C) On fats:

1.↓ lipolysis in fat cells by inhibiting hormone - sensitive (intracellular) lipase enzyme →↓FFAs mobilization to blood.

2.↑ lipogenesis:

Converts glucose →→ fats mainly in adipose tissue.

Insulin + lipoprotein lipase are complementary.

Insulin ↑fat synthesis (from glucose) in liver and ↑blood triglycerides & cholesterol levels. Then lipoprotein lipase (in capillaries) → conversion of triglycerides in lipoprotein to free fatty acids → circulation → export of triglycerides (via VLDL) to adipose tissue. More in metabolic syndrome.

3.↓ formation & ↑ uptake of ketone bodies.

In fed state insulin release ↑glycolysis, glycogenesis & lipogenesis.

In fasting: ↑growth h., glucagon & epinephrine →↑fatty acids oxidation (→ fewer free radicals → antioxidant & anti-inflammatory), ↓glucose oxidation & ↑gluconeogenesis → preserve glucose for brain.

D) Vascular insulin actions: ↑NO, VD, ↓vascular smooth m. proliferation, ↑microvascular blood flow & ↓platelet aggregation.

Antagonizes renin angiotensin actions which → opposite…..& ↓glucose uptake.

- A, B & C : metabolic.
- D : vascular.

Control of insulin release

Normally 50% of daily insulin is basal & 50% PP.

Insulin daily requirements: 0.5- 1 u/Kg. ↑in puberty, pregnancy & medical diseases.

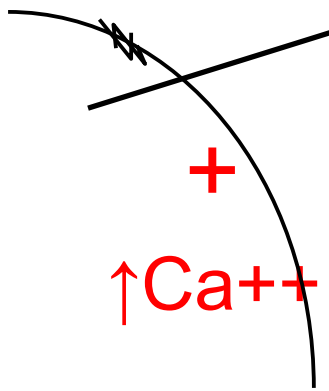
Increase by

1. Glucose → ↑ATP → closure of ATP- sensitive K+ channels → depolarization → opening of voltage dependent Ca++ channels → ↑Ca++ influx → release of stored insulin (rapid) followed by slow release (newly formed insulin).

The 1st phase (& later phase 2) is impaired in T2DM, both in T1DM.

Amino acids & free fatty acids augment glucose – induced insulin release.

Insulinogenic: carbs > proteins > fats.



Control of insulin releas

احنا قلنا إنه الـ insulin ← receptor و ← diabetes

طبيب إذا زاد الـ insulin برضو مش كويس

وزنه الـ insulin هو anabolic بخلي metabolic ↑ و بصير obisty

في DM1 المشكلة عندنا هي نقص الـ insulin فـ العشاكل اللي فوق كلها ما رح تصير

لكن DM-2 ← اللي هو اصلا ٩٠٪ من الـ diabetes بتكون مشكلته بالـ receptor.

ومشكلة الـ receptor بتبدأ في metabolic syndrom

↳ receptor number ↓ → insulin action try to ↑ → metabolic syndrome happend → obisty + ↑ fat in Liver & circulation

metabolic syndrom + ↑ insulin action → may end by a cancer

increased by:

.2. Sulfonylurea: by closing ATP- sensitive K+ channels

3. - 10...

- عكس ↓ بالسلايد الي قبل

Decrease by:

hypokalemia the most ion that cause hyperglycemia

1. Hypokalemia by e.g. thiazides, loop diuretics & diazoxide. They are K+ channel openers, increasing K+ efflux → hyperpolarization.....

used also in hypertesive crisis

Types of Diabetes Mellitus

multiple manifestation

It is a syndrome characterized by disturbance in carbohydrate, protein & fat metabolism beside vascular complications.

Manifested by polyuria, polydepsia, polyphagia, ↑ or ↓body wt. &....

Clinical in 16% of population (diagnosed in 8%).

40%/50% according to life time prevelance

How know have diabetese

75% of inpatients are diabetics.

