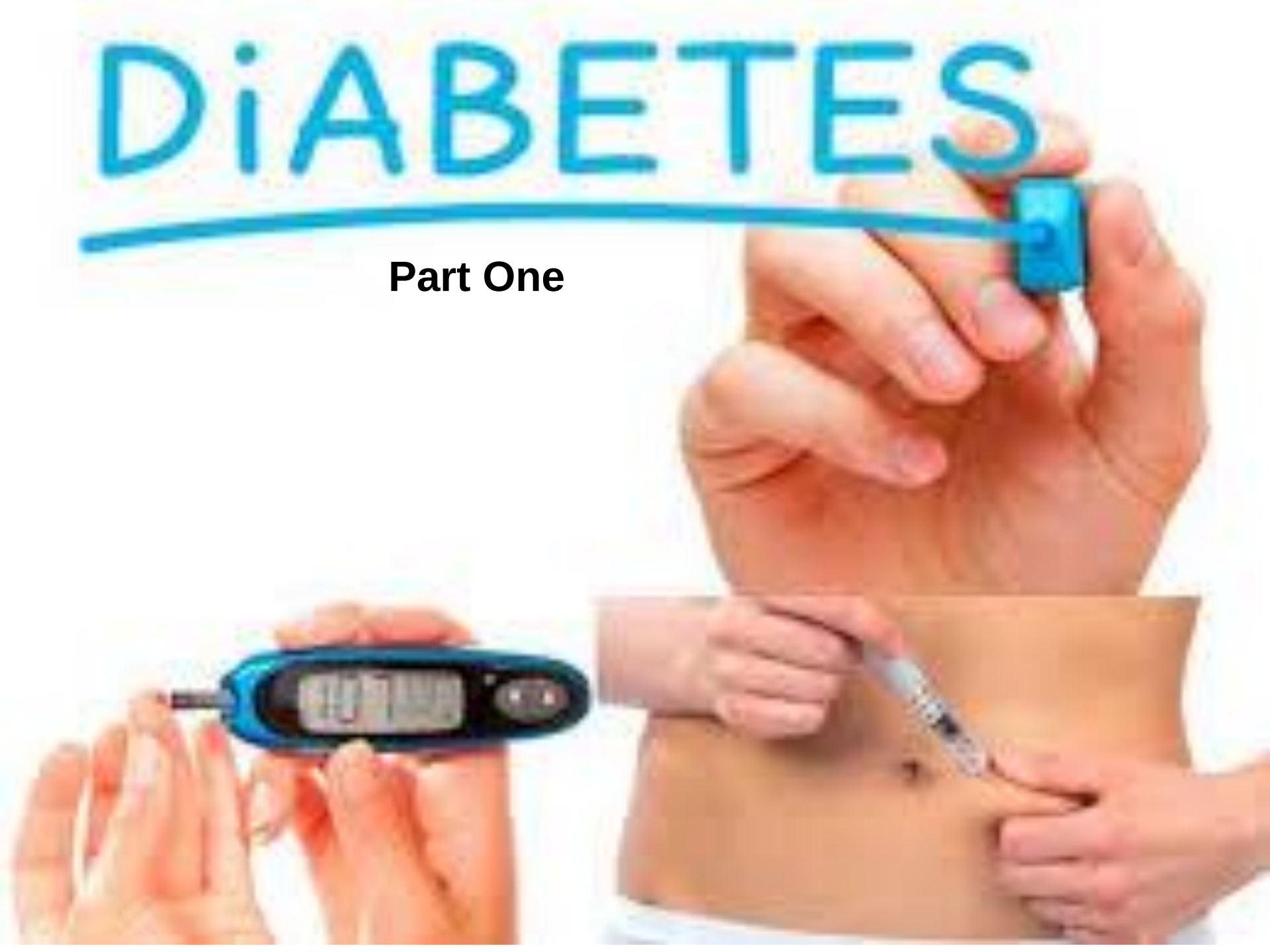
DiABETES

Part One

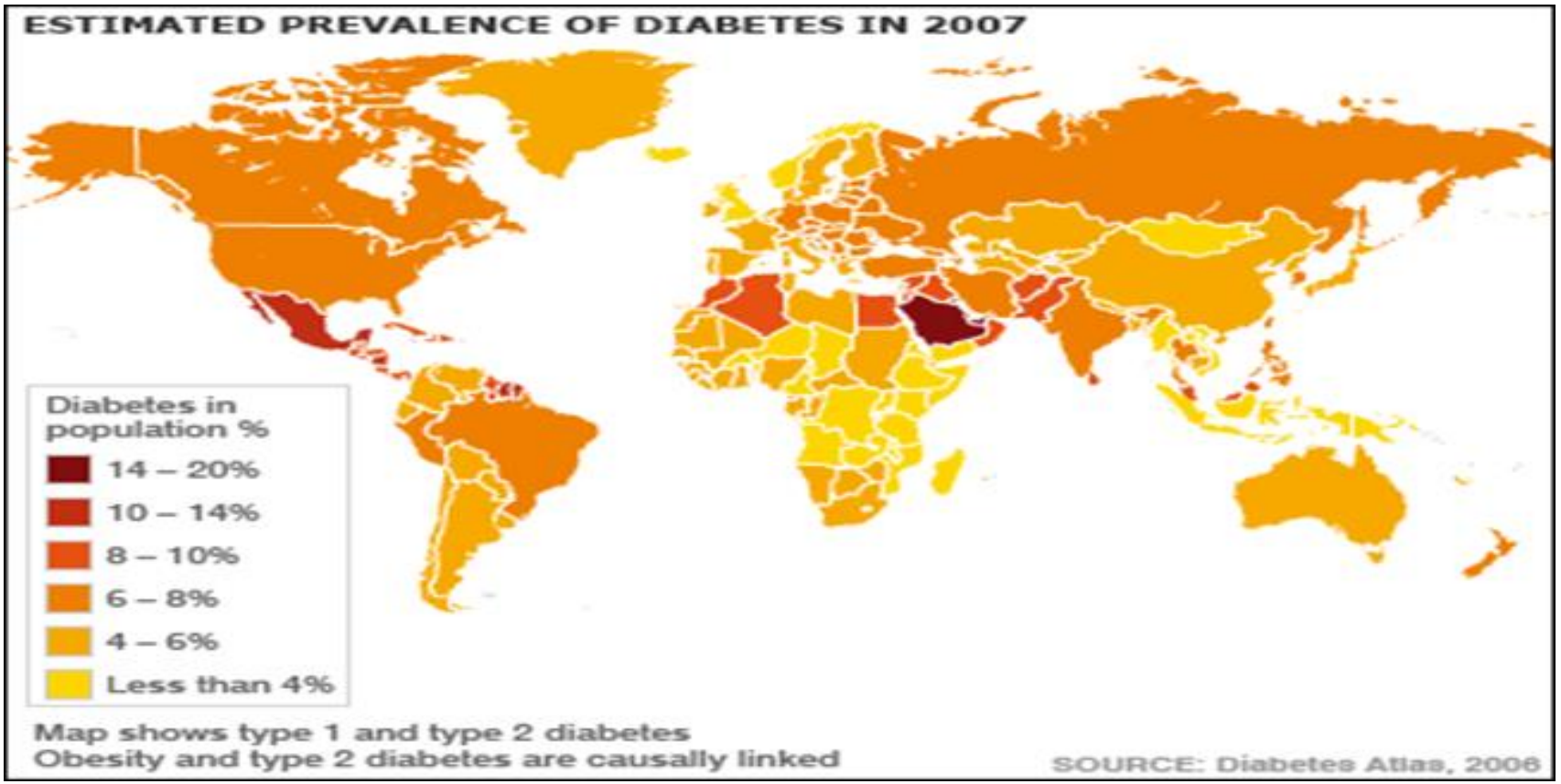


INTRODUCTION

- Diabetes comes from a Greek word meaning 'to pass or flow through' and mellitus means 'sweet'.
- DM is a **group of metabolic disorders** characterized by hyperglycemia.
- It is associated with **abnormalities in carbohydrate, fat, and protein** metabolism and results in chronic complications including **microvascular, macrovascular, and neuropathic disorders**.
- The **feet and eyes** are at special risk and need **special care** and regular checks.
- Diabetes is **controlled not curable**

INTRODUCTION

- Type **2** diabetes has a strong **genetic predisposition.**
- About **1 person in 30 gets diabetes**. It tends to increase as we get older because the pancreas, like other organs, tends to wear out.



CLASSIFICATION OF DIABETES

- The vast majority of diabetic patients are classified into one of three broad categories:
  - Type 1 diabetes
  - Type 2 diabetes
  - Gestational diabetes

- Gestational diabetes:
  - Occur if women develop diabetes because of the stress of pregnancy. Ending after childbirth
- Type 1 diabetes:
  - Type 1 diabetes caused by **an absolute deficiency of insulin.**

- Type 2 diabetes:
  - Type 2 diabetes defined by the presence of **insulin resistance** with an **inadequate compensatory increase in insulin secretion**.

Type 2 Diabetes

- Most individuals with type 2 diabetes exhibit **abdominal obesity, metabolic syndrome causes insulin resistance** with an increased risk of developing **macrovascular complications**.

- **Five Components of the Metabolic Syndrome**
- **(Individuals with at Least 3 Components Meet the Criteria for Diagnosis)**

1-Abdominal obesity Waist circumference

- Men >102 cm (>40 in)
- Women >88 cm (>35 in)

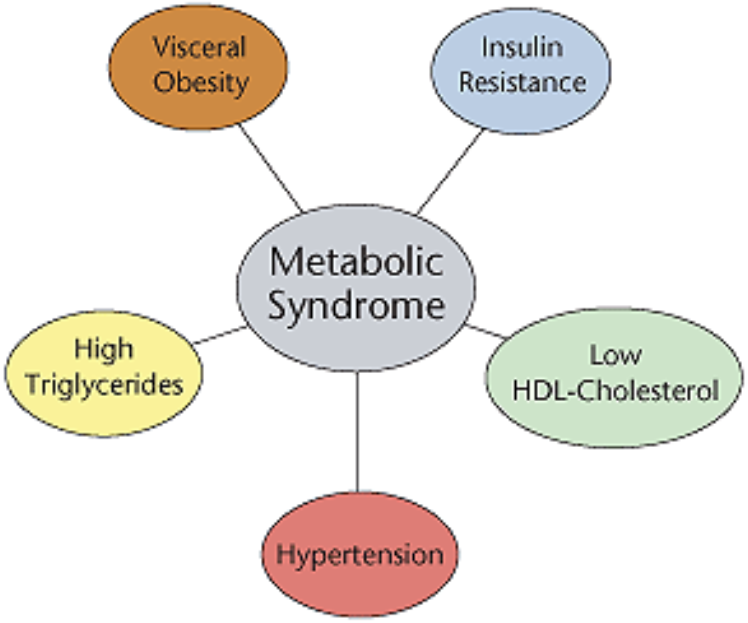
2-Triglycerides ≥150 mg/dL (≥1.70 mmol/L)

3-High-density lipoprotein C

- Men <40 mg/dL (<1.03 mmol/L)
- Women <50 mg/dL (<1.29 mmol/L)

4-Blood pressure ≥130/≥85 mm Hg

5-Fasting glucose ≥110 mg/dL (≥6.1 mmol/L)



CLASSIFICATION OF DIABETES

- Finally, uncommon types of diabetes caused by infections,, endocrinopathies, pancreatic destruction, known genetic defects (Named **MODY from 1-7**) are classified separately.

Drugs:

- Nicotinic acid
- **Glucocorticoids**
- Thyroid hormone
- Diazoxide
- *β*-Adrenergic agonists
- Thiazides
- Phenytoin

Gestational Diabetes Mellitus

- GDM is defined as glucose intolerance that is first recognized during pregnancy under the effect of **placental hormones on insulin function**
- approximately **7%** of all pregnancies.
- Clinical detection (routine check at clinic visit) is important, as therapy will reduce perinatal morbidity **(fetal macrosomic baby)** and mortality.
- Treated by **insulin and lifestyle modification**.
- A **repeat OGTT** should be carried out **6 weeks** after delivery, to confirm the diabetes has disappeared.

