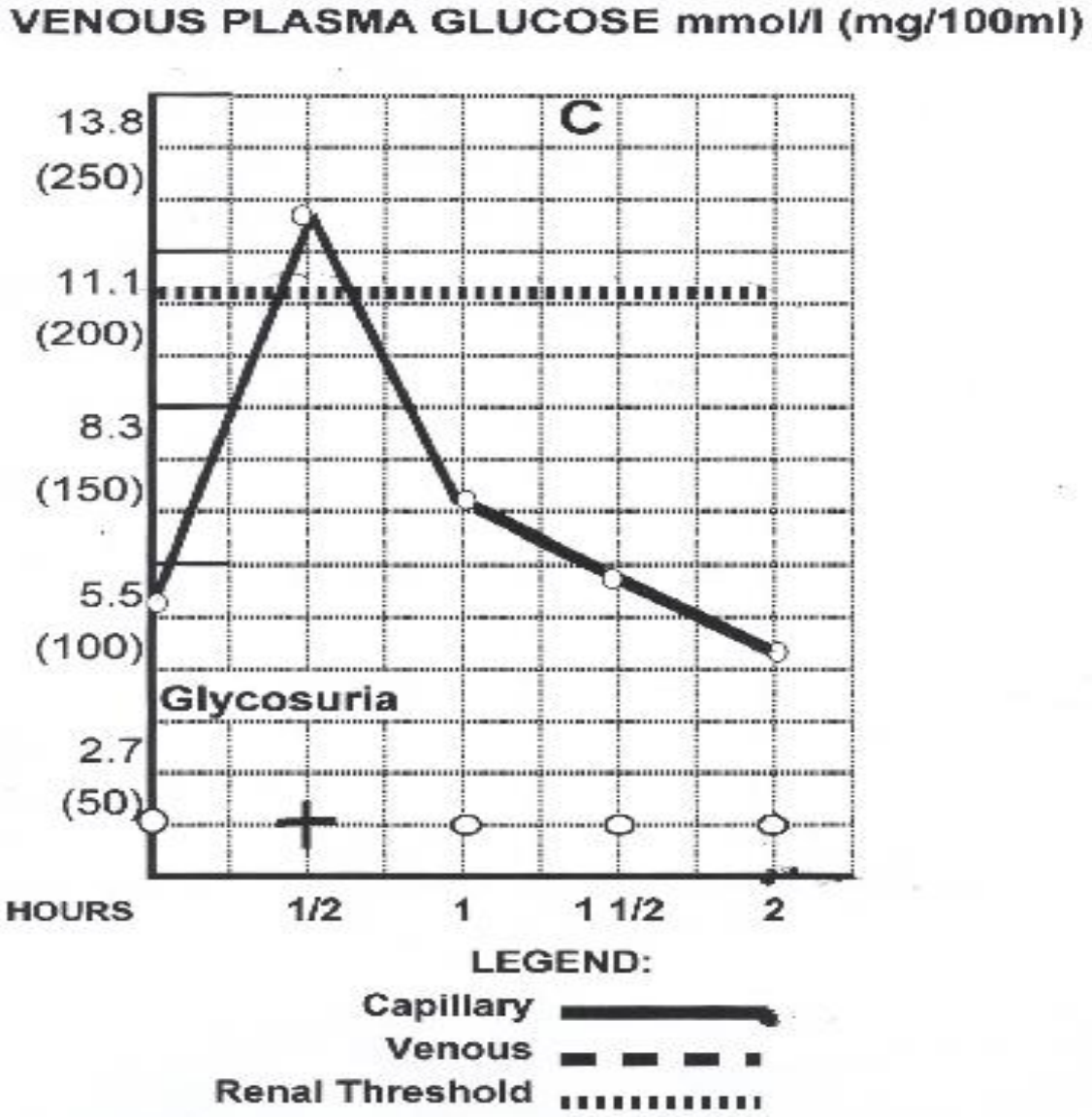
Such persons need careful follow up because it leads to frank diabetes

2.Impaired fasting Glycemia

- **In this condition fasting blood glucose level is above the normal range but 2 hr blood glucose(PP2BS) level is within normal range.**