B) Secondary diabetes: by endocrine diseases causing hyperglycemia as Cushing disease, acromegaly, pheochromocytoma and by hyperglycemic drugs **(type 3)**. Gestational (pregnancy) diabetes is **type 4**. In 5-10% of pregnant. 30 - 60 %→ T2DM.

DM-2→ receptor-dependant

DM-1→ insulin not Found not have anabolic action

A) Primary: → type (1&2) of DM

	Type 1 DM (IDDM)	Type 2DM (NIDDM)
	Insulin dependent	**Insulin receptors dependent**
Age:	Young (<30 years)	Adult (>40 years)
	At 1-2 & 17 years in 75%.	Now…..younger.
%	< 10%	> 90%
Symptoms:	Appear rapidly, with marked hyperglycemia.	Slowly, with mild or mod. hyperglycemia.
Ketosis:	Common	Rare (insulin is enough to prevent ketosis but not hyperglycemia)
Obesity:	Not common (thin) due to ↓insulin (anabolic)	Common (the anabolic insulin is present)
Insulin	↓	Variable (↑ then↓)
ttt.	Insulin	Oral antidiabetics
Family hist.	Not common (10%)	Common

manly dont have insulin → for young → have distruction of pancreas

→ it link to metabolic syndrom

يجيه إذا كان ناصح و تخاف عليه لسا بمرحلة receptor-dependant يمكن يربحها بس ينحف لكن اذا كان نحيف صار insulin-dependant نتيجة exhaustion of pancreatic cell

insulin hormone الزلمة حكينا عنه

والجسم عنا ٩٠٪ reserve و بظل يطلع insulin زيادة و هون عنا hyperinsulinemia لكن ما عنا hyperglycemia لانه الـ insulin اللي زاد بكون compasatory للنقص و بشتغل اد ٩٠٪ و لما الـ insulin يخلص رح يصير عند الشخص diapetis و بعدين hyperglycemia

T1DM

Type Ia: >95%. Autoimmune.

Viral infection of β-cells in genetically predisposed pts. → mild hyperglycemia → healing & recovery (honey moon period) → autoimmune reactions → destruction of these cells (>90% at diagnosis) → severe hyperglycemia.

Contribution is genetic (1/3) in pts. with HLA-DR3 & 4 (regulate immune response) and environmental (by viruses).

Screening done at time of diagnosis shows high circulating levels of antibodies to insulin and components of insulin receptors .

Type Ib: <5%. Idiopathic.

T2DM

A) Hereditary. Contribution is mainly genetic (strong). Mainly in 1st degree family history relatives (parents & siblings).

need to see what ↓ receptor of insuline

B) Environmental:

1. Obesity. Mainly visceral (metabolic) obesity more than SC abdominal fat due to its link with insulin resistance.

2. ↑diet sugars & other Food with high glycemic or insulin index.

pepsi

3. Lack of exercise.

4. Emotions. stress → depression, anixity, happy → cause releas of hormone → all of are hyperglycemic ex. insulin

5. Periodontitis, intestinal dysbiosis and vitamin & mineral deficiency.

inflammation of teeth

Insulin resistance (receptor or post-receptor defect) →

IRS / adaptor protein

1. ↑insulin release.

2 .↓insulin release by exhaustion of β-cells (2ry failure).

insuline

oral antidiaptic

Metabolic syndrome

(insulin resistance syndrome, X syndrome)

Most important factor in development of T2DM.

Very common, with many associations:

1. ↑body wt .
2. ↑BP.
3. ↑plasma lipids .
4. ↑plasma insulin then glucose.
5. ↑prothrombotic & proinflammatory state (↑CRP), thrombophilia & oxidative stress. Astherosclerosis. → thrombosis
6. ↑uric acid. → Gout
7. Fatty liver. NAFLD is better predictor of cardiovascular disease & mortality. Also cholecystitis & gall stones. ↑GGT. → biological marker of metabolic syndrom → GGT
8. Polycystic ovary syndrome. 20% of female in 12-20 years
9. Rheumatoid arthritis.