Screening for diabetes

The recommended screening test is the fasting plasma glucose (FPG), HbA1c, or (OGTT).

Type 1 Diabetes Mellitus

The prevalence of type 1 DM is low. screening for type 1 DM in the asymptomatic general population is **not recommended**.

Only, in **high-risk family members**, screening for ***β*-cell autoantibody** status may be appropriate.

Screening for Diabetes

- The American Diabetes Association (ADA) recommends screening for type 2 DM at any age in individuals who are:

1- **Overweight (BMI ≥25 kg/m2)** and have at least **one** other risk factor for the development of type 2 DM.

2-Risk factors include:

Age>45

physical inactivity

Hypertension

low HDL

history of cardiovascular disease.

prediabetes

first-degree relative with diabetes

high triglycerides

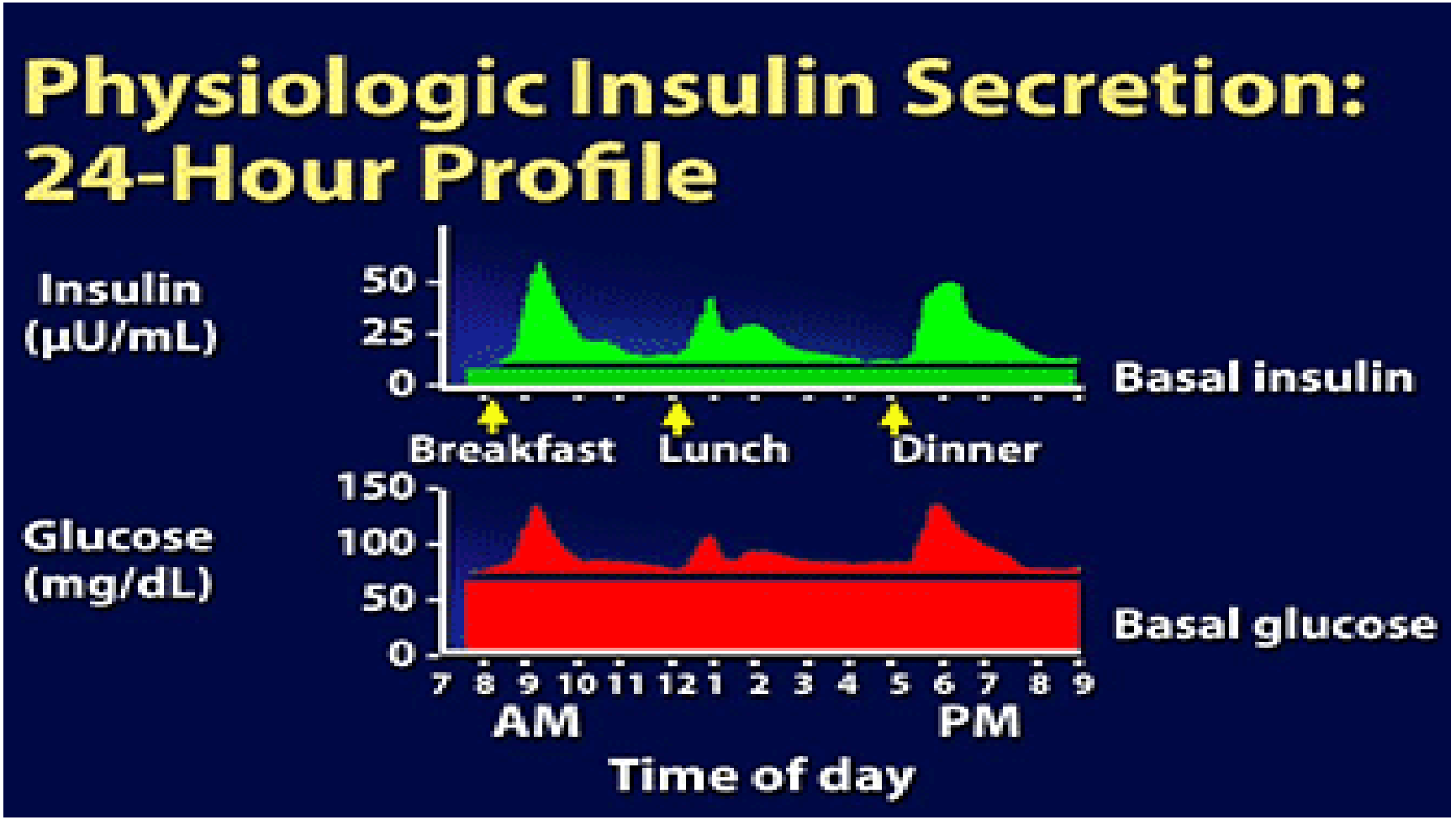
polycystic ovary syndrome

Glucose Monitoring device

- The pharmacist should educate people on how to use these devices.

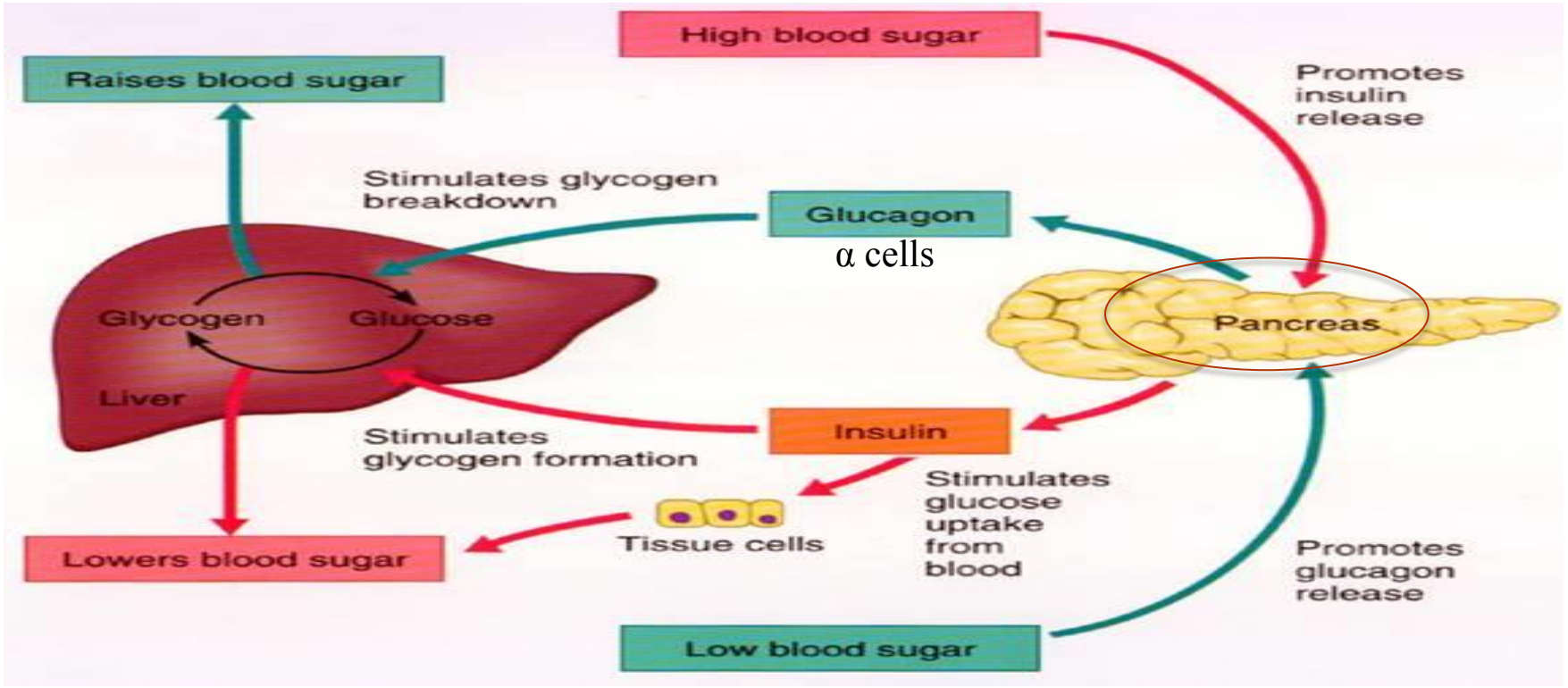
Normal Insulin Action In the fasting state	Normal Insulin Action In the fed state
-75% of total body glucose disposal takes place in non–insulin-dependent tissues: the **brain and splanchnic tissues (liver and gastrointestinal [GI] tissues**) -The remaining 25% of glucose metabolism takes place in muscle (insulin-dependent).	carbohydrate ingestion increases the plasma glucose concentration and stimulates insulin release from the pancreatic β cells. **The resultant hyperinsulinemia stimulates glucose uptake by peripheral tissues**. The majority (80–85%) of glucose taken up by peripheral tissues is disposed of in muscle, with only a small amount (4–5%) being metabolized by adipocytes. **The resultant hyperinsulinemia suppresses of free fatty acid release from fat cells** NB: Increased levels of free fatty acids lead to **insulin resistance in liver and muscle**.
approximately **85%** of glucose production is derived from the **liver**, and the remaining amount is produced by the **kidney**.	**The resultant hyperinsulinemia suppresses hepatic glucose production**

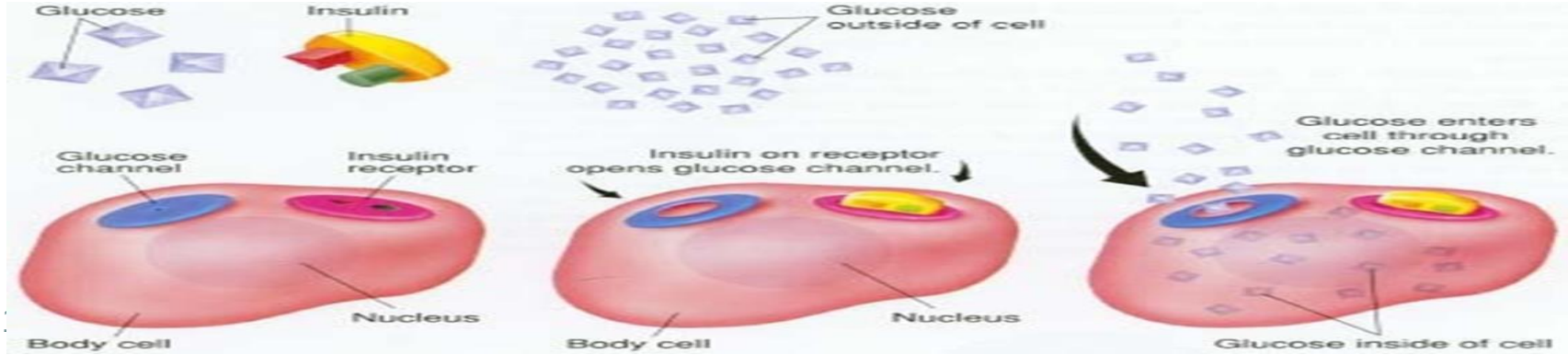
Insulin (the amazing man)



- Secreted in response to glucose
- Attempts to maintain **euglycemia**

Think Back: Insulin





Incretins

- This increased insulin secretion in response to an **oral** glucose stimulus is referred to as **“the incretin effect”** and suggests that **gut-derived hormones** when **stimulated by glucose from food** lead to an **increase in pancreatic insulin secretion**.

- In the **type 2 diabetic patient**, decreased postprandial insulin secretion is due to both impaired pancreatic β-cell function and a reduced stimulus for insulin secretion from gut hormones.

- It is now known that two hormones, **Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)**, are responsible for over 90% of the increased insulin secretion seen in response to an oral glucose load.

