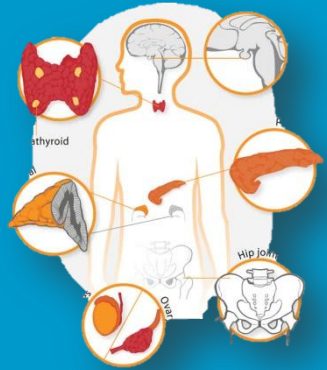


[lecture 10]

Metabolic Syndrome



Endocrine system



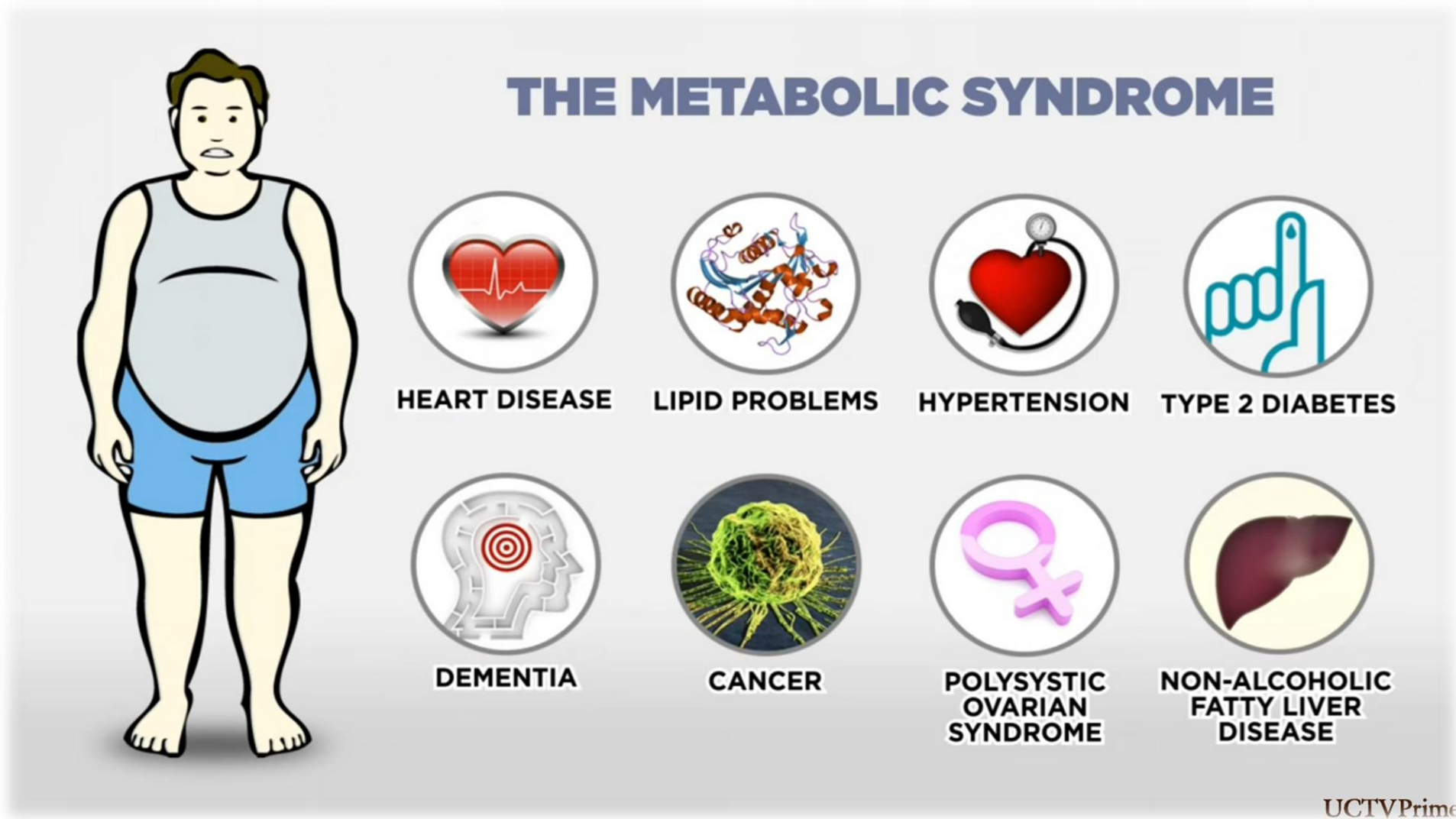
The Objectives

Not given 😞

Red =
Important

Blue =
explain

Green =
addition
notes



Metabolic Syndrome

Metabolic Changes Observed in Obesity:

