METABOLIC SYNDROME

OBJECTIVES:
- ➤ 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

❖ **Important**　　❖ Extra　　❖ **Biochemistry Edit**

ENDOCRINE BLOCK

METABOLIC SYNDROME

Metabolic Syndrome : A combination of metabolic abnormalities which increase the risk of **heart disease, diabetes and other diseases.**

➢ **Obesity is a component of metabolic syndrome**

➢ **Signals from adipocytes in obesity cause metabolic abnormalities such as:**

- ❖Dyslipidemia
- ❖Glucose intolerance
- ❖Insulin resistance
- ❖Hypertension

- Dyslipidemia is an early indicator of insulin resistance

-Liver fat plays a major role in dyslipidemia due to insulin resistance[1]

Features of metabolic syndrome:

- ✓ Obesity
- ✓ High serum triglycerides (TGs)
- ✓ Low HDL cholesterol
- ✓ Hypertension
- ✓ Hyperglycemia
- ✓ Insulin resistance (hyperinsulinemia)

1.Because proinflammtory cytokines produced by adipocytes will go from the portal vein to the liver>>decrease insulin senstivty+increase TAG synthasis>>VLDL release.

METABOLIC ABNORMALITIES

❖ Insulin resistance

- Cells become <u>less</u> <u>responsive</u> <u>to</u> <u>insulin</u> → high plasma insulin → hyperglycemia
- <u>Hydrolysis</u> <u>of</u> stored <u>fats</u> → high plasma FFAs
- <u>Reduction</u> of <u>glucose</u> <u>uptake/use</u> by cells Reduction of <u>glycogenesis</u> →
- <u>hyperglycemia</u>
- Compensatory <u>hyperinsulinemia</u> causes down regulation of insulin receptor
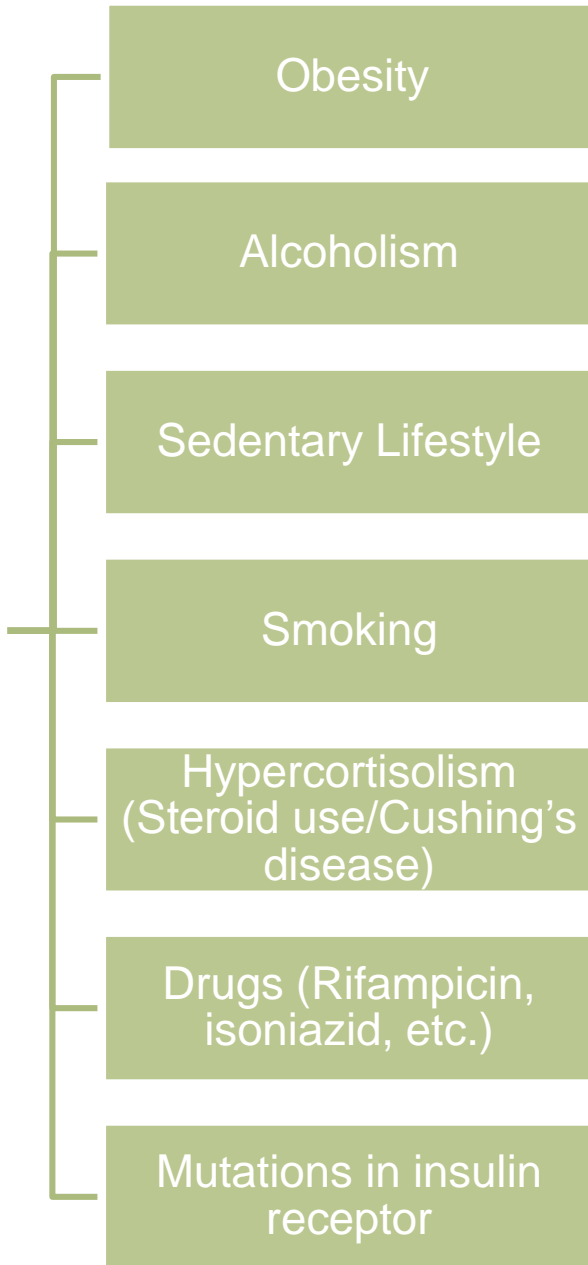- <u>Defects</u> in insulin <u>receptor</u>.