GLP-1	GIP
secreted from the distal intestinal mucosa	secreted by K cells in the intestine
The action of GLP-1 is glucose dependent, and for GLP-1 to enhance insulin secretion, glucose concentrations must be higher than 90 mg/dL (5 mmol/L).	a role with insulin secretion during near-normal glucose levels
GLP-1 **suppresses glucagon secretion, slows gastric emptying, and reduces food intake by increasing satiety**.	**-act as an insulin sensitizer in adipocytes.** GIP has no effect on glucagon secretion, gastric motility, or satiety

- Both hormones rise within minutes of food ingestion
- The half-lives of GLP-1 and GIP are short (<10 minutes).
- Both hormones are rapidly inactivated by removal of two N-terminal amino acids by the enzyme **dipeptidyl peptidase-4 (DPP-4**).

Criteria for the diagnosis of DM

- The diagnosis of diabetes depend on a **blood glucose level.**
- The **ADA recommends using the fasting glucose test** as the principal tool for the diagnosis of DM in **non-pregnant adults.**

- **The fasting and postprandial glucose levels do not measure the same physiologic processes** and do not identify the same individuals as having diabetes.

- **The fasting glucose reflects hepatic glucose production, which depends on insulin secretory capacity of the pancreas.**

- **The postprandial glucose reflects uptake of glucose in peripheral tissues (muscle and fat) and depends on insulin sensitivity of these tissues.**

Criteria for the diagnosis of DM

Symptoms of diabetes plus casual[b] plasma glucose concentration ≥200 mg/dL (11.1 mmol/L)

or

Fasting[c] plasma glucose ≥126 mg/dL (7.0 mmol/L)

or

2-hour postload glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT[d]

Fasting plasma glucose (FPG)	**2-Hour postload plasma glucose (oral glucose tolerance test)**
Normal: FPG <100 mg/dL	Normal: Postload glucose <140 mg/dL
Prediabetes: Impaired fasting glucose (IFG) 100–125 mg/dL	Prediabets: Impaired glucose tolerance (IGT): 2-hour postload glucose 140–199 mg/dL
Diabetes mellitus: FPG ≥126 mg/dL	Diabetes mellitus: 2-hour postload glucose ≥200 mg/dL

Pathogeneses of Type 1 Diabetes

- This form of diabetes results from **autoimmune destruction** of the β cells of the pancreas leading **absolute lack of insulin secretion**.
- Markers of immune destruction of the β cell (islet cell antibodies and antibodies to insulin) are present at the time of diagnosis in 90% of individuals.
- The most commonly detected antibody associated with type 1 DM is the **islet cell antibody**.
- Also, unknown or idiopathic processes can contribute.

Pathogenesis of type 2 diabetes

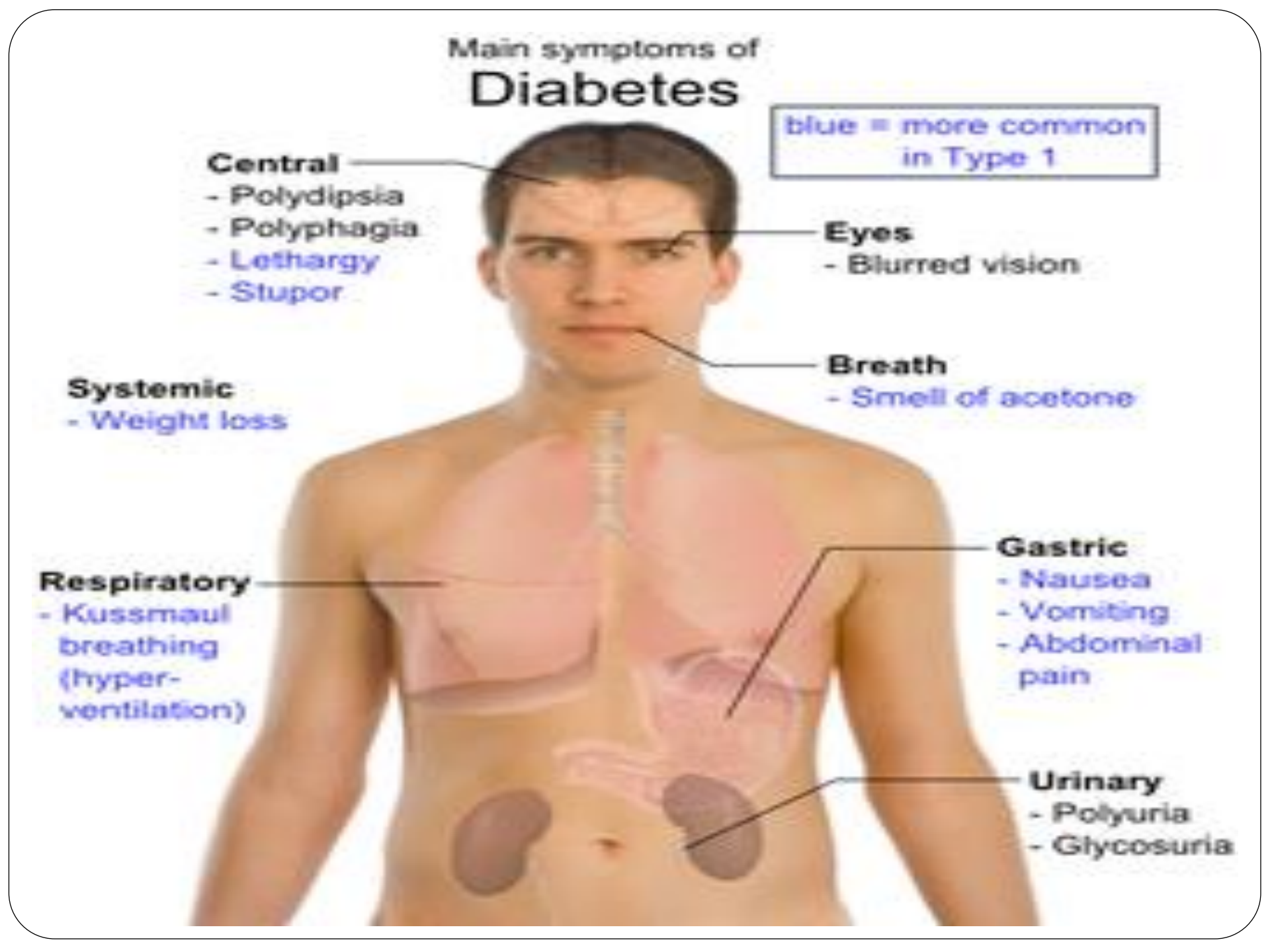
- **Impaired insulin secretion** is a uniform finding in type 2 diabetic patients due to β-cell dysfunction.
- When the FPG concentration **exceeds 140 mg/dL, the β cell is unable to maintain its elevated rate of insulin secretion**, and the fasting insulin concentration declines precipitously.
- This **decrease in fasting insulin leads to an increase in hepatic glucose production, which results in an elevated FPG concentration.**

Pathogenesis of type 2 diabetes

- In the type 2 diabetic patient, decreased postprandial insulin secretion is caused **by impaired pancreatic β-cell function (msy be from insufficient incretin hormones)**.
- **Abdominal fat** is **resistant to the antilipolytic effects of insulin**, resulting in the release of excessive amount of free fatty acid, which in turn lead to **insulin resistance in the liver and muscle**.
- The effect is an **increase in gluconeogenesis in the liver and inhibition of insulin mediated glucose uptake in the muscles**.
- These both result in increased levels of circulating glucose.

CLINICAL PRESENTATION

- Individuals with type 1 DM are often **thin** and are prone to develop diabetic ketoacidosis.
- About **20-40% percent of patients with type 1 DM present with diabetic ketoacidosis after several days of polyuria, polydipsia, polyphagia, lethargy and weight loss.**
- Patients with type 2 DM often present **without symptoms**, even though **complications** tell us that they may **have had type 2 DM for several years**.
- Often these patients are **diagnosed secondary to unrelated blood testing**.
- **later on, polyuria, nocturia, and polydipsia** can be seen in type 2 diabetes.

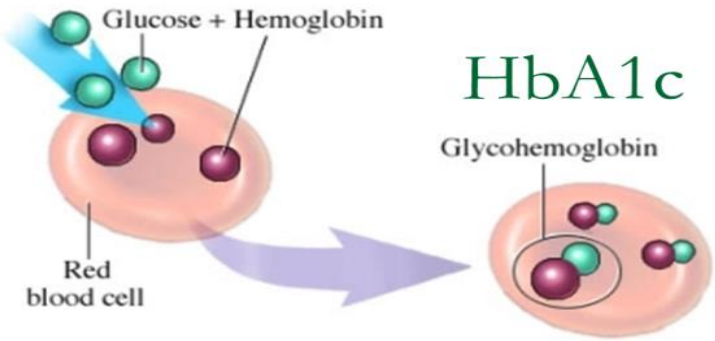

Main symptoms of
Diabetes
blue = more common in Type 1
Central
- Polydipsia
- Polyphagia
- Lethargy
- Stupor
Eyes
- Blurred vision
Breath
- Smell of acetone
Systemic
- Weight loss
Gastric
- Nausea
- Vomiting
- Abdominal pain
Respiratory
- Kussmaul breathing (hyper-ventilation)
Urinary
- Polyuria
- Glycosuria

Characteristic	Type 1 DM	Type 2 DM
Age	<30 years[b]	>30 years[b]
Onset	Abrupt	Gradual
Body habitus	Lean	Obese or history of obesity
Insulin resistance	Absent	Present
Autoantibodies	Often present	Rarely present
Symptoms	Symptomatic[c]	Often asymptomatic
Ketones at diagnosis	Present	Absent[d]
Need for insulin therapy	Immediate	Years after diagnosis
Acute complications	Diabetic ketoacidosis	Hyperosmolar hyperglycemic state
Microvascular complications at diagnosis	No	Common
Macrovascular complications at or before diagnosis	Rare	Common

Treatment

DESIRED OUTCOME

- reduce the risk for microvascular and macrovascular disease complications
- Relieve symptoms
- reduce mortality, and to improve quality of life
- Maintain **FBG<126** and **HbA1c target of <7%**



GLYCEMIC GOAL SETTING AND THE HEMOGLOBIN A1c

- **Glycemic control is paramount in reducing microvascular complications in both type 1 DM and type 2 DM.**

- HbA1c measurements are the gold standard for following **long-term glycemic control**.

- A HbA1c target of <7% is appropriate and lower values should be targeted if significant hypoglycemia and/or weight gain can be avoided.

HbA_{1c} Levels and Blood Glucose Equivalents	
HbA_{1c} Level (%)	Average Blood Glucose (mg/dL)
14	360
13	333
12	300
11	270
10	240
9	210
8	180
7	150
6	120
5	80