The metabolic abnormalities of obesity reflect molecular signals originating from the increased mass of adipocytes

The predominant effects of obesity include-

- ★ dyslipidemias
- ★ glucose intolerance
- ★ and insulin resistance
- ★ hypertension

Metabolic Syndrome

★ A cluster of closely related medical conditions which increase the risk of developing heart disease and diabetes

★ Features comprising Metabolic Syndrome

- Obesity (specifically visceral)
- High serum TGs
- Low HDL cholesterol
- Hypertension
- Hyperglycemia
- Hyperinsulinemia (insulin resistance)

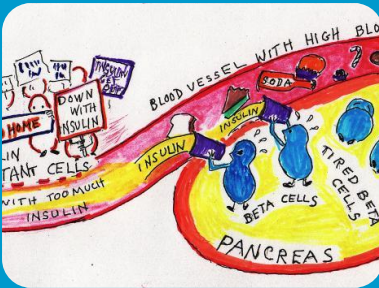
Effects of Insulin Resistance



Hydrolysis of stored TGs or fats, leading to elevation of plasma FFA



Reduction of glucose uptake or glucose utilization among muscle cells and reduction of glycogenesis- both lead to hyperglycemia



Compensatory hyperinsulinemia causes down regulation of insulin receptors



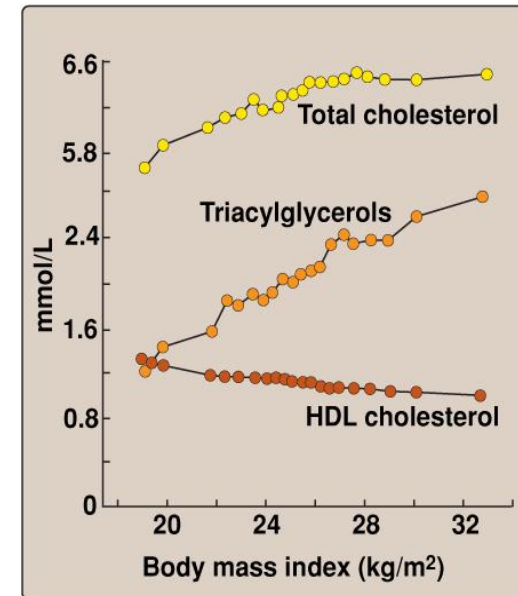
Dyslipidemia

- **Insulin resistance in obese individuals leads to**
 - ⌘ increased production of insulin in an effort by the body to maintain blood glucose levels
 - ⌘ causes increased activity of hormone-sensitive lipase, resulting in increased levels of circulating fatty acids
- These fatty acids are carried to the liver and converted to **TGs and cholesterol**
- Excess TGs and cholesterol are released **as VLDL**, resulting in elevated serum triacylglycerols
- Concomitantly, **HDL levels are decreased**.

