Diabetes Mellitus

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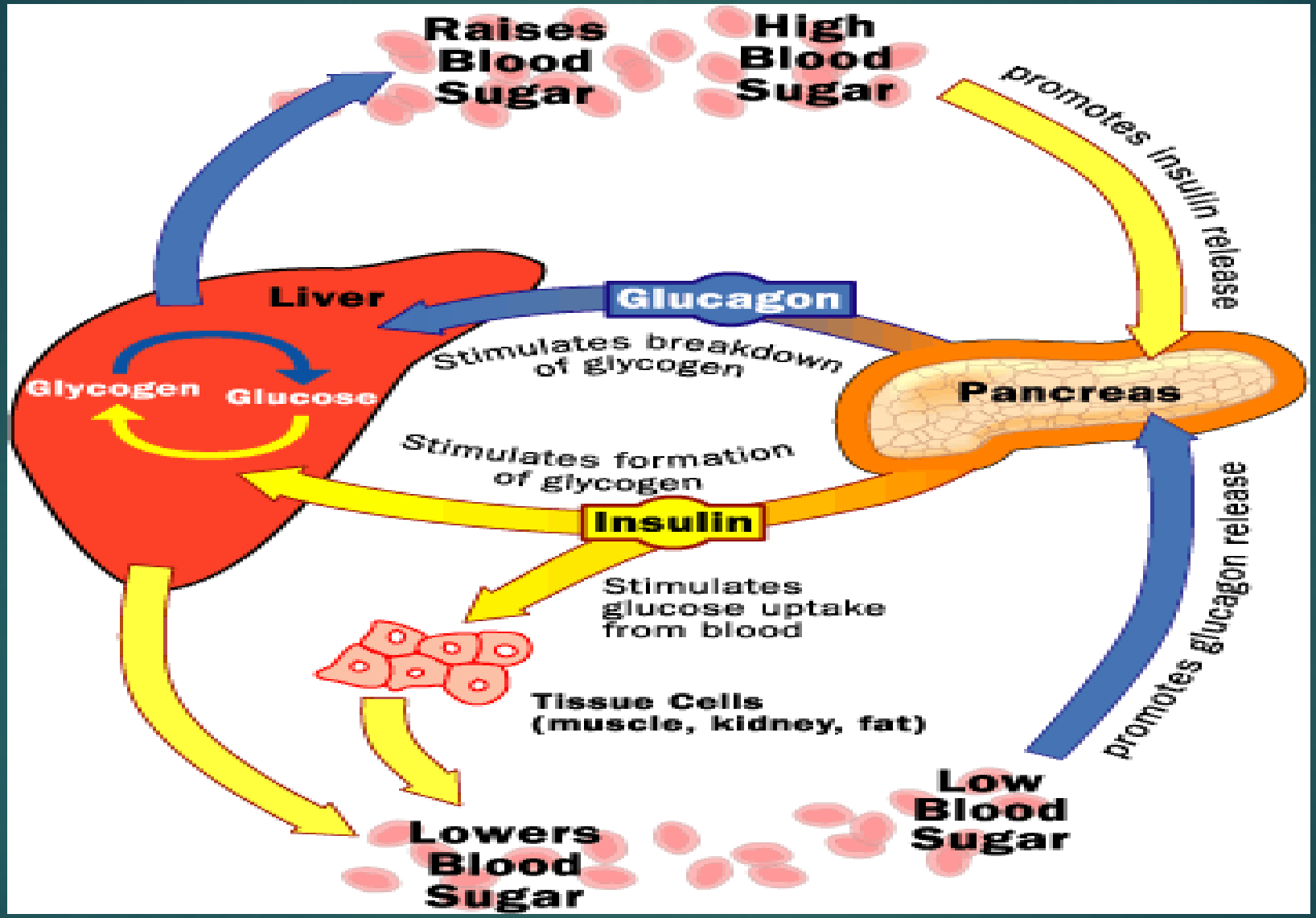
SVU


Raises Blood Sugar
High Blood Sugar
promotes insulin release
Liver
Glucagon
Glycogen
Glucose
Stimulates breakdown of glycogen
Pancreas
Stimulates formation of glycogen
Insulin
Stimulates glucose uptake from blood
Tissue Cells (muscle, kidney, fat)
promotes glucagon release
Low Blood Sugar
Lowers Blood Sugar

Diabetes mellitus

- Definition:
- It's a **clinical syndrome** in which there is an error of CHO metabolism ; due to insulin deficiency, resistance or both, ending in : chronic hyperglycemia ± glucosuria, vasculopathy & neuropathy.

