Diabetes Mellitus

What is diabetes?

- Diabetes mellitus (DM) is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin production, insulin action, or both.

Diabetes

- Diabetes mellitus may present with characteristic symptoms such as thirst, polyuria, blurring of vision, and weight loss.

- In its most severe forms, ketoacidosis or a non–ketotic hyperosmolar state may develop and lead to stupor, coma and, in absence of effective treatment, death.

Long-term Effects

▶ The long–term effects of diabetes mellitus include progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, and/or neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction, including sexual dysfunction.

▶ People with diabetes are at increased risk of cardiovascular, peripheral vascular and cerebrovascular disease.

Burden of Diabetes

▸ The development of diabetes is projected to reach pandemic proportions over the next10-20 years.

▸ International Diabetes Federation (IDF) data indicate that by the year 2025, the number of people affected will reach 333 million –90% of these people will have Type 2 diabetes.

▸ In most Western societies, the overall prevalence has reached 4-6%, and is as high as 10-12% among 60-70-year-old people.

▸ The annual health costs caused by diabetes and its complications account for around 6-12% of all health-care expenditure.

Types of Diabetes

- Type 1 Diabetes Mellitus
- Type 2 Diabetes Mellitus
- Gestational Diabetes
- Other types:
  - ❖ MODY (maturity-onset diabetes of youth)
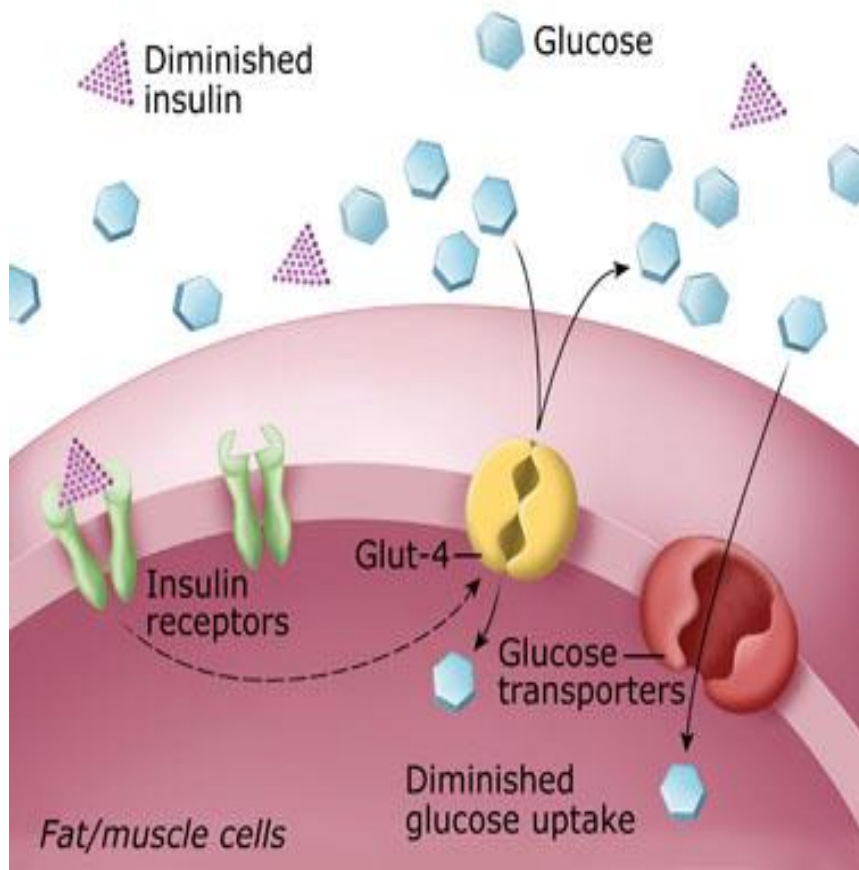 - ❖ Secondary Diabetes Mellitus

Type 1 diabetes

- Type 1 diabetes develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin that regulates blood glucose.