❖ Dyslipidemia

- ➢ Insulin resistance in adipocytes → increased activity of hormone-sensitive lipase → high plasma FFAs
- ➢ FFAs → TGs/cholesterol in the liver
- ➢ Excess TGs/cholesterol are released as VLDL in the blood.

- HDL levels are decreased
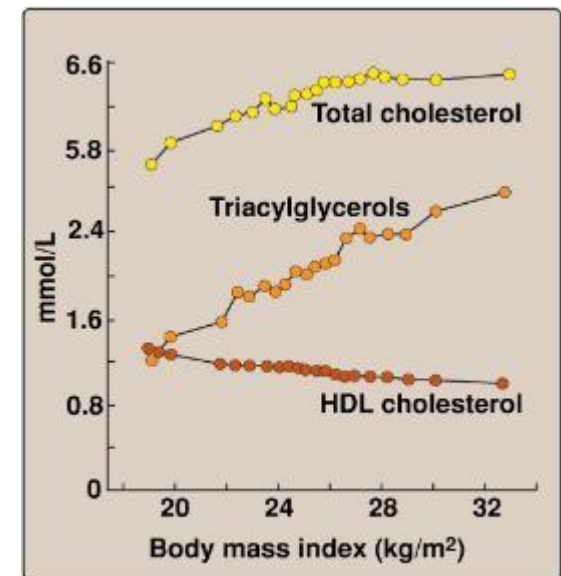
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Risk factors for metabolic syndrome

- Obesity
- Alcoholism
- Sedentary Lifestyle
- Smoking
- Hypercortisolism (Steroid use/Cushing's disease)
- Drugs (Rifampicin, isoniazid, etc.)
- Mutations in insulin receptor

Metabolic syndrome is linked to:

A) Heart diseases
1 .5-3 fold increase in atherosclerosis

B) Type-2 diabetes mellitus
5-fold increase

C) Kidney disease

D) Reproductive abnormalities in women
- ✓ Polycystic ovarian syndrome[1]
- ✓ Impaired ovulation and fertility
- ✓ Irregular menstruation

E) Nonalcoholic steatohepatitis (fatty liver disease) Related to impaired lipid metabolism

F) Cancer
-Obesity is a major risk factor for cancer of esophagus, colon and rectum, liver, gall bladder
-Being overweight and obese accounts for 14% of all cancer deaths in men and 20% of those in women

1.Polycystic ovary syndrome (PCOS) is the most common cause of infertility in women, is characterized by ovulatory dysfunction and hyperandrogenism.

DIAGNOSIS

❖ WHO Criteria 1999

✓ Impaired glucose tolerance

✓ Diabetes mellitus

✓ Insulin resistance

PLUS any of these two

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 General obesity	Waist to hip ratio >0.9 in men, >0.85 in women And/or BMI >30
Microalbuminuria	Urinary albumin excretion rate ≥ 20ug/min or albumin:creatinine ratio ≥ 30mg/g

❖ NCEP[1] ATP[2] III Guideline (2002)