Diagnostic criteria of diabetes mellitus (WHO)

- Symptoms:

(polyuria, polydipsia, weight loss, DKA, HHS) +

- Random blood glucose level ≥ 11.1 mmol/l (≥ 200 mg/dl)

or

- Fasting blood glucose level ≥ 7.0 mmol/l(≥ 126 mg/dl),(no caloric intake 8h)

or

- Post 2 hours blood glucose in OGTT ≥ 11.1 mmol/l (≥ 200 mg/dl)

or

- HbA1c ≥ 6.5 %

Oral glucose tolerance test : (OGTT)

- i. Patient should be fasting over night.
- ii. Fasting blood sugar is done.
- iii. The patient is fed 75 gm glucose orally.
- iv. Take blood & urine samples every 1/2 h. for 2 h.
- v. Normal curve : *3 criteria*
- 1) Fasting : 70-110 mg %
- 2) Reach maximal point in 1h. but still under 180 mg %
- 3) Return to normal within 2 h.

- 2 h. post-prandial : (*after ingestion of 75 gm glucose*).
- □ < 140 mg % → normal.
- □ > 200 mg % → DM.
- □ 140 - 200 mg % → impaired glucose tolerance (IGT)

Fasting blood glucose : (*no caloric intake for at least 8 hours*)

- □ 70 - 110 mg % → normal.
- □ > 126 mg % → DM.
- □ 110 - 126 mg % → impaired fasting glucose (IFG).

Stages of DM :

I. **Pre diabetes** : (*impaired glucose tolerance*)

a. It refers to a group of people who have glucose values too high to be considered normal but not fit the criteria for the diagnosis of DM (fasting blood glucose > 110 & < 126 mg%)

b. It's an intermediate category between normal & DM.

c. There is risk factor for future diabetes & CVS diseases.

d. This group includes :

i. +ve family history.

ii. obesity.

iii. ♀with bad obstetric history → macrosomia.

iv. renal glucosuria.

II. **Latent diabetes** :

Diabetes appears only on exposure to stress & disappears after removal of stress e.g. pregnancy.

III. Chemical diabetes : Raised blood glucose with no symptoms.

IV. **Clinical diabetes** :

a. ***Uncomplicated*** : Classic triad of symptoms : 3 **p**

- **p**olyuria : due to osmotic diuresis induced by sugar.
- **p**olydepsia : due to loss of fluid.
- **p**olyphagia with weight loss : ↓ insulin → no glucose can enter satiety center → ↑↑ of satiety center. While loss of weight is caused by fluid depletion , fat & muscle breakdown.

b. ***Complicated*** : May be the 1st presentation.

Classification of diabetes

1- Type 1 diabetes:

results from beta cell destruction, leading to absolute insulin deficiency

2- Type 2 diabetes:

results from a progressive insulin secretion defect on a background of impaired insulin function

3- Gestational diabetes mellitus (diagnosed during pregnancy)

4- Other specific types of diabetes:

a. Pancreatic causes e.g. Chronic pancreatitis .

b. Endocrinal : Cushing , Acromegaly , Thyrotoxicosis.

c. Drugs : Cortisone, Thiazide , Contraceptive pills.

d. Genetic.

Pathogenesis :

Type 1 : 10%.

- An autoimmune destruction of the pancreatic β-cells leads to absolute insulin deficiency.
- Genetic factor play an important role (*the combination of HLA**DR3*** *& **DR4** makes a person more likely to develop type 1 DM*)
- viral infection may play a role.
- without insulin, these patients are prone to develop ketoacidosis.
- Although typically diagnosed before age 30, it can present at any age due to variability in rate of β-cell destruction

Type 2 : 85%

- It's characterized by peripheral insulin resistance, so hyperglycemia develops despite above average level of insulin.
- In addition, it may be due to abnormal structure of insulin or due to anti-insulin hormones e.g. glucagons.
- Factors that may play a role in pathogenesis include : genetic predisposition & obesity.