- Risk factors for type 1 diabetes may include autoimmune, genetic, and environmental factors.
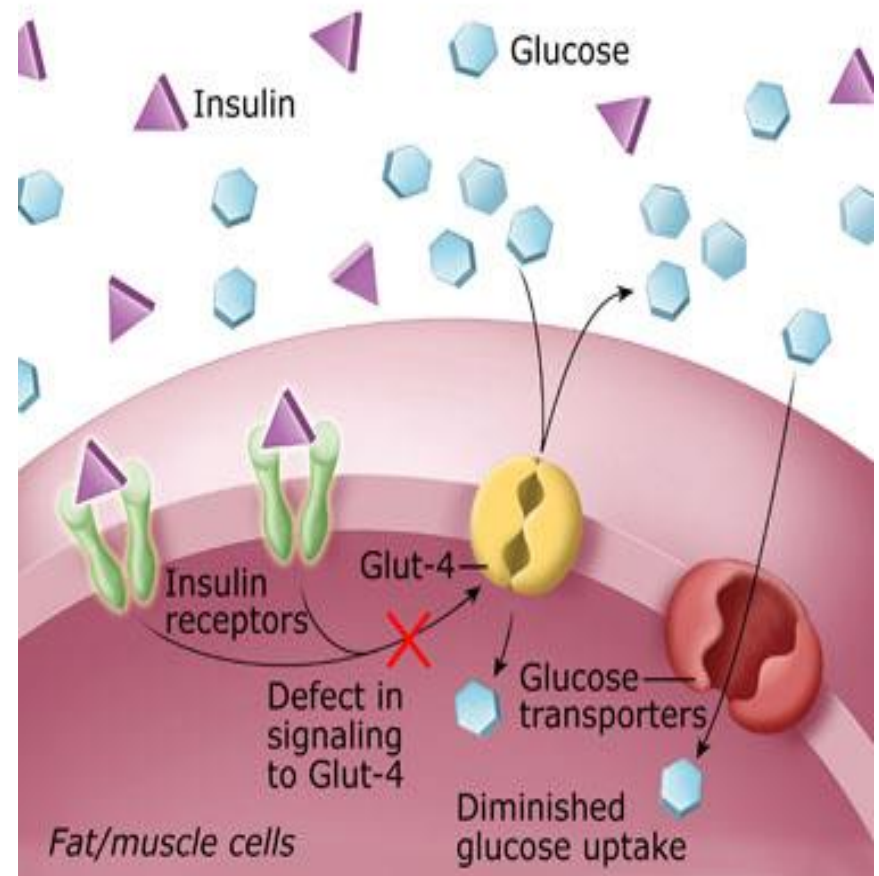
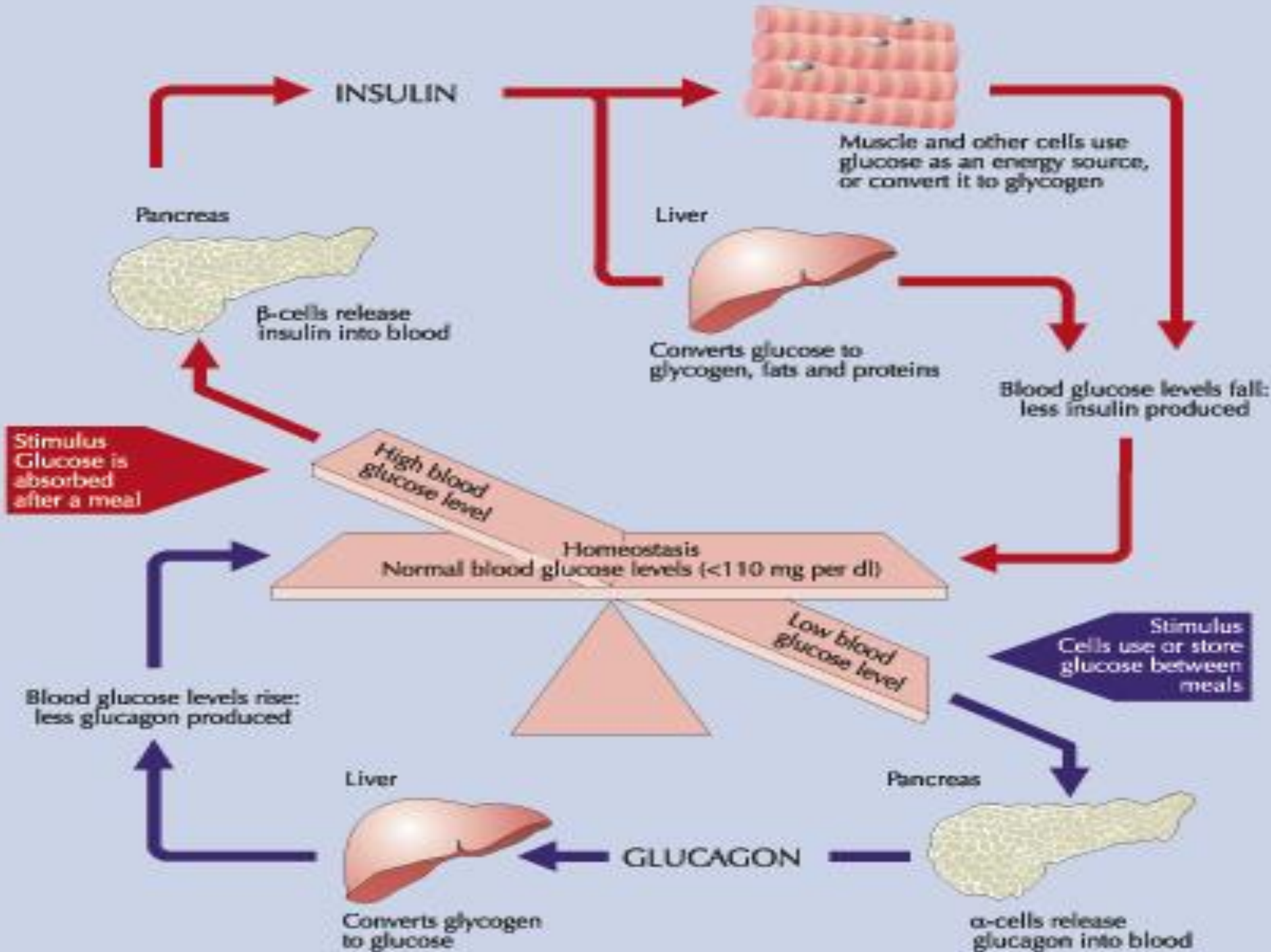# Type 2 diabetes