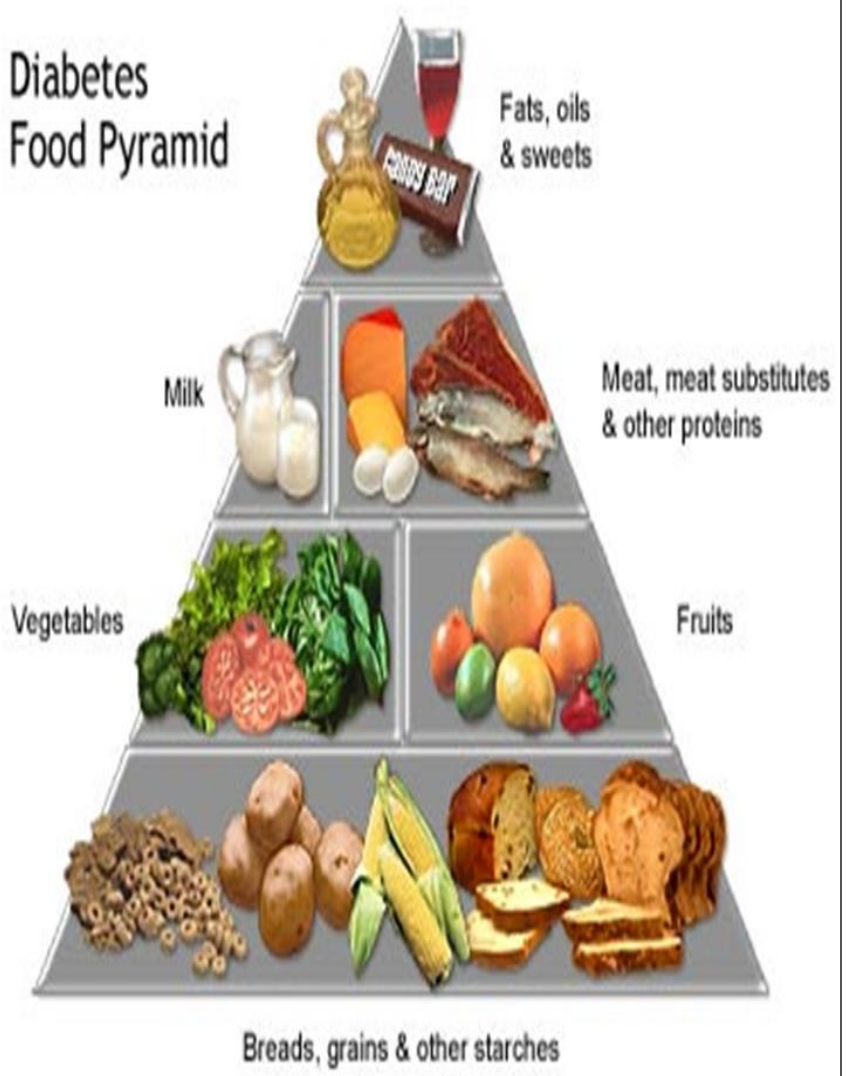
NONPHARMACOLOGIC THERAPY

Diet

- Medical nutrition therapy is recommended for all persons with DM.
- For individuals with type 1 DM, a meal plan that is **moderate in carbohydrates and low in saturated fat (<7% of total calories),** with a focus on **balanced meals is recommended**.
- In addition, patients with type 2 DM often require **caloric restriction to promote weight loss**.
- As most patients with type 2 DM are overweight or obese, **bedtime and between-meal snacks should be avoided.**

Diet

- eating good food **regularly** (not skimping)
- **spacing the meals** throughout the day (three main meals)
- **cutting down fat to a minimum**
- avoiding **sugar and refined carbohydrates (e.g. jam, honey, chocolates, sweets, pastries, cakes, soft drinks)**.
- eating a balance of **more natural carbohydrates (starchy foods) such as wholemeal bread, potatoes and cereals**
- eating a good variety of **fruit and vegetables**



Diet check list

This chart will help you determine which foods are high in sugar or fat. It suggests alternatives. You may want to look over the chart with your doctor, so that he or she can see what changes you will be making to your diet.

Foods to avoid or limit	*Suitable alternatives*
High in sugar	
sugar, honey	tablet or liquid artificial sweetener
spreads: jam, marmalade, syrups, Nutella	low joule jam/marmalade, Promite, Vegemite, meat/fish paste
sweet drinks: cordial, soft drink, flavoured mineral water, tonic water, fruit juice drinks, ordinary flavoured milk, milkshakes	low joule cordial/soft drink, plain mineral/soda water, pure fruit juice (limit to 1 small glass a day), coffee, tea herbal teas
sweet wine/sherry, port, liqueurs, ordinary beer	dry wine or spirit or low alcohol beer (1 to 2 drinks a day)
confectionery: lollies, cough lollies, chocolate (ordinary/diabetic/carob), muesli/health bars	low joule pastilles
sweet biscuits (e.g. cream, chocolate, shortbread), cakes, doughnuts, iced buns, sweet pastries	crispbreads, Cruskits, wholemeal crackers, wheatmeal or coffee biscuits, scones, 'no added sugar' fruit loaf
sweet desserts: ordinary jelly, fruit in sugar syrup, fruit pies, cheesecakes, puddings, ordinary flavoured yoghurt or ice-cream, ice-cream toppings	low joule jelly, fresh or tinned/stewed fruit without added sugar, custard or junket made with liquid sweetener plain or diet-lite 'no added sugar' yoghurt, plain ice-cream (1 scoop occasionally), low joule ice-cream toppin
sweet cereals: some mueslis, Nutrigrain, Cocopops, Honeysmacks, Sugar Frosties	most other cereals, e.g. porridge, Weetbix, All-Bran, Ready Wheats
High in fat	
mayonnaise, oily dressings, cream sauces, fatty gravies, sour cream	low joule dressings, vinegar, lemon juice, low joule Gravox, plain yoghurt
fat on meat, chicken skin, fatty meats (sausages, bacon, salami)	lean cuts of meat with skin and fat removed
deep-fried foods, pies/pasties	foods cooked without fat, or with a minimal amount of vegetable oil
snack foods: nuts, crisps, corn chips	crisp, raw vegetables, fruit, plain popcorn
large amounts of margarine, butter, oil, cream, peanut butter, dripping, lard,	limit to 3-6 teaspoons a day, preferably polyunsaturated margarine or oil

Activity

- Regular exercise, in any form, can help **reduce the risk of developing diabetes if prediabetic** .
- Activity can also **reduce the risk of developing complications of diabetes such as heart disease, stroke, kidney failure, blindness, and leg ulcers**.
- As **little as 20 minutes of walking three times a week** has a proven beneficial effect.
- If the patient has complications of diabetes (eye, kidney, or nerve problems), they may be limited both in type of exercise and amount of exercise they can safely do without worsening their condition.
- **Consult with your health care provider before starting any exercise program**.

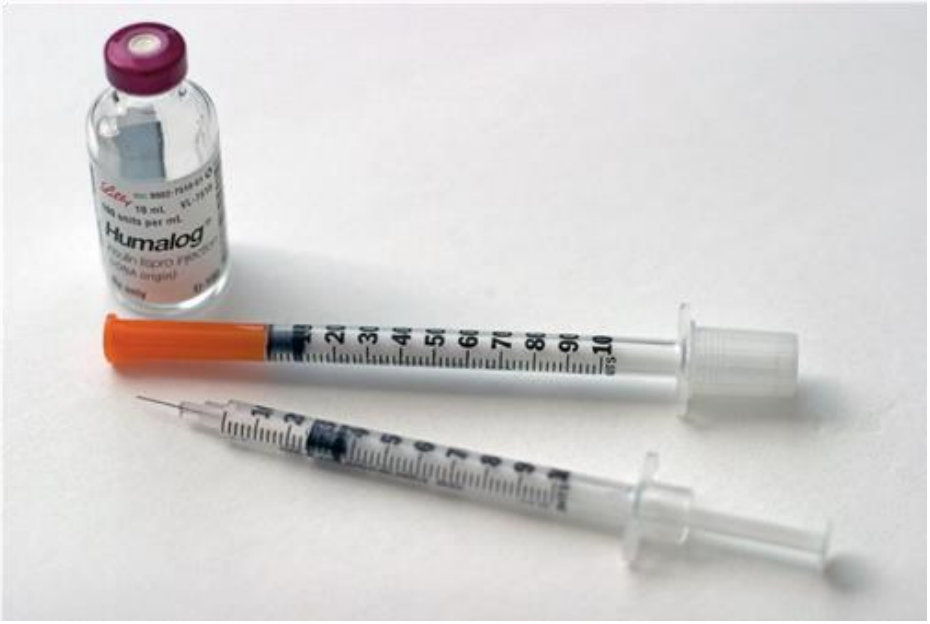
Alcohol and smoking

- For men, no more than two drinks a day and for women, one is recommended

- insulin, or certain oral diabetes medications, such as a sulfonylurea (glipizide, glyburide) or meglitinide (Prandin) that stimulate the pancreas to produce more insulin, drinking alcohol can cause a **dangerous low blood sugar** because your liver has to work to remove the alcohol from your blood instead of its main job to regulate your blood sugar

- *Smokers* with *diabetes* have higher risks for **serious complications**, including: Heart and kidney disease. **Poor blood flow in the legs and feet that can lead to infections, ulcers, and possible amputation** (removal of a body part by surgery, such as toes or feet) **Retinopathy** (an eye disease that can cause blindness). So, smoking should be avoided.

INSULIN THERAPY
IN
TYPE 1 DM



INSULIN THERAPY

- All patients with **type 1 DM** require treatment with insulin in order to survive.
- Exogenous insulin is used to **mimic the normal physiological pattern** of insulin secretion as closely as possible, for each individual patient.
- However, a **balance is needed between tight glycemic control and hypoglycemia risk**. If the risk of hypoglycemia is high, then it may be necessary to aim for less glycemic control.
- **Insulin role in type 1 treatment:**

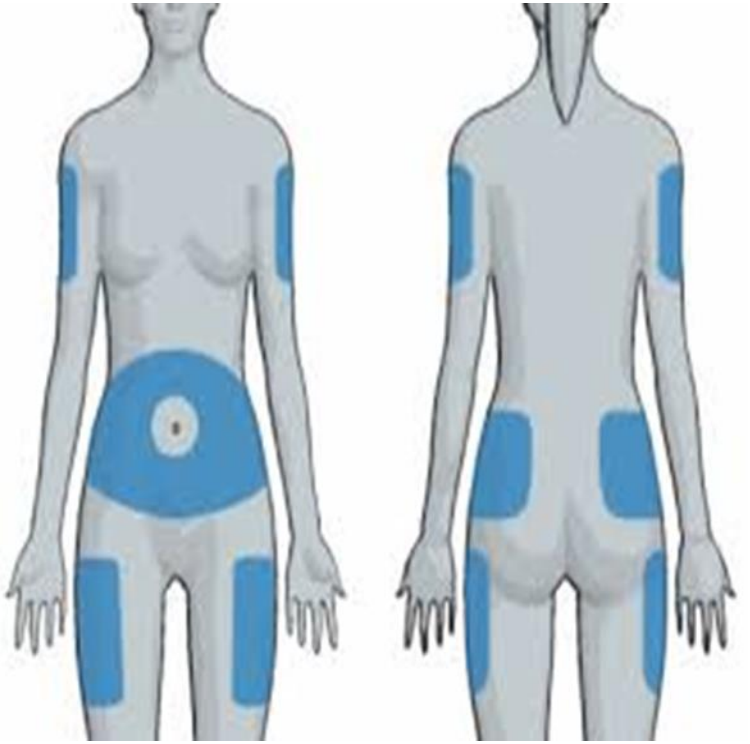
1. Replace the absolute deficiency in insulin secretion,
2. no ceiling for A1c reduction,
3. Reduces microvascular complications
4. Highly adjustable and individualized

INSULIN THERAPY

- There is a wide variety of insulin preparations which differ in:
  - **Species of origin, formulations or action**

Insulin formulations:

- Soluble insulin:
- Biphasic insulin:
- Isophane insulin
- Insulin zinc suspension
- Protamine zinc
- Long acting analogues

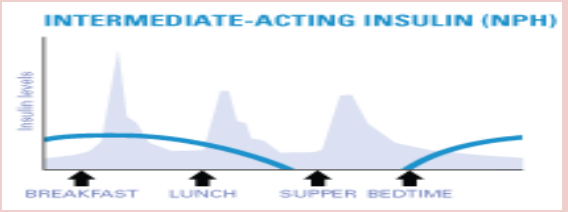
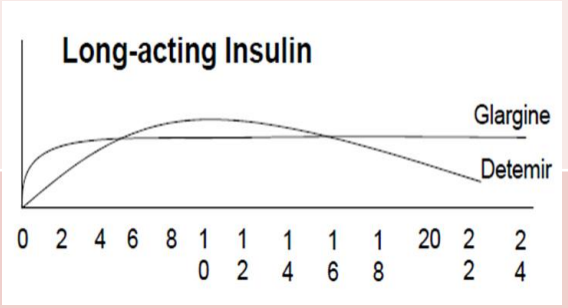