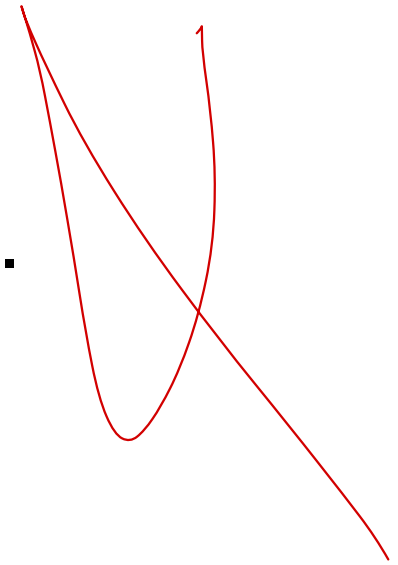
Causes of metabolic syndrome:

1. Life style….
2. Periodontitis:

Bidirectional relationship between periodontitis & DM.

Predictor of mortality.

3. Intestinal dysbiosis:
4. Deficiency of Mg, K, vit. D, omega 3 fatty acids, ….



Insulin resistance ttt.:

1. Life style modification of diabetics…….
2. Metformin.
3. Pioglitazone (insulin sensitizer).
4. ACEIs & ARBs:

Stages of diabetes – induced metabolic syndrome

A. Impaired glucose tolerance (prediabetes): 10 years, with complications.

B. Metabolic diabetes: Hyperglycemia.

Hypoglycemia → many complications as cardiovascular & ↑mortality.

Brittle diabetes is that with unstable blood glucose levels (marked fluctuations). Food →marked hyperglycemia. Normally this is compensated by ↑insulin release → ↑glycogen storage & ↑ glucose uptake & utilization. ↓insulin activity in diabetics reduces glycogen storage & ↓ glucose uptake & utilization. Fasting → hypoglycemia because low glycogen stores cannot supply enough glucose by ↑glycogenolysis induced by other hormones.

actual age

C. Vascular diabetes: Microvascular (& macrovascular) complications (we are as old as our arteries, carotid intima media thickness).

test for artery → ↑thick → accumulation of lipid

Tight glycemic control improves micro & not macroangiopathy.

less age → vascular complication

في علاقة ما بين GH & insulin

↓1% HbA1c → ↓microvascular complications by 40% & mortality by15%.

D. Cancer: By ↓immunity, ↑insulin→ ↑growth..., cancer cells need glucose.

because in DM → ↓protein + ↑ of gln → ↓ nutrition of Bacteria → ↓ immunity

in metabolic syndrom ↑ insulin to compansate ↓insulin receptor → ↑growth of tumar cell

Ⓐ impaired Glucose tolerance → blood Glu stil in border line
not normal or very high (prediabetes)

بعني بقله الدكتور & مصابح استنا جوي → هون طبعا الدكتور خيبان

و اذا سمع كلامه من وقتها لـ ١٥ سنين بالكثير بيكون اجا مضاعفات

↳ not come only in diapetise → also begin in prediabetic

→ then diapetis come to this pateint

Ⓑ Metabolic diabetes → hyperglycemia

hyperglycem ⇐ eat ⇐ يلا بينا نتخيل .. النهاردة اتسدرنا

⇓

Insulin release

(good test is P.P glucose level)

بكرا بيني العكس (وقت الصيام)

الانسولين كله طلع وما ضل عندي اصلا ⇐ stored ⇐ فانا يكون بحاجة لغلوكوز بس ما تخزن علا يكون في حتى يتحول لغلوكوز فما في عنا glucose لعشان هيك بتلاحظ انه عند DM اول ما يوكلوا ع بيصير على طول لانه ما عنده hyperglycemia و نفس الاشي لما يكون ع insulin ع يجي نوعه hypo لانه ما في مخزن غلوكوز على شكل غلايكوجين

فلهذا هيك بلاحظ انه مريض DM يكون عنده fluctuted في blood.G ... fast ⇐ hypo

hyper ⇐ eater

⟹ Brittle diabits (sever flacuted)

ولابد احسن flacuted اشي

ويزود complicatio والاصل يكون عنا stable ⇐