- It usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce insulin.

- Type 2 diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity.

Type 1 Diabetes: Insufficient Insulin

Diminished insulin

Glucose

Insulin receptors

Glut-4

Glucose transporters

Diminished glucose uptake

Fat/muscle cells

Type 2 Diabetes: Insulin Resistance

Insulin

Glucose

Insulin receptors

Glut-4

Defect in signaling to Glut-4

Glucose transporters

Diminished glucose uptake

Fat/muscle cells

INSULIN

Pancreas

β-cells release insulin into blood

Muscle and other cells use glucose as an energy source, or convert it to glycogen

Liver

Converts glucose to glycogen, fats and proteins

Blood glucose levels fall: less insulin produced

Stimulus Glucose is absorbed after a meal

High blood glucose level

Homeostasis
Normal blood glucose levels (<110 mg per dl)

Low blood glucose level

Stimulus Cells use or store glucose between meals

Blood glucose levels rise: less glucagon produced

Liver

Converts glycogen to glucose

GLUCAGON

Pancreas

α-cells release glucagon into blood

Gestational diabetes

- During pregnancy, gestational diabetes requires treatment to normalize maternal blood glucose levels to avoid complications in the infant.

- Women who have had gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5-10 years.

Other types of DM

- Other specific types of diabetes result from specific genetic conditions (such as maturity-onset diabetes of youth), surgery, drugs, malnutrition, infections, and other illnesses.

- Such types of diabetes may account for 1% to 5% of all diagnosed cases of diabetes.

Diagnosis

Values of Diagnosis of Diabetes Mellitus

Values for diagnosis of diabetes mellitus and other categories of hyperglycaemia

	Glucose concentration, mmol l^{-1} (mg dl^{-1})		Plasma*
	Whole blood		
	Venous	Capillary	Venous
Diabetes Mellitus:			
Fasting	≥ 6.1 (≥ 110)	≥ 6.1 (≥ 110)	≥ 7.0 (≥ 126)
or			
2-h post glucose load	≥ 10.0 (≥ 180)	≥ 11.1 (≥ 200)	≥ 11.1 (≥ 200)
or both			
Impaired Glucose Tolerance (IGT):			
Fasting (if measured)	< 6.1 (< 110)	< 6.1 (< 110)	< 7.0 (< 126)
and			
2-h post glucose load	≥ 6.7 (≥ 120) and < 10.0 (< 180)	≥ 7.8 (≥ 140) and < 11.1 (< 200)	≥ 7.8 (≥ 140) and < 11.1 (< 200)
Impaired Fasting Glycaemia (IFG):			
Fasting	≥ 5.6 (≥ 100) and < 6.1 (< 110)	≥ 5.6 (≥ 100) and < 6.1 (< 110)	≥ 6.1 (≥ 110) and < 7.0 (< 126)
and (if measured)			
2-h post glucose load	< 6.7 (< 120)	< 7.8 (< 140)	< 7.8 (< 140)

Prevention or delay of diabetes:
Life style modification

- Research studies have found that lifestyle changes can prevent or delay the onset of type 2 diabetes among high-risk adults.