1999 WHO Diabetes criteria – Interpretation of Oral Glucose Tolerance Test

Glucose levels	NORMAL		**Impaired Fasting Glycaemia**		**Impaired Glucose Tolerance**		**Diabetes Mellitus**	
			(I.F.G.)		**(I.G.T.)**		**(D.M.)**	
Venous Plasma	Fasting	2 hrs	Fasting	2 hrs	Fasting	2 hrs	Fasting	2 hrs
(mmol/l)	< 6.1	< 7.8	≥6.1 & <7.0	<7.8	< 7.0	≥ 7.8	≥ 7.0	≥11.1
(mg/dl)	< 110	< 140	≥110 & <126	<140	< 126	≥ 140	≥ 126	≥ 200


VENOUS PLASMA GLUCOSE mmol/l (mg/100ml)
13.8
(250)
11.1
(200)
8.3
(150)
5.5
(100)
2.7
(50)
C
Glycosuria
+
HOURS
1/2
1
1 1/2
2
LEGEND:
Capillary
Venous
Renal Threshold

MCQ

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1. GTT Is for

a) Diagnosis of Diabetes

b) Treatment of Diabetes

c) Follow up of Diabetes

d) All of above

2. Type 2 Diabetes mellitus is due to

a) Insulin deficiency

b) Cells resistance

c) Glucagon deficiency

d) All of above

3. Normal Blood glucose level in fasting is

a) 300-400 mg%

b) 70-110 mg%

c) 20-30 mg%

d) All of above

4. Impaired fasting glycaemia

a) Fating is in normal range

b) PP2BS is in normal range

c) Fasting is above normal range

d) None of above

5. Normal Blood glucose level in Post prandial blood glucose is

a) 300-400 mg%

b) 110-140 mg%

c) 20-30 mg%

d) All of above

Thank You!

Diabetes Mellitus

10% of total population 25% of persons above 50 years
Incidence in increasing; “Silent killer”

Greek, Dia = through;
Bainein = pass
Diabetes = pass through
Body mass is passed through urine
Mellitus = sweet

Type 1

5% of all diabetics; Insulin deficient Generally in young; adolescence Auto immunity Insulin is the drug of choice

Type 2

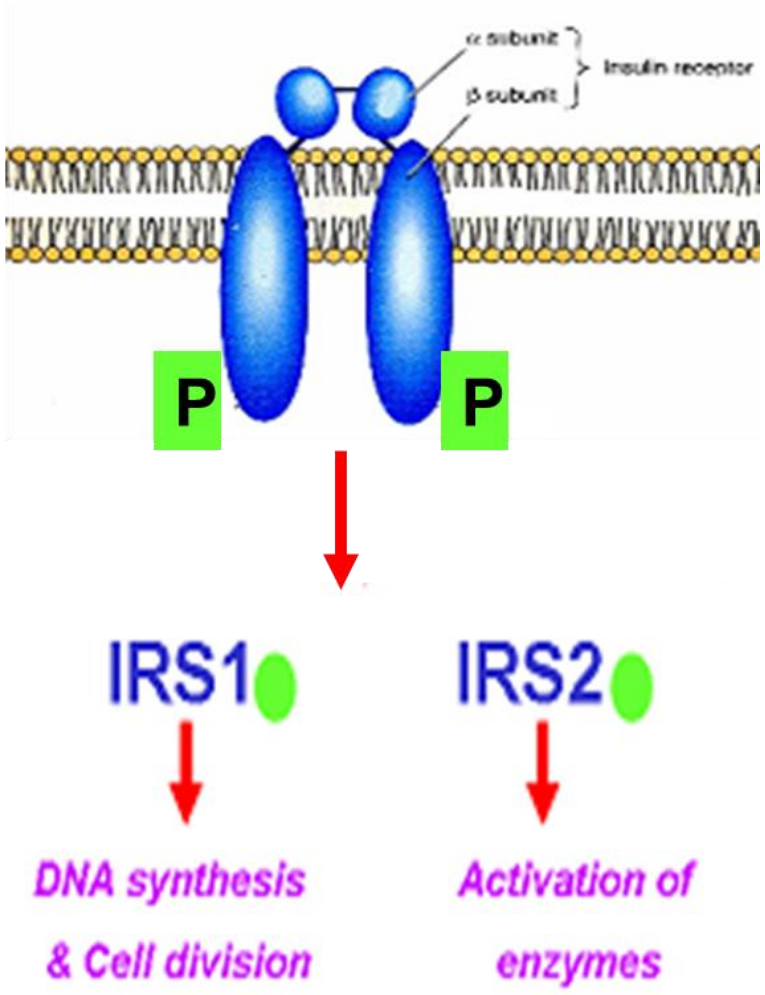
90% of all diabetics Insulin level normal or high