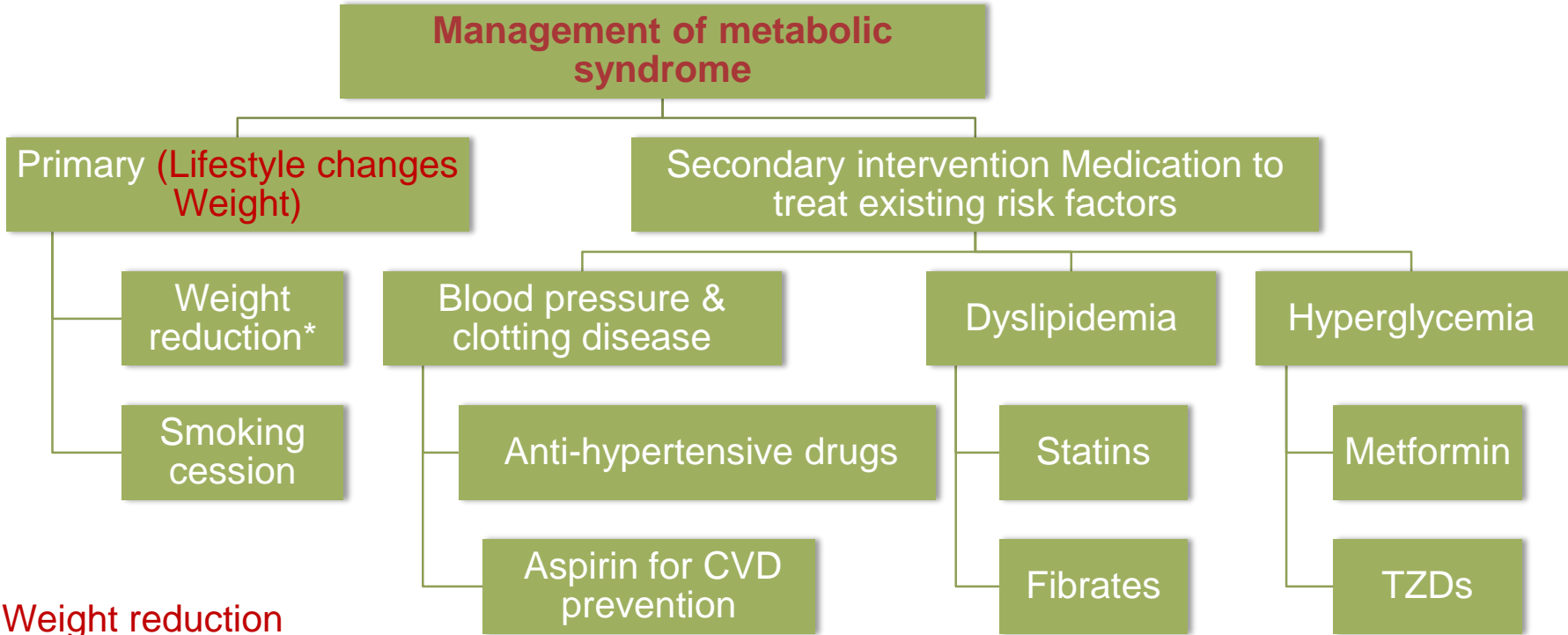❑ Diagnosis: If <u>any 3 or more</u> of these risk factors are present:
✓ Waist circumference:
   Men >102 cm (>40 in)
   Women >88 cm (>35 in)
✓ Triglycerides >150 mg/dL
✓ HDL cholesterol:
   Men <40 mg/dL
   Women <50 mg/dL
✓ Blood pressure 130/ 85 mm Hg
✓ Fasting glucose >100 mg/dL

1.NCEP: National Cholesterol Education Program
2.ATP: Adult Treatment Panel

❖ Markers of metabolic syndrome

- ➢ Lipoproteins (LDL, HDL)
- ➢ Adipokines (Leptin, adiponectin)
- ➢ Inflammatory markers
  - ✓ c-reactive protein, TNF-a, IL-6, IL-8
- ➢ Hemostatic marker
  - ✓ Plasminogen activator inhibitor-1

Management of metabolic syndrome

Primary (Lifestyle changes Weight)

Secondary intervention Medication to treat existing risk factors

Weight reduction*

Smoking cession

Blood pressure & clotting disease

Anti-hypertensive drugs

Aspirin for CVD prevention

Dyslipidemia

Statins

Fibrates

Hyperglycemia

Metformin

TZDs

*Weight reduction
- ✓ Target BMI < 25
- ✓ Reduced intake of calories and fats
- ✓ More physical activity

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HYPERTENSION AND CLOTTING DISORDERS

LIFE STYLE MODIFICATIONS AND THEIR IMPACT ON LOWERING BP

Modification	Recommendation	Average drop in SBP
Weight loss	Maintain normal body weight	5-10 for every 22lbs loss
Healthy eating plan	Meals rich in fruits, vegetables; low fat dairy; low saturated fats and cholesterol	8-14
Sodium restriction	< 2400 mg/day	2-8
Regular physical activity	30 min. most of the week	4-9