- In the Diabetes Prevention Program, a large prevention study of people at high risk for diabetes, the development of diabetes was reduced 58% over 3 years.

Management of Diabetes Mellitus

Management of DM

- The major components of the treatment of diabetes are:

A	• **Diet and Exercise**
B	• **Oral hypoglycaemic therapy**
C	• **Insulin Therapy**

Diet

▶ Diet is a basic part of management in every case. Treatment cannot be effective unless adequate attention is given to ensuring appropriate nutrition.

▶ **Dietary treatment should aim at:**
  ◦ ensuring weight control
  ◦ providing nutritional requirements
  ◦ allowing good glycaemic control with blood glucose levels as close to normal as possible
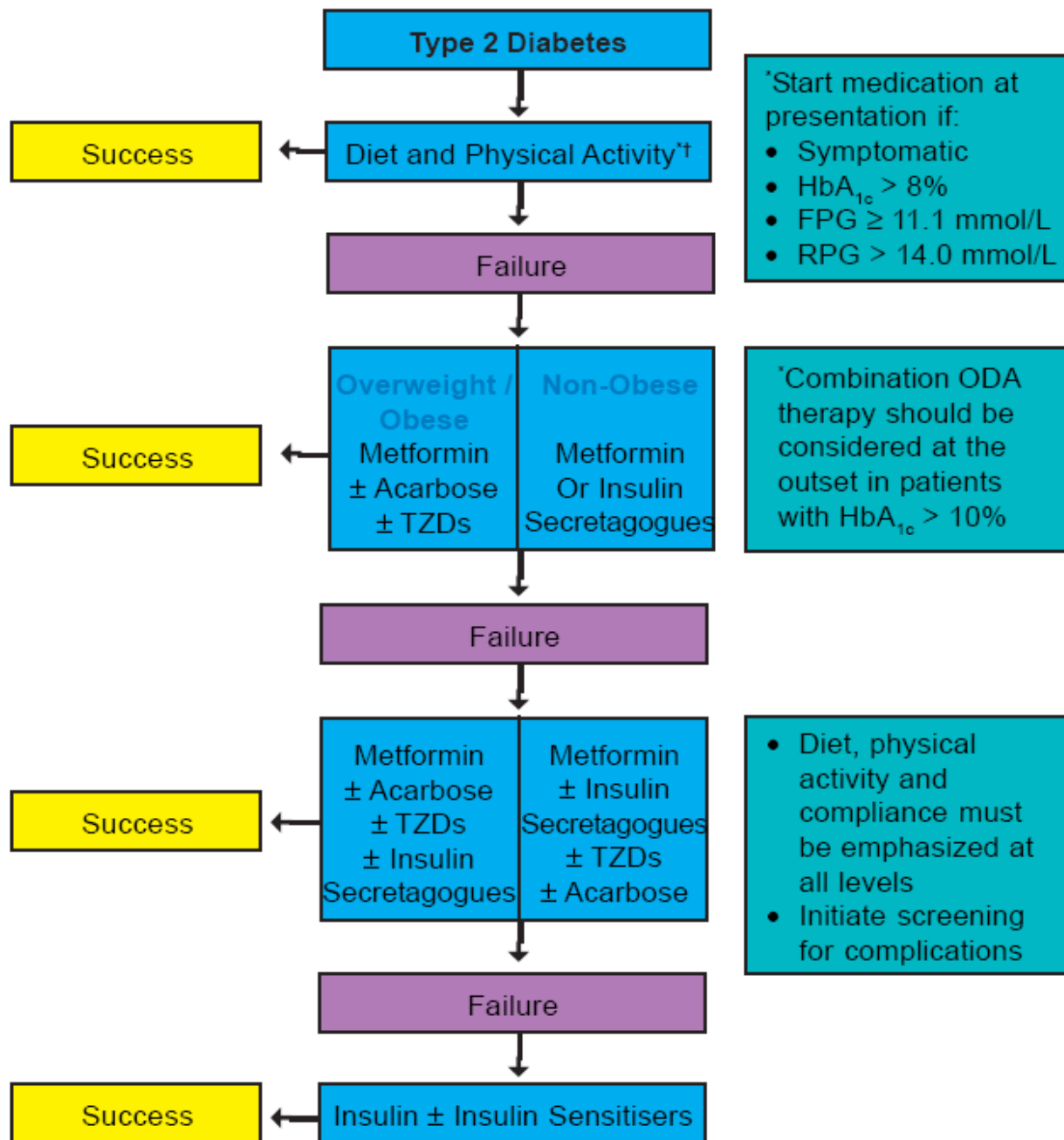 ◦ correcting any associated blood lipid abnormalities