	Type 1	Type 2
▪ **Incidence :**	10 %	85%
▪ **Pathogenesis :**	Insulin deficiency due to damage of β-cells.	Insulin resistance.
▪ **Insulin level :**	↓↓	Normal or even ↑↑
▪ **Age of onset :**	Younger (usually < 30y).	Older (usually > 30y).
▪ **Body weight :**	Thin.	Obese (usually 80 %).
▪ **Hereditary :**	- 30% in identical twins - usually no family history.	- Near 100% - strong family history.
▪ **C / P :**		
- **Severity :**	Sever.	Mild or moderate.
- **Ketoacidosis :**	Common.	Rare, need ppt factors.
- **Complication :**	More common.	Less common.
▪ **Treatment :**		
- **Oral hypoglycemic**	Ineffective.	Effective.
- **Insulin :**	Necessary (*essential for life*)	Usually not required

Gestational diabetes (GDM)

Diagnosed during pregnancy

- Test for undiagnosed DM at first prenatal visit in those with risk factors (HbA1c)
- Screen!: 24-28 weeks of gestation, 75 g OGTT
- Screen women with GDM for persistent diabetes 6-12 weeks postpartum

Diagnostic criteria for GDM One-step strategy

- 24-28 weeks, without previous DM diagnosis
- OGTT, 75 g, any of the following values
- FBG ≥ 5.3 mmol/l (95 mg/dl)
- 1 hour BG: ≥ 10.0 mmol/l (180 mg/dl)
- 2 hour BG: ≥ 8.5 mmol/l (153 mg/dl)

N.B:

TTT with insulin as most oral drugs are teratogenic

Complications of DM

- **Cutaneous :**

1. Infection : carbuncles & recurrent abscesses.
2. Pruritis : pruritis vulvae.
3. Delayed healing of the wounds.
4. Xanthelasma ; due to hyperlipidemia.
5. Cutaneous features of diabetic foot.
6. Acanthosis nigricans : black patches due to insulin spillover into the skin in type 2 DM.
7. Lipodystrophy : at the sites of insulin injection

- **Cardiovascular :**

1. Microangiopathy :

a) Diabetic retinopathy → retina. b) Diabetic nephropathy → glomeruli.

c) Diabetic neuropathy → vasa nervosa.

2. Macroangiopathy :

a) cerebral : thrombosis & ischemia.

b) coronary : angina & MI ,may be painless due to neuropathy

c) peripheral : gangrene & intermittent cludication.

d) renal : reno-vascular hypertension.

3. Cardiomyopathy : due to microangiopathy.

4. Blood pressure :

a) systemic hypertension.

b) postural hypotension due to autonomic neuropathy.

Chest :

1. Recurrent chest infection e.g. T.B. **(*T.B. follows DM as its shadow*)**.
2. Kussmaul respiration (*air hunger*) & acetone smell in DKA.

Gastrointestinal : *Diabetics **never** have normal bowel habits*

1. **Mouth** : gingivitis , loosening of teeth.
2. **Stomach** :

o gastroparesis .

o Nausea , vomiting & abdominal pain in DKA.

3. **Intestine** :

o Diarrhea : due to sympathetic neuropathy , vasculopathy& GIT infections.

o Constipation : due to vagal neuropathy.

4. **Liver** : fatty liver.
5. **Gall bladder** : chronic cholecystitis , gall stones.

- **Genital :**

1. In ♂ : impotence (*psychological, neuropathy, vasculopathy*)

2. In ♀ : infections & pruritis vulvae.3.

Effects of DM on pregnancy :

- On mother : i. Eclampsia. ii. post Partum hemorrhage. iii. puerperal sepsis.

- On fetus :iv. High birth weight. v. Hypoglycemic baby.

- vi. Congenital anomalies.