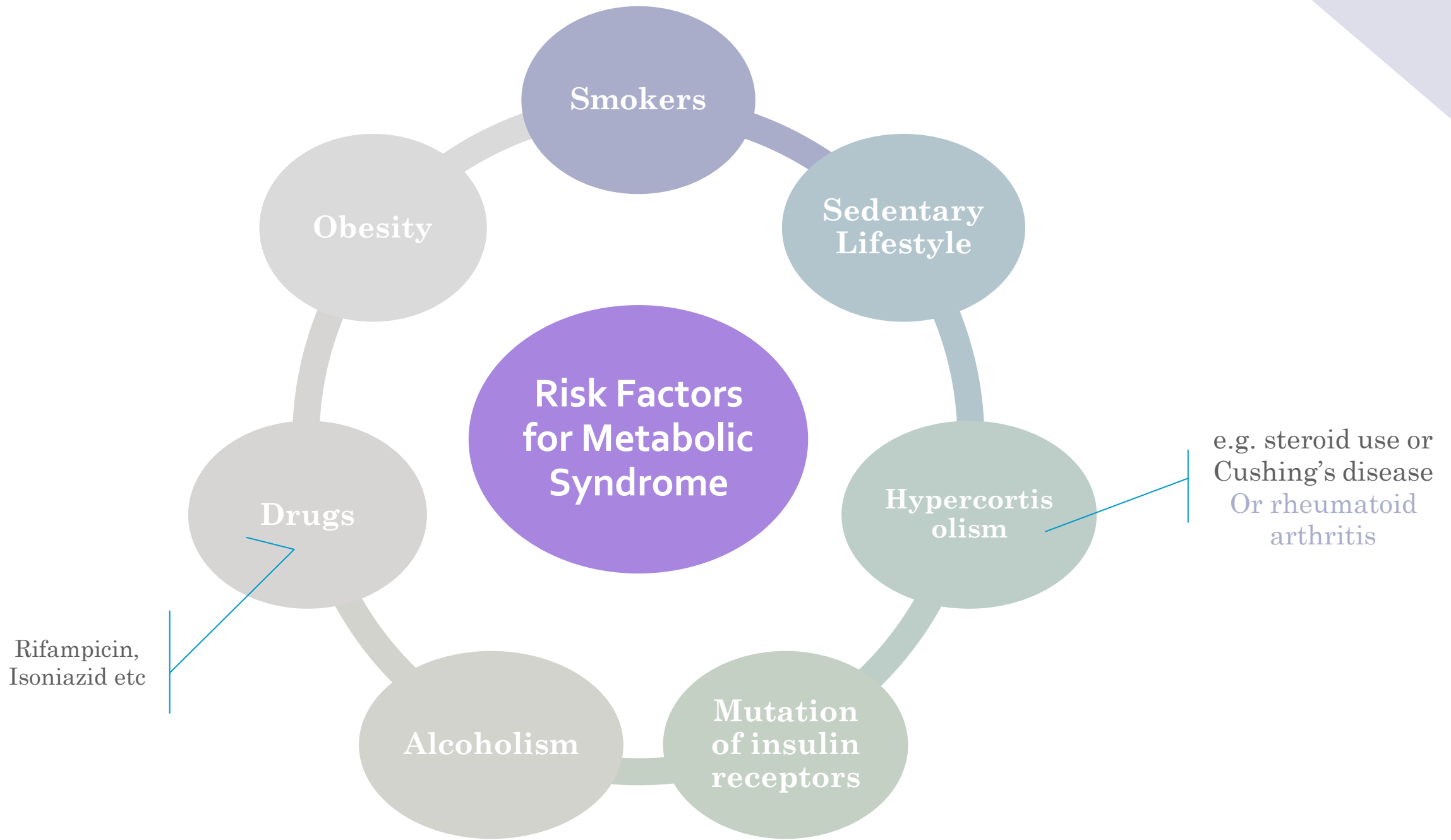
Dyslipidemia and the Metabolic Syndrome an inseparable couple?

- ⌘ Dyslipidemia is an early and consistent component of insulin resistance
- ⌘ Liver fat seems to be the unifying factor between dyslipidemia and insulin resistance

- metabolically healthy obese individuals: obese people who live without the increased risk of health complications that are typically associated with obesity like HTN .
- Normal weight obesity: means you may have the same serious health risks as does someone who's obese.



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Metabolic Syndrome is Linked to:

Med432 Biochemistry Team

Heart disease

- 1.5 - 3 fold increase for atherosclerotic CVD

Type 2 Diabetes Mellitus

- 5 fold increase

Kidney disease

Reproductive abnormalities in women

- PCOS “polycystic ovary syndrome”, difficulty with ovulation and fertility, irregular periods

Nonalcoholic steatohepatitis (fatty liver)

- Related to distorted lipid metabolism

Cancer

- Obesity is major risk factor for cancer of the esophagus; colon and rectum; liver; gall bladder etc
- Being overweight and obese accounts for 14% of all cancer deaths in men and 20% of those in women



Obesity is chronic inflammation
During inflammation free radical
are made.
Free radical can lead the cells to
become cancerous
Because they affect cell's DNA and
make them malignant

DIAGNOSIS – WHO CRITERIA (1999)

- ◆ Impaired glucose tolerance; DM or insulin resistance ; along with at least two of the below mentioned components:

Component	Criterion
Hypertension	BP >140/90 mmHg
Dyslipidemia	High plasma TGs (>1.7mmol/L) Low HDL cholesterol (men <0.9, women <1.0 mmol/L)
Central or Genenral obesity	Waist to hip ratio >0.9 in men, >0.85 in women And/or BMI >30
Microalbuminuria	Urinary albumin excretion rate \geq 20ug/min or albumin:creatinine ratio \geq 30mg/g

Managing Metabolic Syndrome

Markers!