Exercise

- Physical activity promotes weight reduction and improves insulin sensitivity, thus lowering blood glucose levels.

- People should, however, be educated about the potential risk of hypoglycaemia and how to avoid it.

Oral Anti-Diabetic Agents

• There are currently four classes of oral anti-diabetic agents:

i. Biguanides

ii. Insulin Secretagogues – Sulphonylureas

iii. Insulin Secretagogues – Non-sulphonylureas

iv. α-glucosidase inhibitors

v. Thiazolidinediones (TZDs)

Combination Oral Agents and Insulin

- Combination of insulin+ oral anti-diabetic agents (BIDS) has been shown to improve glycaemic control in those not achieving target despite maximal combination oral anti-diabetic agents.

- Insulin dose can be increased until target FPG is achieved.

Type 2 Diabetes

Success ← Diet and Physical Activity[*][†]

'Start medication at presentation if:
- Symptomatic
- $HbA_{1c} > 8\%$
- $FPG \geq 11.1$ mmol/L
- $RPG > 14.0$ mmol/L

Failure

Overweight / Obese	Non-Obese
Metformin ± Acarbose ± TZDs	Metformin Or Insulin Secretagogues

Success ←

'Combination ODA therapy should be considered at the outset in patients with $HbA_{1c} > 10\%$

Failure

Metformin ± Acarbose ± TZDs ± Insulin Secretagogues	Metformin ± Insulin Secretagogues ± TZDs ± Acarbose

Success ←

- Diet, physical activity and compliance must be emphasized at all levels
- Initiate screening for complications

Failure

Success ← Insulin ± Insulin Sensitisers

Diabetes Management Algorithm

Insulin Therapy

Short-term use:

- Acute illness, surgery, stress and emergencies
- Pregnancy
- in marked hyperglycaemia
- Diabetic ketoacidosis, hyperosmolar nonketotic coma, lactic acidosis, severe hypertriglyceridaemia
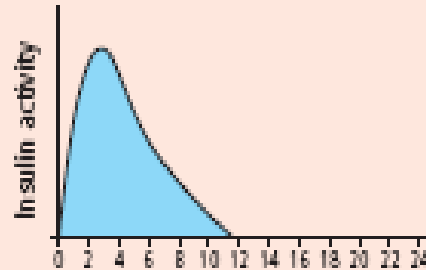
Long-term use:

- If targets have not been reached after optimal dose of combination therapy or BIDS, consider change to multi-dose insulin therapy.
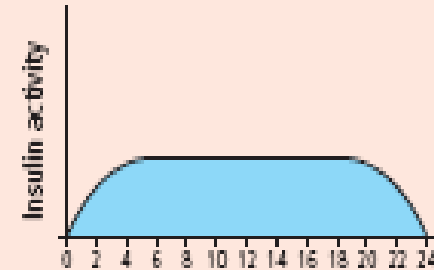
Overview of Insulin and Action

Soluble Human Insulin: Actrapid, Humulin S

Onset:	30 mins
Peak:	2-4 hours
Duration:	6-8 hours

Long Acting Basal Analogues: Glargine (Lantus), Detemir (Levemir)