- **Eye :**1. **Lids** : infection (chalazion , conjunctivitis) , Xanthelasma.

2. **Iris** : New vessels formation in iris (rubeosis iridis)

3. **Lens** :

 Senile cataract (*occur at an earlier age*)

 Repeated error of refraction secondary to osmotic lens changes with fluctuating glucose level :

- Hyperglycemia leads to myopia.
- Hypoglycemia leads to hypermetropia.

4. **Nerves** :Optic neuritis , Cranial nerve palsy (3, 4 & 6 nerves).

5. ***Diabetic retinopathy***

Kidney(Diabetic nephropathy):

- Clinical picture :

i. Long standing DM especially poorly controlled diabetes after about 10-20 years .

ii. Proteinurea : *the early clinical sign of diabetic nephropathy*

1. micro-albuminuria : 30-300 mg/day It is reversible by **ACEIs** .
2. macro-proteinuria : > 300 mg/day
3. heavy proteinurea (nephrotic syndrome)

Nearly 100% with gross proteinuria will progress to End Stage CRF in 5 – 15 y

- **Diabetic foot :**

Definition : Trophic changes in foot of diabetic patients (ulcers, falling of hair & gangrene).

- **Etiology :** vasculopathy, neuropathy & infection combine to produce

tissue necrosis.

Neurological :

I. **Diabetic macroangiopathy :** (*due to atherosclerosis*)

a. Cerebral hemorrhage. b. Cerebral thrombosis.

II. Diabetic neuropathy : paraethesia followed by sensory loss

3. Autonomic neuropathy :

- **P**ostural hypotension.
- **P**ainless myocardial infarction.
- **P**ersistent tachycardia .
- Gastroparesis : delayed gastric empting.
- Diarrhea : severe, nocturnal & alternating with constipation.
- **I**mpotence.
- **I**ncontinence.

Diabetic comas :

1. Hypoglycemic coma. (insulin reaction)
2. Diabetic ketoacidosis. (DKA)
3. Hyperglycemic hyperosmolar non ketotic coma.
4. Diabetic lactic acidosis.

Treatment of DM :

I. General measures.

II. Diet.

III. Oral hypoglycemic.

IV. Insulin.

V. Treatment of complications

I. General measures :

a. Reassurance.

b. Education about nutrition & lifestyle modifications.

c. Exercise.

Diet :

a. Diet alone can control mild cases of type II D.M.

b. **Total calories/day :** *depending on weight & physical activity*

i. Mild activity → 1500 cal/d. ii. Moderate activity → 2500 cal/d.

iii. Severe activity & pregnancy → 3500 cal/d.

d. Food components :

i. CHO : 50% of calories . avoid simple sugars.

ii. fat : 30% of calories . avoid saturated fat.

iii. protein : 20% of calories.

iv. vitamins : B-complex & vit. A

v. ↑↑ fibers : ↑ satiety.

e. Number of meals :

3 main meals + 2 snacks in between, to avoid hyperglycemia or hypoglycemia .

III. Oral hypoglycemic

a. Sulphonylureas :

- mechanismof action :

1. ↑↑insulin secretion from pancreas.
2. ↑↑ peripheral action of insulin.
3. ↓↓ hepatic production of glucose.

e.g: glimipride(amaryl)

Gliclazide(diamicron)

Biguonides :

- Mechanism of action :

1. ↑ anaerobic glycolysis.

2. ↓↓ intestinal glucose absorption. 3. ↓↓ appetite.

- preparations : Metformin *(Cidophage)* 500 - 850 mg t.d.s.

- Indications :

1. type 2 DM not controlled by diet alone esp. in obese patients.

2. combined with suphonylurea or insulin to achieve control.