Sites for insulin injections

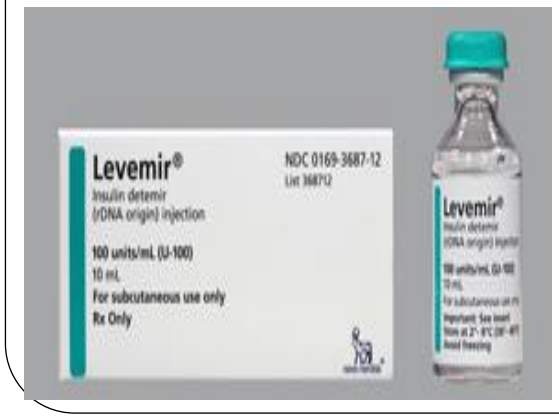
TYPES OF INSULIN

- These types are classified according to how quickly they begin working and how long the insulin lasts
  - **Rapid-acting (Humalog, Apidra)**
  - **Short-acting (eg, insulin regular (Novolin R, Humulin R))**
  - **Intermediate-acting (eg, insulin NPH (Novolin N, Humulin N))**
  - **Long-acting (eg, insulin glargine [Lantus®], insulin detemir [Levemir®])**
  - **Premixed (Mixtard 70/30)**

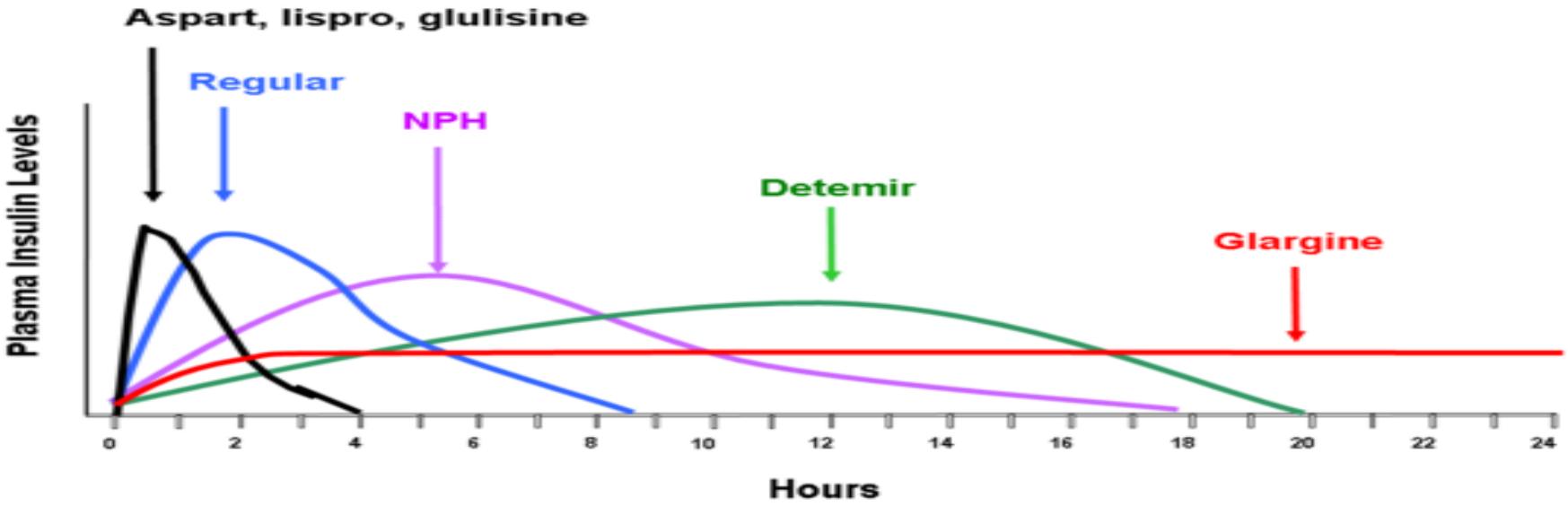
- Standard formulations- U 100
- **Concentrated formulations – U 500, U 300**

Category	Insulin Name	Onset	Peak	Duration	
Rapid acting	Aspart/ Lispro/ Glulisine	**5-15 minutes**	0.5-2 hours	**4-5 hours**	
Short acting	Regular	**30 minutes**	2-4 hours	**5-8 hours**	
Intermediate acting	NPH	**30-60 min**	4-12 hours	**10-16 hours**	
Long acting	Detemir	**2-4 hours**	6-8 hours	**20-23 hours**	
	Glargine	**1-2 hours**	No peak	**~24 hours**	

TYPES OF INSULIN

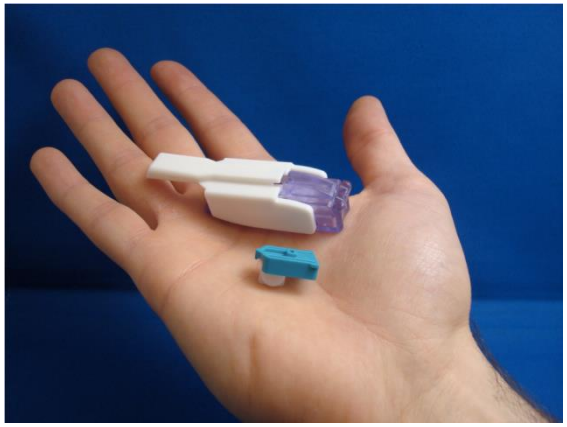


Insulin Kinetics and storage



Insulin should be stored in 4C (not in -20 ◦C or room temperature)

Inhaled Insulin



- Afrezza approved in 2014
- Exubera discontinued in 2007

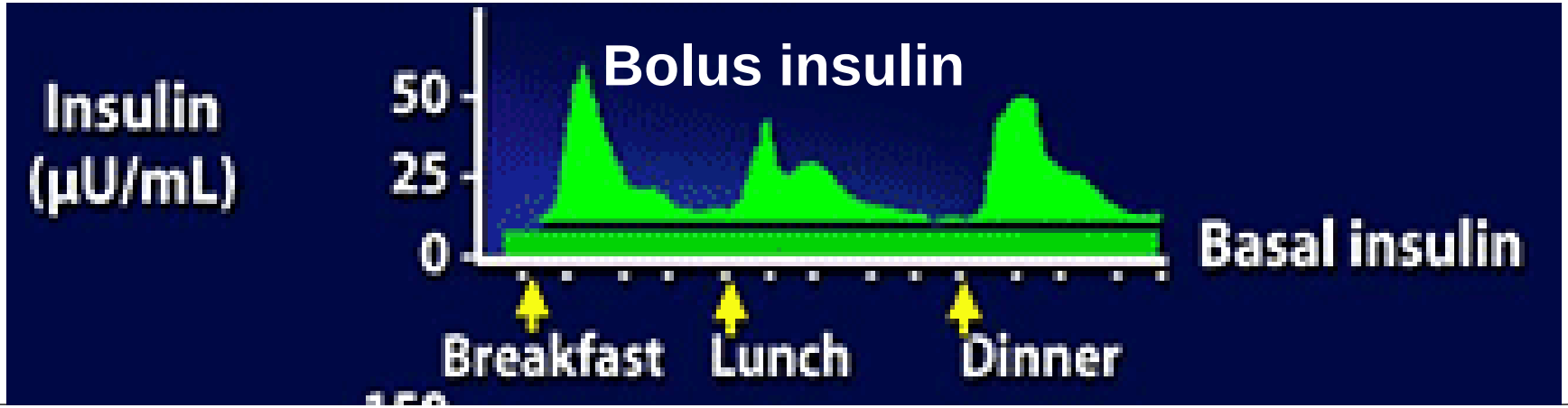
- Dosed in mg instead of units (need conversion as shown)

- Warnings:
  - Acute bronchospasm risk
  - Contraindicated
    - Asthma
    - COPD

Injected Mealtime Insulin Dose	AFREZZA® Dose	# of 4 unit (blue) cartridges needed		# of 8 unit (green) cartridges needed
up to 4 units	4 units			
5-8 units	8 units			
9-12 units	12 units		+	
13-16 units	16 units			
17-20 units	20 units		+	
21-24 units	24 units			

What are we Trying to Control?

Fasting Plasma Glucose (FPG)	Post-prandial Plasma Glucose (PPG)
Basal insulin	Bolus or prandial
Intermediate or Long-acting	Rapid-acting or Short-acting
Suppress glucose rises between meals and overnight	Limits hyperglycemia after meals
Nearly a constant level	Immediate rise in insulin
Typically 50% of daily need	Typically 50% of daily need Divided between each meal of day



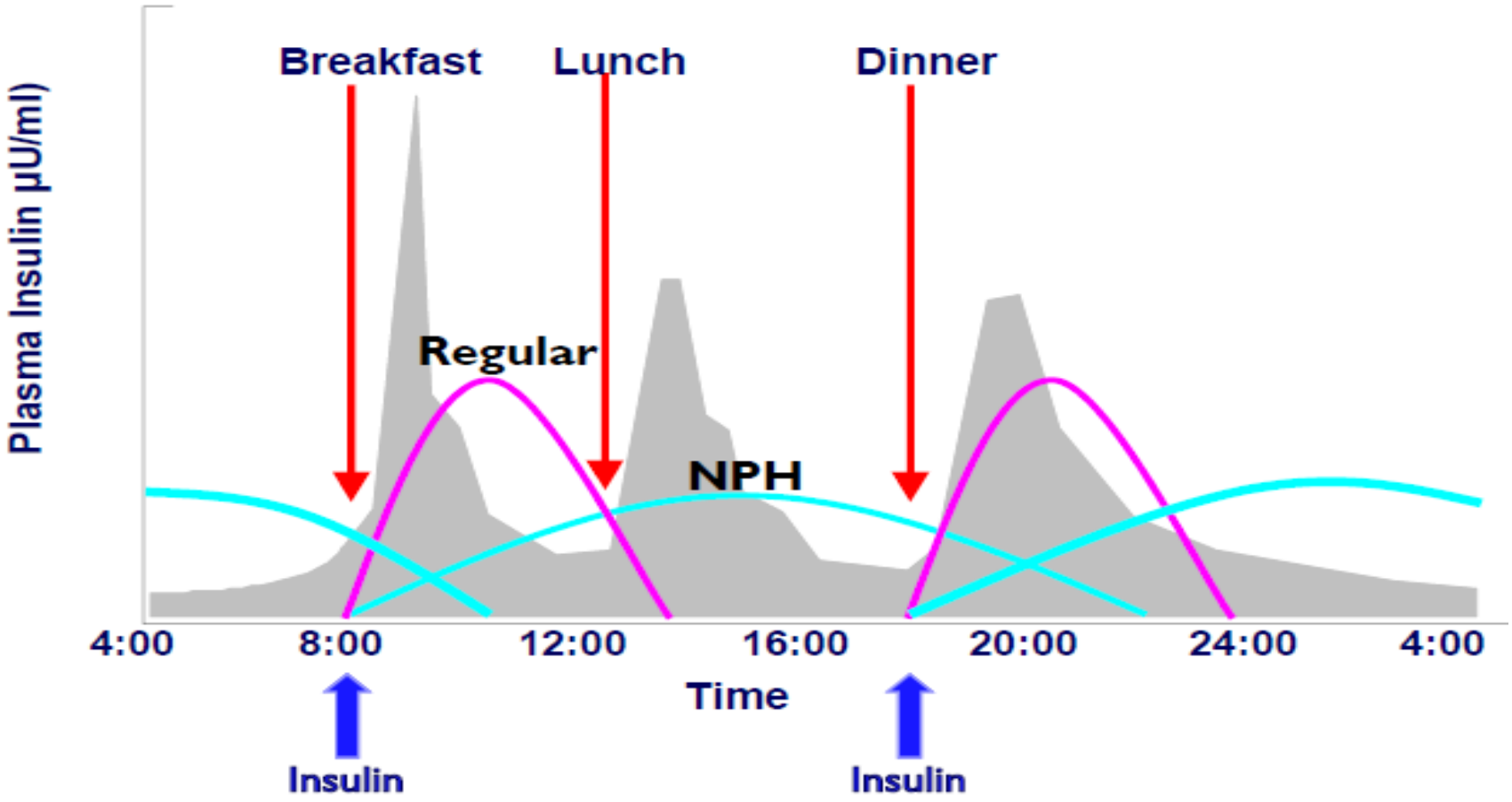
INSULIN REGIMEN for Type 1 DM

1. **Mealtime plus basal regimens (basal-bolus regimen)**
2. **Twice-daily regimen**

Mealtime plus basal regimens (basal-bolus regimen)