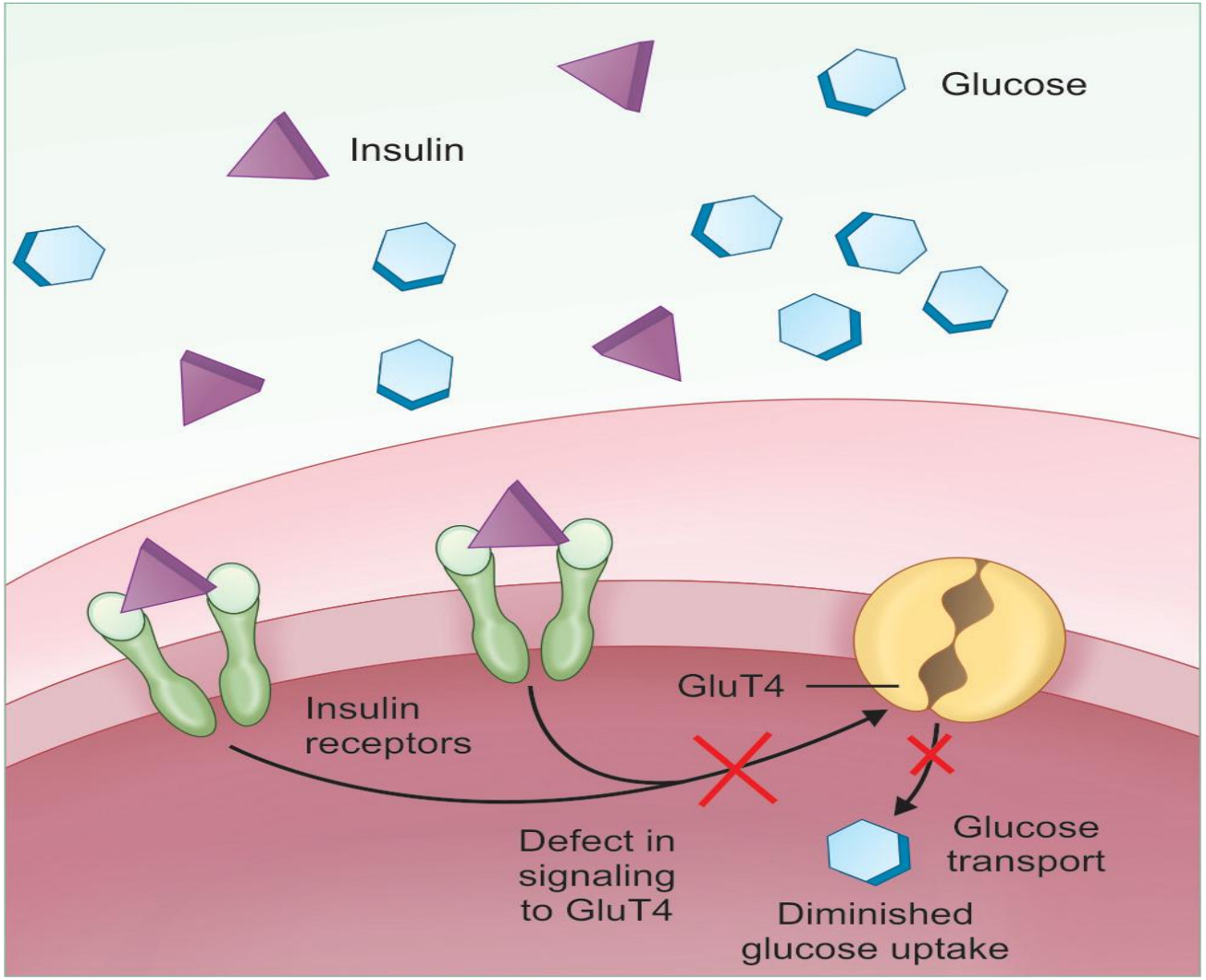
Generally adults, above 40 years Exercise, anti-diabetic drugs

Metabolic Changes in Type 2

- ↓ number of insulin receptors on the peripheral tissues

- Lack of normal response to Insulin





Insulin resistance in diabetes mellitus type 2. GluT4 receptors are defective in muscle cells.