1) Treat hypertension to goal (< 130/80 mmHg)   **2) Low dose diuretics**

3) ACE inhibitor

4) Aspirin:

❖ To treat clotting disorders
❖ Daily low dose aspirin (81-325mg) for: (Men > 45 + Postmenopausal women)

❖ DYSLIPIDEMIA

- Fibrates

- **Reduce blood lipid levels**
- **Activate transcription factor:**
  - ❖ Peroxisome proliferator activated receptor-α (PPAR-α)
- **Activated PPAR- α → transcription of genes of lipid degradation / uptake by the cells:**
  - ❖ Carnitine:palmitoyl transferase I (enhances FA uptake into mitochondria)
  - ❖ Lipoprotein Lipase
  - ❖ Stimulates apoAI and apoAII protein synthesis (major proteins in HDL)

❖ HYPERGLYCEMIA

1) Metformin
- Reduces blood glucose levels by inhibiting hepatic gluconeogenesis
  - ❖ Hepatic gluconeogenesis is active in patients due to liver's resistance to the effects of insulin
- Reduces lipid synthesis in the liver
- Helps reducing blood lipids
2) Thiazolidinediones (TZDs)
- Used for the treatment of insulin resistance and type-2 diabetes mellitus
- TZDs activate PPAR-γ class of transcription factors expressed primarily in the adipose tissue
- Activates the transcription of adiponectin
- Adiponectin reduces the fat content of the liver and enhances insulin sensitivity

SUMMARY

- **Signals from adipocytes in obesity cause metabolic abnormalities such as:**

  -Dyslipidemia

  - Glucose intolerance

  - Insulin resistance

  - Hypertension

  ✓ Obesity is a component of metabolic syndrome.

- **Compensatory hyperinsulinemia causes down regulation of insulin receptor and may lead to Defects in the receptor.**

- **Dyslipidemia means there is an increased VLDL and decrease HDL levels and others.**

- **Cushing's disease is a risk factor for metabolic syndrome.**

- **Some drugs like (Rifampicin, isoniazid) can cause metabolic syndrome.**

- **Metabolic syndrome is linked to Type-2 diabetes mellitus as well as Heart disease, kidney disease, Nonalcoholic steatohepatitis and cancer.**

- **Primary intervention in metabolic syndrome is lifestyle changing.**

- **Thiazolidinediones (TZDs) it Activates the transcription of adiponectin.**

MCQs & SAQs

Left Column

1- Which of the following is true about Dyslipidemia?

A) High HDL

B) High VLDL

C) A + B

D) Low VLDL

2- which of the following could be an early indicator of metabolic syndrome?

A) Hypertension

B) Glucose intolerance

C) Dyslipidemia

D) None

3- Which of the following is an inflammatory Marker of metabolic syndrome?

A) Interleukin-2

B) Interleukin-4

C) Interleukin-6

D) Interleukin-1

4- To treat and control a hypertensive patient we need to achieve a blood pressure of?

A) < 130/80 mmHg

B) > 140/90 mmHg

C) < 110/60 mmHg

D) < 100/50 mmHg

Right Column

1- Talk briefly about Metabolic Syndrome:

A combination of metabolic abnormalities which increase the risk of heart disease, diabetes and other diseases.

2- Name 3 Features of metabolic syndrome:

A) Low HDL cholesterol

B) Hypertension

C) Hyperglycemia

3- What are the Risk factors for metabolic syndrome? (Mention 4)

- Obesity

- Alcoholism

- Sedentary Lifestyle

- Smoking

4- Name 2 Markers of metabolic syndrome:

Lipoproteins:(LDL, HDL).

-Adipokines: (Leptin, adiponectin).

Biochemistry Bandits 434

اللهم إني استودعك ما قرأت وما حفظته وما تعلمت فرده
لي عند حاجتي إليه إنك على كل شيء قدير

DONE BY:

Moaath Al-sheikh

Abdullah Alkhamshi

REVISED BY:

Mohammad Alotaibi

For questions and comments. contact us **Biochemistry434@gmail.com**