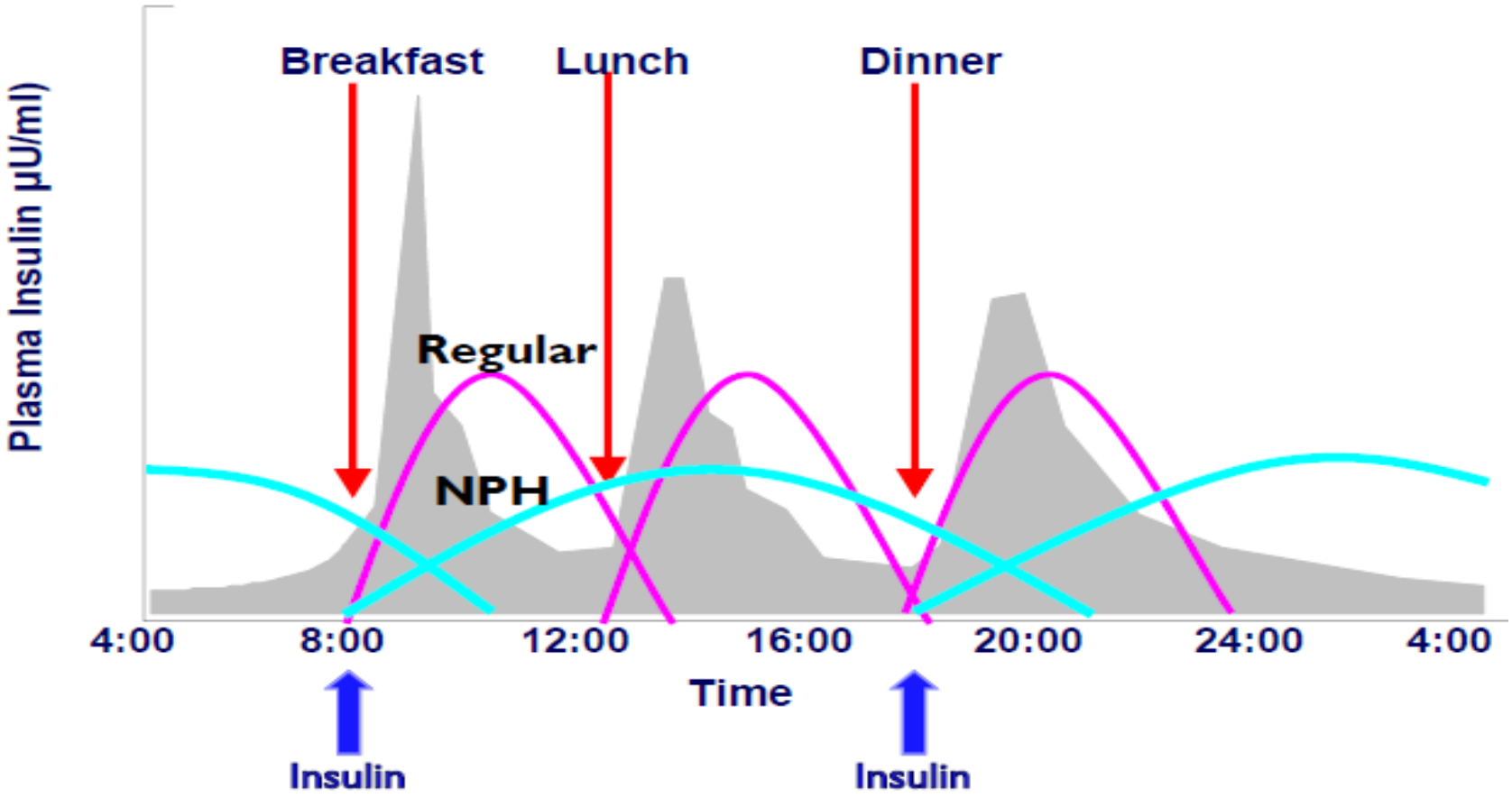
- This regimen requires
  - mealtime injections of insulin with a fast acting preparation
  - One or two injections of a basal (intermediate or long acting) insulin.
- This regimen offers the **most flexibility of dosing and eating habits** and often **better glucose control**.
- The disadvantage of this regimen is that it require **multiple injections and requires regular blood glucose monitoring**.

2 Injection Schedule (basal + prandial)



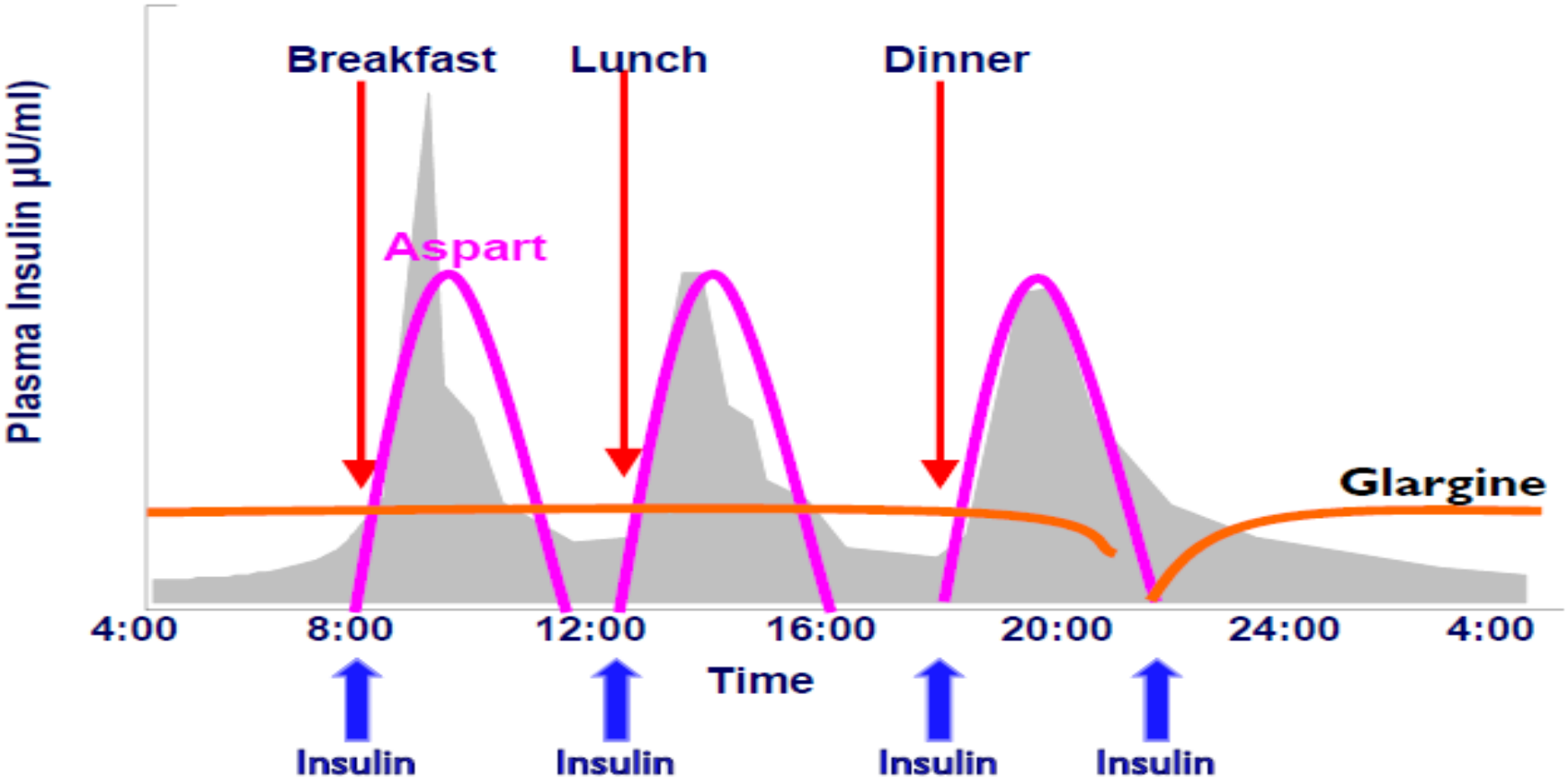
2 Regular + 2 NPH

3 Injection Schedule (basal + prandial)



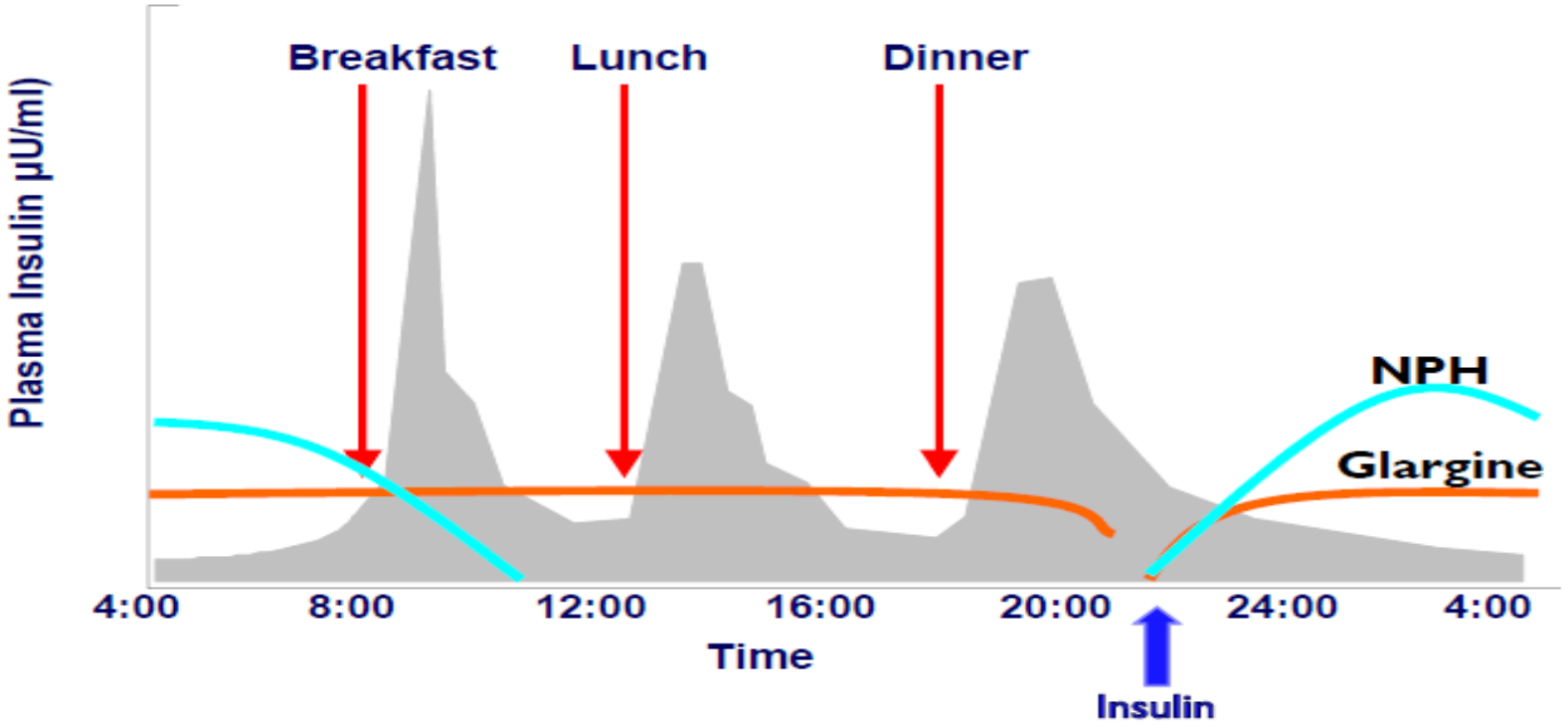
3 Regular + 2 NPH

4 Injection Schedule (basal + prandial)



3 apsart + 1 glargine

1 Injection Schedule (basal only) exception)



Special case: Once nightly injections of NPH or glargine will control the increase in FBG that often **results from cortisol release** and subsequent glucose release from the liver (**Dawn phenomenon**)