- ★ Lipoproteins- LDL, HDL
 - ★ Adipokines-
 - Leptin
 - Adiponectin
 - ★ Inflammatory markers- CRP, TNF-a, IL-6, IL-8
- Because obesity is a low grade chronic state
- ★ Hemostatic marker – Plasminogen Activator inhibitor-1
- Inhibit fibrinolysis : some people have thrombosis

1

Primary intervention

- ★ Lifestyle changes
 - ★ Weight reduction (strive for BMI less than 25)
 - Reduced caloric intake and dietary fat
 - Increased physical activity
 - Set realistic goals: 5-10% weight loss from baseline
 - ★ Smoking cessation

2

Secondary intervention

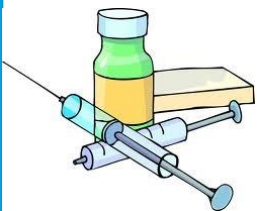
- ★ Pharmacotherapy (for existing risk factors)
 - ★ Management of
 - blood pressure (anti-hypertensives)
 - Lipids (statins, fibrates)
 - Blood glucose (metformin, TZDs)
 - ★ Aspirin for CVD prevention

Modification	Recommendation	Average drop on SBP
Weight Loss	Maintain normal body weight	5-10 for every 22lbs loss
Healthy eating plan	Meal plan rich in fruits, vegetables, low fat dairy and low in saturated fat and cholesterol	8-14
Sodium Restriction	Less than 2400 mg/day	2-8
Regular physical activity	30 min most days of the week	4-9

SBP : systolic blood pressure

Hypertension and clotting disorders

- * Treat hypertension to goal (<130/80 mmHg)
- * Low dose diuretic
- * ACE inhibitor (if also have DM)
- * No particular agent is preferred for metabolic syndrome
- * Aspirin- to treat clotting disorders
 - Daily low dose aspirin (81-325mg) for men over age 45 and postmenopausal women



Metformins	Fibrates	Thiazolidinediones (TZDs)
<ul style="list-style-type: none"> ⌘ Metformin reduces blood glucose levels by inhibiting hepatic gluconeogenesis <ul style="list-style-type: none"> ▪ Hepatic gluconeogenesis is active in patients due to liver's resistance to the effects of insulin ⌘ Metformin also reduces lipid synthesis in the liver which aids in modulating blood lipid levels in these patients 	<ul style="list-style-type: none"> ⌘ Used to reduce the lipid levels ⌘ Target for fibrates is a transcription factor- peroxisome proliferator activated receptor- αPPAR- when activated, leads to the transcription of genes involved in lipid degradation, or uptake by the cells. E.g. <ul style="list-style-type: none"> • Carnitine: palmitoyl transferase I- enhances the uptake of FA into the mitochondria • Lipoprotein Lipase • Stimulates apoAI and apoAII protein synthesis (major proteins in HDL) 	<ul style="list-style-type: none"> ⌘ Used for the treatment of insulin resistance and type 2 diabetes mellitus e.g. pioglitazone ⌘ TZDs activate PPAR-γ class of transcription factors expressed primarily in the adipose tissue ⌘ Activates the transcription of adiponectin ⌘ The increase in adiponectin reduces the fat content of the liver and enhances insulin sensitivity

summary

Metabolic Syndrome :

A cluster of closely related medical conditions which increase the risk of developing heart disease and diabetes.

Managing Metabolic Syndrome by:

Primary intervention (life style)

Secondary intervention (pharmacotherapy)

Metformins: reduces blood glucose levels and lipid synthesis.

Fibrates: -reduce the lipid levels
-the target for fibrates is a transcription factor peroxisome proliferator activated receptor **PPAR- α** .

Thiazolidinediones (TZDs): -Used for the treatment of insulin resistance and type 2 diabetes mellitus e.g. pioglitazone.
-activate **PPAR- γ** .

Test your knowledge ...!

1)_Target for fibrates is :

- A. PPAR- α
- B. PPAR- γ
- C. PPAR-d

2)-We used **Metformins** to treat patient with metabolic syndrom because it is :

- A. inhibiting hepatic gluconeogenesis
- B. reduce the lipid levels
- C. reduces blood glucose levels& reduces lipid synthesis

3)-Which one is marker for **Metabolic Syndrome**:

- A. Increase LDL
- B. Increase HDL
- C. Decrease leptin



If you find any mistake, please contact us =>
Biochemistryteam@gmail.com

Biochemistry team leaders:
Basil AlSuwaine & Manar AlEid

THANK YOU