- Side effects :

- GIT irritation. - lactic acidosis

Recent drugs :

i. **Alpha Glucosidase inhibitors** : Acarbose *(Glucobay)* 50 mg t.d.s.

prevent breakdown of CHO in intestine ↓glucose absorption.

ii. **Pioglitazone** (*Diabetin*) : ↑tissue sensitivity to insulin (*insulin sensitizer*

- DDP-4 inhibitors
- GLP-1 agonists
- SGLT2 inhibitors

Insulin

- **Indications :**

i. All type 1 DM.

ii. Type 2 DM not controlled with diet & oral hypoglycemic.

iii. During pregnancy, infection & surgery.

iv. DKA & HHNK .

v. ↑↑ K (Hyperkalemia)

- **Administration** :

i. S.C.

ii. Insulin pump (**C**ontinuous **S**.C **I**nsulin **I**nfusion , CSII) .

iii. IV infusion or IM : in case of DKA , HHNK

iv. Insulin pens.

v. Oral , nasal → under trial

- Forms:
- -Rapid acting
- -short acting
- -intermediate
- -Long acting
- Regimens:
- Pre meal (before every meal; short acting)
- Premixed)=(2/3 morning---1/3 evening)
- Basal insulin (long acting)

- Side effects :

i. Hypoglycemia & hypoglycemic coma.

ii. Allergy : use human insulin.

iii. Insulin resistance :

o obesity → mild resistance.

o antibodies against insulin.

iv. Insulin lipodystrophy : atrophy or hypertrophy of s.c. fat at the site of insulin injections.

v. Insulin edema : Na & H2O retention Hypertension.

vi. Weight gain.

TTT of complications:

- Complications as described before
- The most important is: Diabetic ketoacidosis " DKA

Definition :

- DKA is an extremely serious metabolic complication of DM due to **sever** insulin deficiency, it's characterized by triad of :
- - Acidosis. - Ketosis. - Hyperglycemia (usually >250 mg %

c. **Pathogenesis & C/P** : sever insulin deficiency leads to :

i. **Glucose can't enter the cells** → hyperglycemia > 250 mg %.

ii. **Fat :** ↑↑ **lipolysis** to produce energy → ↑ production of ketone bodies (β-hydroxy buteric acid, acetoacetic acid & acetone) → ketoacidosis (PH < 7.3)

iii. **Effects of ketoacidosis** : 1- Muscles : a. generalized weakness. b. muscle pain.

2- Kidney:ketonuria together with glucosuria lead to severe polyuria & dehydration.

3- GIT :a. Anorexia , nausea & vomiting. b. **abdominal pain**.

4- Respiration :a. Kussmaul respiration (deep rapid) b. acetone odour of breath.

5- CVS :a. depressed contractility & low blood pressure. b. rapid weak pulse.

iv. **Hyperkalemia** due to Shift of K outside cells in absence of insulin.

v. **Coma** due to combined effect of :

1. ketone bodies. . dehydration. 3. electrolyte disturbance.

d. Investigations :

i. **Blood examination** : o ↑ glucose > 250 mg %. ↑ ketone bodies. Acidosis (PH < 7.3) with high anion gap. ↑ FFA. o Electrolytes : ↑↑ **K** & ↓↓ Na .

ii. **Urine examination** : Polyuria , glucosuria & ketonuria

- Treatment :
- **i. Insulin :**
- short acting soluble insulin.
- Regimen : *2 methods*
- a. IV insulin infusion : 5 – 10 u/ h infusion . when blood glucose < 250 mg /dl → reduce insulin to 2 – 4 u/h
- b. Repeated IM : 20 U at the start then 6 U/ h
- The goal is to decrease the blood glucose by 75mg % / hour.
- **ii. Fluid therapy :**
- 4 – 8 L is usually required.
- 1 L / hour for the first 2 hours followed by 1/2 L / hour until the deficit is replaced.
- At first normal saline is given, then change to dextrose saline when blood glucose < 250 mg/dl.
- iii. **K therapy :**
- The serum K falls during insulin therapy (*intracellular shift*), and this fall may be dramatic. so add (20 – 40 mEq) to each 1L saline.
- iv. **Na bicarbonate :** in sever acidosis [PH < 7.1]
- v. **Treatment of precipitating factors** e.g. infection : antibiotics

- Q : criteria for good diabetic control ?
- **Lab. :**
- - Fasting plasma glucose (90 - 130) mg/dl
- - Post prandial plasma glucose : < 180 mg/dl.
- - HbA1c < 7%.
- **Clinical :**
- - No symptoms of DM : .....

Thank you