Twice-daily regimen

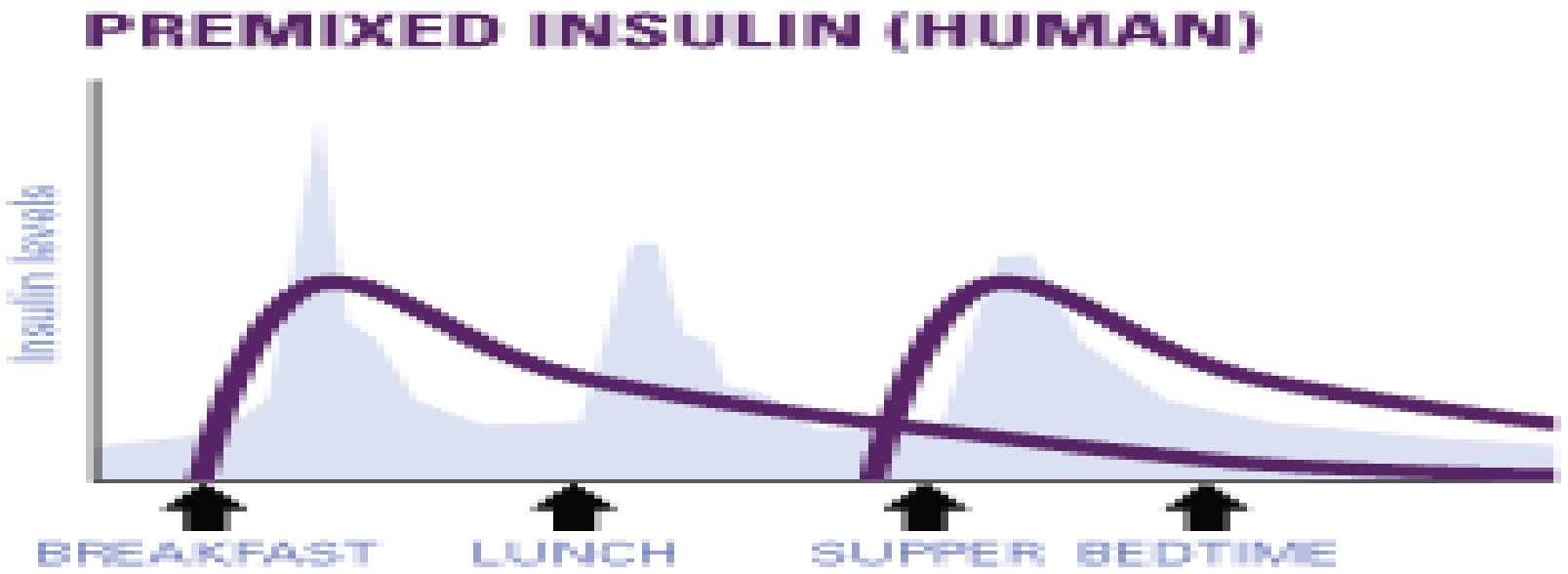
- This regimen uses a premixed insulin, comprising a short or rapid (fast) acting insulin and an **intermediate acting insulin**.
  - The regular human insulin mixes should be **given 30 minutes before breakfast and 30 minutes before evening meal**.

Types:

1. NPH and regular insulin (Humulin 70/30, Mixtard 70/30)
2. Protamine lispro (long-acting) & lispro: Humalog 75/25, Humalog 50/50
3. Protamine aspart & aspart NovoMix 70/30

Twice-daily regimen

- Notes
  - Typically dose twice daily with breakfast and dinner (supper)
  - Less flexibility than with individual insulin doses
  - Less injections (better compliance)
  - Roll/mix before use
  - Available in pens and vials



Insulin conversion

- Common insulin conversions
  - Rapid ↔ Regular
    - 1:1 ratio
  - Lantus ↔ Levemir
    - 1:1 ratio
  - NPH ↔ Levemir
    - 1:1 ratio
  - NPH twice daily ↔ Lantus
    - 80% of daily NPH dose; give once daily

Converting From Mixed Insulin

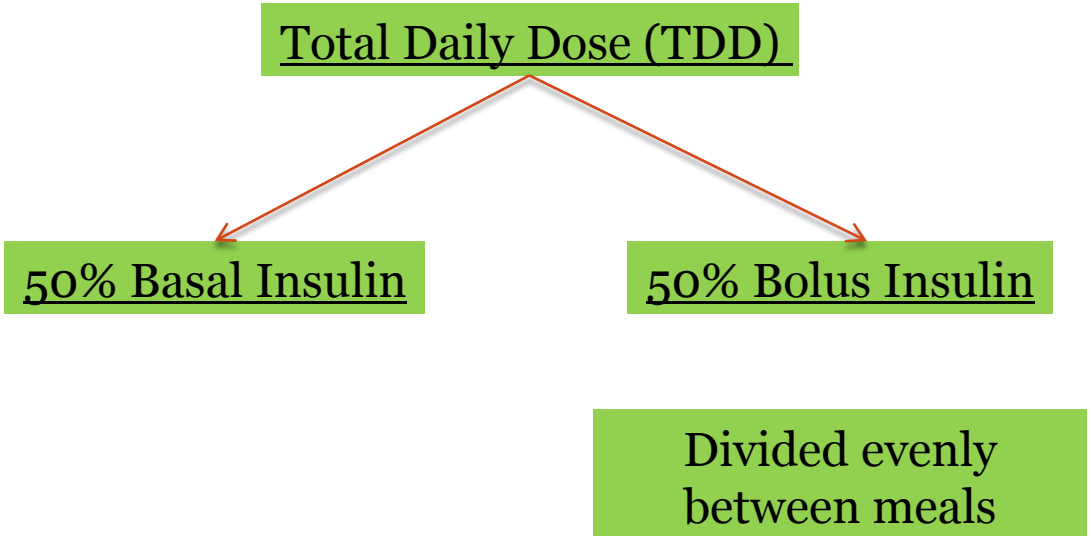
Example:

- Novolin 70/30 (insulin NPH/regular) 40 units qAM and 20 units qPM before meals ➔ insulin lantus once and insulin aspartTID
  - TDD = 60 units
    - NPH dose = 60 (0.7) = 42 units
    - Regular insulin dose = 60 (0.3) = 18 units
  - NPH ↔ detemir (1:1)
    - 42 units NPH = 42x 0.8= 34 units insulin lantus
    - Inject 34 units insulin lantus once daily
  - Regular ↔ rapid (1:1)
    - 18 units regular = 18 units rapid
    - Rapid = TID dosing; 18/3 = 6
    - Inject 6 units insulin lispro TID 15 min before meals

Adjusting insulin dose

- The patient varies the amount of **before meal rapid-acting insulin injected,** depending on the **preprandial BG level, the anticipated activity and anticipated carbohydrate intake.**

- Many patients start with **a prescribed dose** of insulin before meals that they vary by use of an **"correction factor"** to normalize a high premeal plasma glucose reading.



Now you try

JT is a 12-year old male with newly diagnosed T1DM (BG=650 mg/dL, Wt=176 lb). He is going to start insulin therapy with insulin glargine and insulin aspart. Use 0.6 units/kg

- What is his estimated total daily dose?
- What is his estimated insulin glargine dose?
- What is his estimated insulin aspart dose?

Now You Try Answers

- **What is his estimated total daily dose?**
  Weight: 176 lb / 2.2 = 80 kg
  TDD: 80 kg (0.6 unit/kg/day) = 48 units

- **What is his estimated insulin glargine dose?**
  Basal dose: 50% of TDD
  Basal dose: 48 units x 0.5 = 24 units
  Insulin glargine 24 units once daily

- **What is his estimated insulin aspart dose?**
  Prandial dose: 50% of TDD, split between 3 meals
  Prandial dose: 48 x 0.5 = 24 units
  Individual prandial dose: 24 units / 3 meals = 8 units
  Insulin aspart 8 units TID 15 min before meals

Correction factor

- A “correction factor” can be calculated as a starting point to estimate the approximate plasma glucose–lowering effect of 1 unit of short-acting insulin in mg/dL.
- **For regular insulin, one may use a factor of 1,500** divided by the total daily insulin dose in number of units that the patient currently uses.
- **For rapid-acting insulin analogs, a factor of 1,700** is more often used when calculating the correction factor.
- For example, if a patient is currently taking 40 units of basal insulin and 12 units of rapid-acting insulin at each of three meals, the total daily insulin dose (TDD) equals 76 units.
- Using this calculation 1,700 divided by 76 equals 22; thus, each unit of rapid-acting insulin analog will lower the plasma glucose approximately 22 mg/dL.

Insulin Sensitivity Factor (ISF)

- **"Rule of 1800" "Insulin Sensitivity Factor"** for short acting (regular) insulin
  - Estimates the drop in blood glucose (mg/dl) per 1 unit of rapid activity insulin
- **Use "Rule of 1500" for short acting (regular) insulin**
  - Can be used to calculate a correction dose of insulin
- **Rule of 1800 equation**
- **1800 ÷ TDD**
- **Step 1: Determine the pt's total daily insulin requirement**
  - **JT's total daily insulin requirement = 48 units**
- **Step 2: Divide 1800 by total daily insulin requirement**
  - **1800 ÷ 48 units = 37.5 units = 37 or 38 units**
- **Interpretation**
  - **1 unit of aspart will reduce JT's blood glucose by roughly 37 mg/dL**
- **Application**
  - **He can use this to treat unusually high BGs (i.e. during times of illness etc.**

Determining a Correction Dose

1. Calculate the difference between current BG and goal BG
   - Example: current BG – goal BG = mg/dl reduction needed
     - 180 mg/dl – 90 mg/dl = 90 mg/dl
2. Correction dose = BG difference ÷ ISF
   - 90 mg/dl ÷ 37 mg/dl/unit = 2.4 ≈ 2 units
3. **Add correction dose to regularly scheduled insulin dose and inject prior to the meal**

- If JT calculated that he needs 8 units to cover his meal, and his pre-meal glucose was 180 he would inject 10 units total to hopefully get back to goal

Carbohydrate counting (500 rule)

- Carbohydrate counting is a very effective tool for determining the amount of rapid-acting insulin that should be injected preprandially.

- Instead of using a prescribed dose of rapid-acting insulin before meals, patients can **self-adjust their premeal dose based on the estimated grams of carbohydrates that will be consumed**.

- **Rule of 500" for rapid acting insulin / TDD**

- "**Rule of 450" for short acting (regular) insulin/ TDD**

- Therefore, using the example above with a total daily insulin dose of 76 units, we would use 500 divided by 76, which estimates that 1 unit of rapid-acting insulin will cover approximately 7 g of carbohydrate.