Onset:	~ 2 hours
Peak:	None
Duration:	18-24 hours

Rapid Acting Insulin Analogue: Novorapid Aspart, Humalog Lispro, Apidra

Onset:	0-15 mins
Peak:	1-2 hours
Duration:	3-5 hours
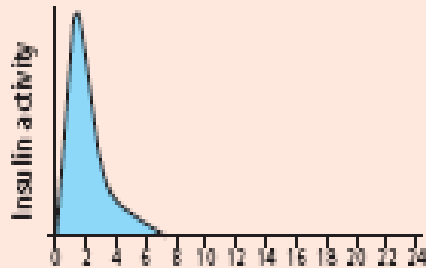
Pre-mixed Human Soluble/Isophane: Mixtard 30, Humulin M3 etc

Onset:	See above
Peak:	See above
Duration:	See above

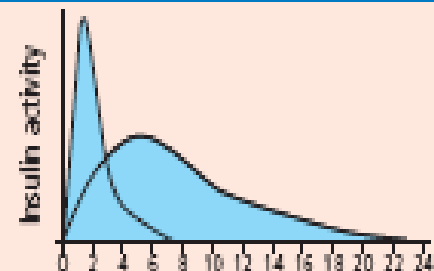Mixtard 30, M3 refers to % of soluble insulin ie. 30% Soluble 70% Isophane
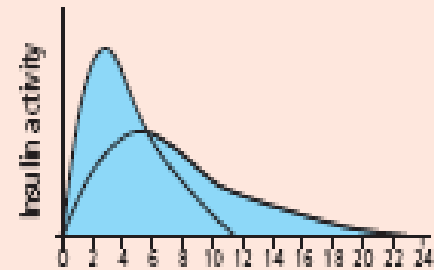
Intermediate Human Isophane Insulin's: Insulatard, Humulin I

Onset:	-
Peak:	4-8 hours
Duration:	14-16 hours
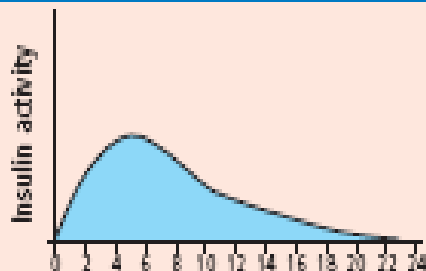
Pre-mixed Analogues/Isophane: Novo Mix 30, Humalog Mix50, Mix25

Onset:	See above
Peak:	See above
Duration:	See above

Novo Mix 30, Humalog Mix50/ Mix25 refers to % of rapid acting analogue insulin

Types of insulin

Insulin type/action (appearance)	Brand names (generic name in brackets)	Basal/bolus	Dosing schedule
Rapid-acting analogue (clear) Onset: 10–15 minutes Peak: 60–90 minutes Duration: 4–5 hours	Humalog® (insulin lispro) NovoRapid® (insulin aspart)	Bolus	Usually taken right before eating or to lower high blood glucose
Short-acting (clear) Onset: 0.5–1 hour Peak: 2–4 hours Duration: 5–8 hours	Humulin®-R Novolin®ge Toronto	Bolus	Taken about 30 minutes before eating, or to lower high blood glucose
Intermediate-acting (cloudy) Onset: 1–3 hours Peak: 5–8 hours Duration: up to 18 hours	Humulin®-N Novolin®ge NPH	Basal	Often taken at bedtime, or twice a day (morning and bedtime)
Extended long-acting analogue (Clear and colourless) Onset: 90 minutes Peak: none Duration: 24 hours	Lantus® (insulin glargine) Levemir® (insulin detemir)	Basal	Usually taken once or twice a day
Premixed (cloudy) A single vial contains a fixed ratio of insulins (the numbers refer to the ratio of rapid- or fast-acting to intermediate-acting insulin in the vial)	Humalog® Mix 25™ Humulin® (20/80, 30/70) Novolin®ge (10/90, 20/80, 30/70, 40/60, 50/50)	Combination of basal and bolus insulins	Depends on the combination

Self-Care

▶ Patients should be educated to practice self-care. Self-care should include:

- Blood glucose monitoring
- Body weight monitoring
- Foot-care
- Personal hygiene
- Healthy lifestyle/diet or physical activity
- Identify targets for control
- Stopping smoking

References

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- **World Health Organization**. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of WHO. **Department of Non-communicable Disease Surveillance. Geneva** 1999

- Academy of Medicine. Clinical Practice Guidelines. Management of type 2 diabetes mellitus. MOH/P/PAK/87.04(GU), 2004

- NHS. **Diabetes - insulin initiation - University Hospitals of Leicester NHS Trust** Working in partnership with PCTs across Leicestershire and Rutland, May 2008.

THANK YOU