Plasma Glucose Levels in OGTT in Normal Persons and in Diabetic Patients

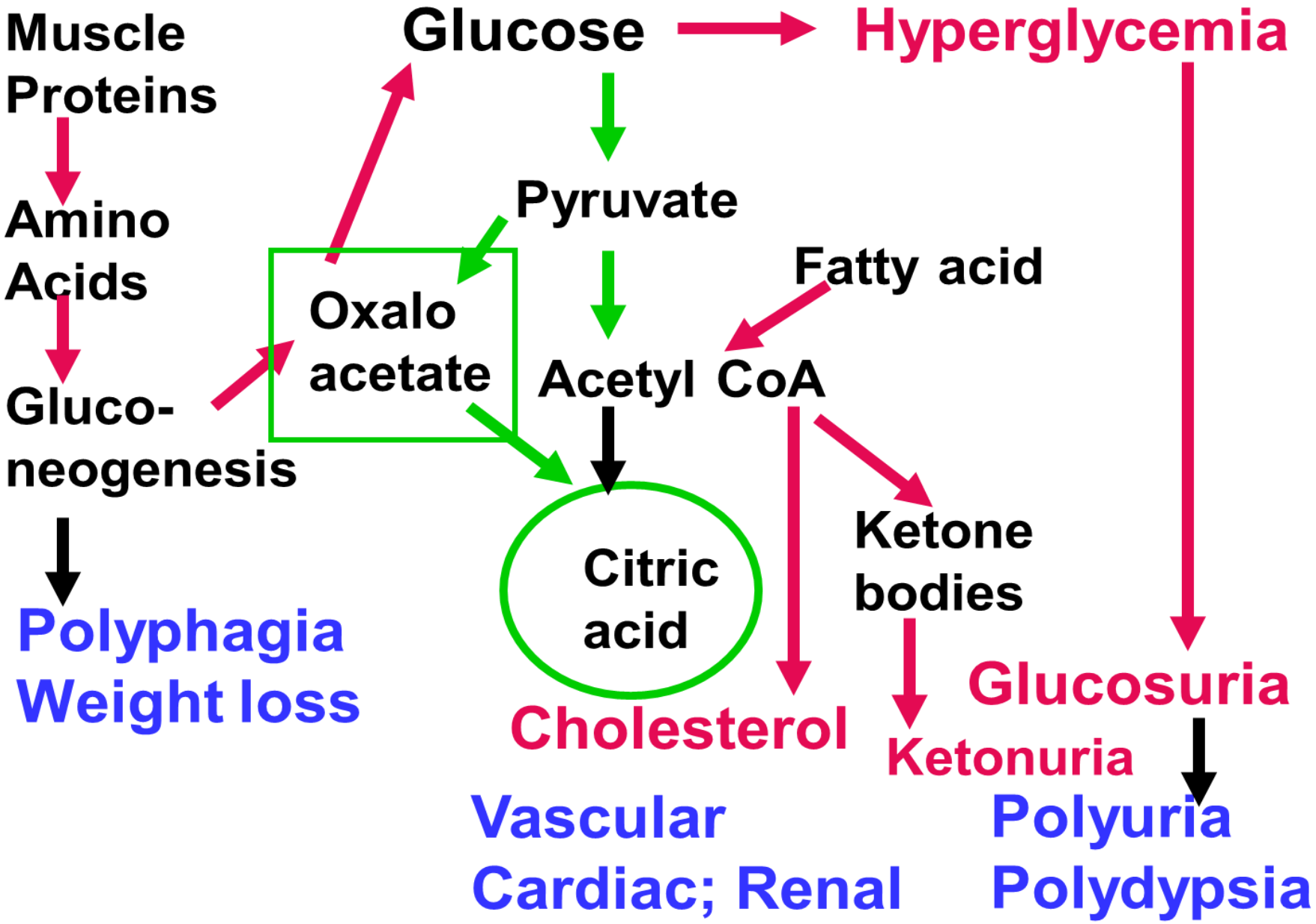
	Normal Persons	Criteria for diagnosing diabetes	Criteria for diagnosing IGT
Fasting	< 110 mg/dl	> 126 mg/dl	110 to 126 mg/dl
1 hr (peak) after glucose	< 160 mg/dl	Not Prescribed	Not Prescribed
2 hr after Glucose	< 140 mg/dl	> 200 mg/dl	140 to 199 mg/dl