Erratic glucose fluctuations

- There are several common errors in the management of patients with type 1 DM that can cause :

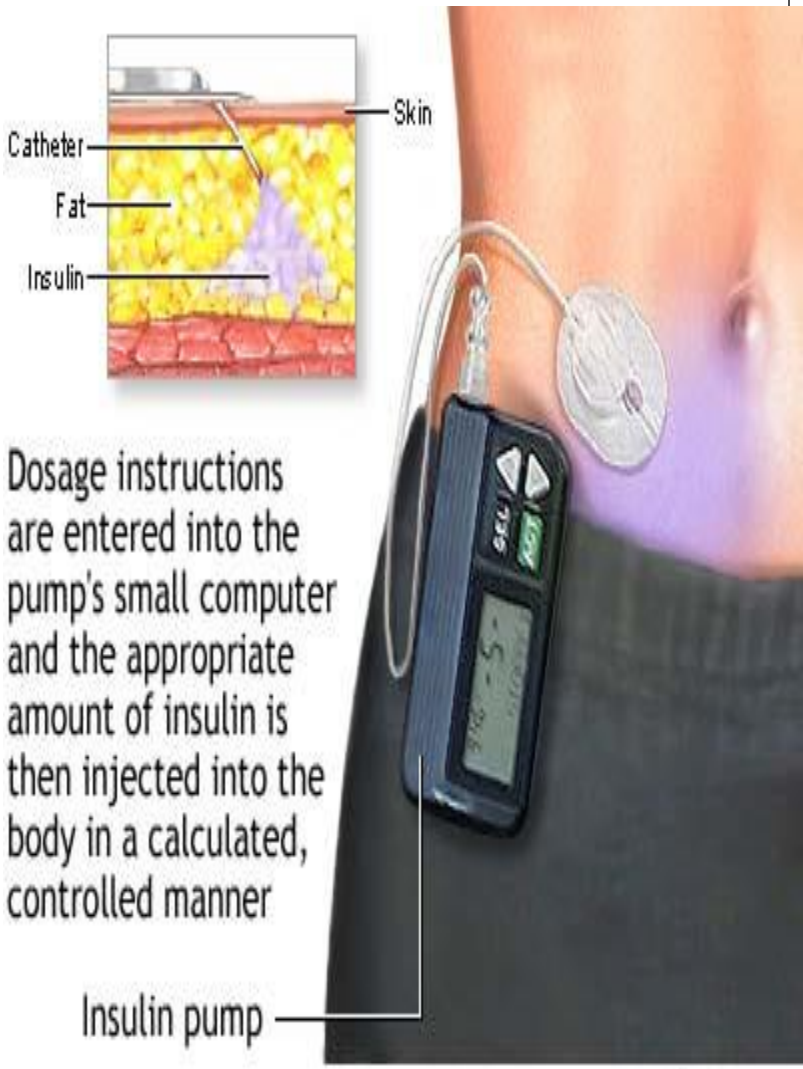
- **Failure to take into account action of insulin**: The timing of meals and/or physical activity must be planned around the peaks of insulin action accordingly.

- **Choice of insulin injection sites**

- **Injection technique and BG monitoring**: When in doubt, always reevaluate the patient's technique for insulin dosing, insulin injection, and BG testing. Sometimes simple errors result in unpredictable glycemic control.

Insulin Pumps

- Primarily used for T1DM
  - **Studies have found similar efficacy between basal/bolus & the pump**
- Typically use rapid-insulin over regular
  - **50% basal dose; 50% bolus dose**
  - **Bolus dose adjusted by patient based on SMBG monitoring**
- Converting from multi-dose insulin to pump
  - **If previously controlled then may reduce TDD by 20%**
  - **If previously uncontrolled then may use same TDD**



How a Pump Works

The insulin is housed inside the pump in a little cartridge called a "**reservoir.**"

Insulin travels into your body through a flexible tube that ends with a tiny needle called a "**cannula**" inserted just under the skin.

The needle is held in place by an "**infusion set,**" a little adhesive patch stuck to your skin.

Compatibility of Mixtures

Insulin	Compatible	Not Compatible
Aspart	NPH, Regular	Glargine, Detemir
Lispro	NPH, Regular	Glargine, Detemir
Glulisine	NPH, Regular	Glargine, Detemir
Regular	NPH	Glargine, Detemir

Always mix **clear** before **cloudy**

- Always draw rapid or regular insulin first Then draw NPH
- **Mixture should be used within 5 minutes of mixing**

Insulin Conversions & side effects

1. Hypoglycemia

   -Most serious adverse effect

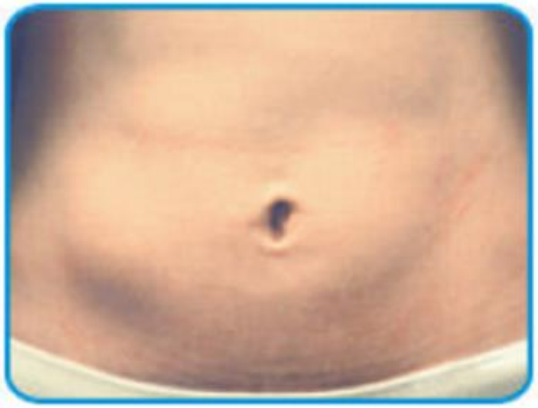
   -Patients must be educated about hypoglycemic symptoms

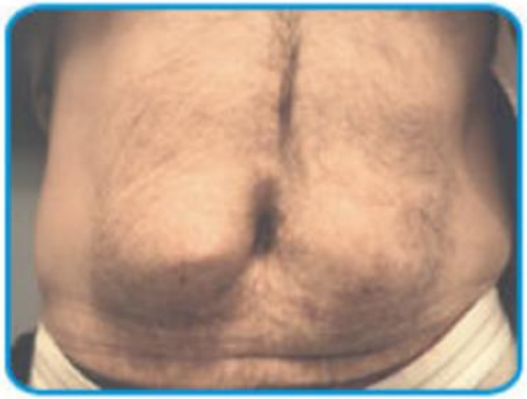
2. Weight gain

3. Injection site pain

4. Lipohypertrophy

(avoided by site rotation)





Why Insulin Causes Weight Gain

- **Diabetes** can cause you to have too much glucose in your bloodstream (blood sugar). If you are not absorbing sugar into your cells, your body will **depend on fat for energy, and this can cause weight loss**.

- When you begin taking insulin, glucose can be absorbed by the cells and used for energy. This helps blood sugars to go down, but it can make **you gain weight if you eat more than you burn in a day. Also, fat is not used for energy and begin to accumulate**

Diabetic Ketoacidosis

- Diabetic ketoacidosis is true diabetic emergencies.
- The absence of insulin in type 1 DM causes increased free fatty acid concentration in the blood and glucose is produced by the liver.
- Ketone bodies (acetone, acetoacetate ester and hydroxybutyrate) are formed in an increased amount and released in the blood.
- Furthermore, **osmotic diuresis is increased due to hyperglycemia, low plasma volume, loss of potassium occur**.
- **Potassium loss** is caused by a shift of potassium from the intracellular to the extracellular space in an exchange with hydrogen ions that accumulate extracellularly in acidosis

Diabetic Ketoacidosis

- Vomiting, dehydration, deep gasping breathing (kussmaul respiration), confusion and occasionally coma are typical symptoms.
- Impaired consciousness and coma developed in 10% of patients.

Risk factors include Infection, injury, a serious illness, missing doses of insulin shots, missing meal emotional stress or surgery.

Diagnosis :

Added to hyperglycemia, **ketones in the blood or on urinalysis and acidosis (pH <7.35)** are demonstrated. Also, acetone smell in breathing (fruity smell).

The American Diabetes Association categorizes DKA :

- *Mild:* blood pH mildly decreased to between 7.25 and 7.35 (normal 7.35–7.45);
- *Moderate:* pH 7.00–7.25, bicarbonate 10–15, mild drowsiness is present
- *Severe:* pH below 7.00, bicarbonate below 10, stupor or coma may occur

Treatment of Diabetic Ketoacidosis

1-Fluid replacement:

Fluid volume expansion (**initially with 0.9% NaCl**) to correct dehydration (**specially if with shock or decrease of conciousness**). rapid infusion of saline (**1 liter for adults**, 10 ml/kg in repeated doses for children) is recommended to restore circulating volume.

2-Insulin:

a bolus (initial large dose) of insulin of **0.1 unit of insulin per kilogram** of body weight. This can be administered immediately after the potassium level is known to be **higher than 3.3 mmol/l**; if the K^+ level is lower, administering insulin could lead to a dangerously low potassium level.

Diabetic Ketoacidosis

Initially, insulin 0.1 unit/kg per hour to reduce the blood sugars and suppress ketone production.

Reducing the dose of insulin once glucose falls below (300 mg/dl)

It is possible to use rapid acting insulin analogs injections **under the skin for mild or moderate cases**

3-Hypokalemia prevention:

measurement of the potassium levels and addition of potassium to the intravenous fluids once levels fall **below 5.3 mmol/l**. If potassium levels fall below 3.3 mmol/l, insulin administration may need to be interrupted to allow correction of the hypokalemia

4-Alkalinizing agents (eg, sodium bicarbonate) but questionable effects

Diabetic Ketoacidosis

Monitoring for response:

Resolution of DKA is defined as **general improvement in the symptoms, such as the ability to tolerate oral nutrition and fluids, normalization of blood acidity (pH>7.35), and absence of ketones in blood (<1 mmol/l) or urine.**

[

Once this has been achieved, insulin may be switched to the **usual subcutaneously administrered regimen**, one hour after which the intravenous administration can be discontinued

Prevention:

by **adherence to "sick day rules"**; these are clear-cut instructions to person on how to treat themselves when unwell. **Instructions** include:

1. advice on how much extra insulin to take when sugar levels appear uncontrolled,
2. an easily digestible diet rich in salt
3. means to suppress fever and treat infection,
4. recommendations when to call for medical help.
5. People with diabetes can monitor their own ketone levels when unwell and seek help if they are elevated

DIABETIC EMERGENCIES

- **HYPOGLYCEMIA:**
  - It occurs both with insulin treatment and oral agents, especially the longer acting sulphonylureas (chlorpropamide and glibenclamide).
  - Hypoglycemia in DM is defined as a blood sugar ≤ 70mg/dl
  - **Sweating, trembling, tachycardia, drowsiness, headache,** confusion, loss of concentration and **coma** are the symptoms.
  - If occur take glucose tablet of carbohydrate juice. if unconcious **IV dextrose or Glucagon vial (1 to 2 milligrams) of glucagon** in an **intramuscular injection**
  - Prevention of the causative factor for hypoglycemia like **heavy activity, eating forgetting**

DIABETIC EMERGENCIES

- If the patient is not aware of hypoglycemia, blood glucose levels may drop further causing **neuroglycopenic syndrome**, **in which the brain is starved of glucose may lead to death**

- Often the patient is confused and to control the hypoglycemia **need assistance**.

LONG TERM DIABETIC COMPLICATIONS

- **1-MACROVASCULAR DISEASES**
- CARDIOVASCULAR DISEASE:
  - The **most common cause of death** in type 2 DM is CVD (estimated 80% death)
  - Most of the patients with type 2 DM are affected by **MI.**
  - Cerebrovascular disease is also more commonly associated with diabetes.
- HYPERTENSION:
  - HTN is **twice as common** in diabetics compared to the normal population.
  - It affects 80% of type 2 diabetic patients.

MICROVASCULAR DISEASES

- RETINOPATHY:
  - Diabetic retinopathy is a **leading cause of blindness in people under the age of 60**.
  - After **20 years** from the onset of DM over **90% of people with type 1 and over 60% of people with type 2** will have diabetic retinopathy.
  - **Tight glycemic control and tight blood pressure control reduce the risk of developing retinopathy.**

MICROVASCULAR DISEASES

- NEPHROPATHY:
  - Nephropathy affects most of the type 1 and type 2 diabetic patients.
  - The presence of nephropathy is indicated by **Microalbuminuria**.
  - **Proteinuria signifies the more severe renal damage**.
  - **Tight control of both glycemic levels and blood pressure reduces the risk of nephropathy**.

MICROVASCULAR DISEASES

- DIABETIC FOOT:
  - **Infected diabetic foot ulcers are the leading cause of amputations.**
  - There are three kinds of foot ulcers: Neuropathic, ischaemic and Neuroischaemic.
  - Neuropathic ulcers occur when peripheral neuropathy causes **loss of pain sensation**.
  - Ischaemic ulcers result from peripheral vascular disease and poor blood supply causing **reduction in available nutrients and oxygen required for healing**.

Why are doctors so concerned about your feet?

- **Foot problems can develop without your being aware of them.**
- **A foot problem can be very difficult to heal once it has set in.**

What type of problems occur?

- Pressure sores can develop on the soles of your feet from things such as **corns, or calluses** nails in your shoes.
- **Minor injuries such as cuts and splinters** can become a major problem through poor healing.
- Problems with **toenails such as *paronychia* (infection around the nail) and ingrowing nails** can get out of control.

What should the patient do?

1. Check your feet *daily*. Make sure you check between the toes.
2. Wash your feet daily with medicated soap:
3. Soften dry skin- especially around the heels- with lanoline.
4. Clip your toenails regularly in the right way.
5. Wear clean cotton or wool socks daily
6. Exercise your feet each day to help the circulation in them.
7. Avoid injury to your foot by not walking barefoot, especially out of doors.

Type 2 DM Treatment (Part Two)