Diagnostic Criteria for Diabetes Mellitus

1. If the fasting plasma sugar is more than 126 mg /dl, on more than one occasion

2. Or, if 2-hr post-glucose load value of GTT is more than 200 mg /dl (even at one occasion).

3. If the random plasma sugar level is more than 200 mg/dl, on more than one occasion. Diagnosis should not be based on a single random test alone; it should be repeated.


Muscle Proteins
Amino Acids
Gluco-neogenesis
Polyphagia
Weight loss
Glucose
Hyperglycemia
Pyruvate
Oxalo acetate
Fatty acid
Acetyl CoA
Citric acid
Ketone bodies
Cholesterol
Ketonuria
Glucosuria
Vascular
Cardiac; Renal
Polyuria
Polydypsia

Cardinal Symptoms

Blood glucose level exceeds renal threshold; glucose in urine. Due to osmotic effect, more water accompanies the glucose (polyuria).

To compensate for this loss of water, more water is taken (polydypsia).

Breakdown of protein. loss of weight. To compensate the loss of glucose and protein, patient will take more food (polyphagia).

Immediate Complications

Infections

Ketosis, ketonuria

Hypercholesterolemia

Hypertension

Chronic complications

Myocardial infarction

Micro angiopathy

Diabetic retionopathy; Cataract

Diabetic renopathy; renal failure

Neuropathy; Diabetic gangrene

Diabetic Ketoacidosis

Ketosis is more common in type 1 diabetes mellitus. When the rate of synthesis exceeds the ability of extrahepatic tissues to utilize them, there will be accumulation of ketone bodies in blood.

This leads to **ketonemia**, excretion in urine (**ketonuria**) and smell of **acetone** in breath. All these three together constitute the condition known as **ketosis**.

Diagnosis of Ketosis

Detection of ketone bodies in urine by **Rothera's test**. Supportive evidence may be derived from estimation of serum electrolytes, acid-base parameters and glucose estimation.

Causes for Ketosis

- **Diabetes mellitus:**

The combination of hyperglycemia, glucosuria, ketonuria and ketonemia is called **diabetic ketoacidosis** (DKA). Untreated diabetes mellitus is the most common cause for ketosis.

Ş̧tarvation:

- In starvation, the dietary supply of glucose is decreased. Available oxaloacetate is channeled to gluconeogenesis.
- The increased rate of lipolysis provides excess acetyl-CoA which is channelled to ketone bodies. The high **glucagon** favours ketogenesis.
- In both diabetes mellitus and starvation, the oxaloacetate is channelled to gluconeogenesis;
- So, the availability of oxaloacetate is decreased. Hence, acetyl-CoA cannot be fully oxidized in the TCA cycle.

Consequences of Ketosis

- **Metabolic acidosis:** Acetoacetate and beta-hydroxy butyrate are acids. There will be an increased **anion gap.**
- **Reduced buffers in blood**
- **Kussmaul's respiration:** due to compensatory hyperventilation.
- **Smell of acetone** in patient's breath.
- **Osmotic diuresis** induced by ketonuria may lead to dehydration.
- **Sodium loss:**
- **High potassium:** Due to lowered uptake of potassium by cells in the absence of insulin.
- **Dehydration:** The sodium loss further aggravates the dehydration.
- **Coma:** Hypokalemia, dehydration and acidosis contribute to the lethal effect of ketosis.

Management of Ketosis

- Administration of insulin and glucose by intravenous route to control diabetes.
- „Intravenous bicarbonate to correct th acidosis.
- „Correction of water imbalance by normal saline.
- „Correction of electrolyte imbalance. Insulin induces glycogen deposition, and along with that, extracellular potassium is distributed intracellularly. This leads to dangerous hypokalemia, which is to be immediately corrected.

Hyperosmolar Nonketotic

It can result due to elevation of glucose to very high levels (900 mg/dL or more).

This would increase the osmolality of extracellular fluid (ECF).

Osmotic diuresis leads to water and electrolyte depletion.

The coma results from dehydration of cerebral cells due to hypertonicity of ECF.