Disorders of lipid metabolism

Most of disorders of lipid metabolism associated with hyperlipidemia .rarely the lipids accumulate in tissues not in plasma , accumulation in tissue is usually the result of sever and prolonged hyperlipidemia and cause cell damage

Clinical manifestation of hyperlipidemia

1- arterial wall the commonest and the most important manifestation ,it gives atherosclerosis → LDL and IDL are atherogenic.

2- subcutaneous tissues ,Xanthomatosis

3- Tendon . Xanthomata .

4- Cornea .corneal arcus.

Hypertriglyceridemia due to chylomicrons , VLDL or both causes turbidity of plasma , if it occur for long time → abdominal pain and acute pancreatitis.

There is a positive correlation between ischemic heart disease and raised plasma total and LDL cholesterol and negative one with plasma HDL .

Disorders of lipids can be considered under three headings :

- Predominant hypercholesterolemia .
- Predominant hypertriglyceridemia .
- Mixed hyperlipidemia .

Predominant hypercholesterolemia

- If Plasma cholesterol concentration reaches 200mg/dl The risk of cardiovascular disease increases. It is more in men than women .
- Hypercholesterolemia either:-
- primary which is familial inherited disorder with a high risk of cardiovascular disease. or
- Secondary hypercholesterolemia , the main causes are:

- Primary hypothyroidism .
- Diabetes mellitus .
- Nephrotic syndrome .
- Cholestasis .
- Drugs like thiazide , frusemide , and *B*- blockers .

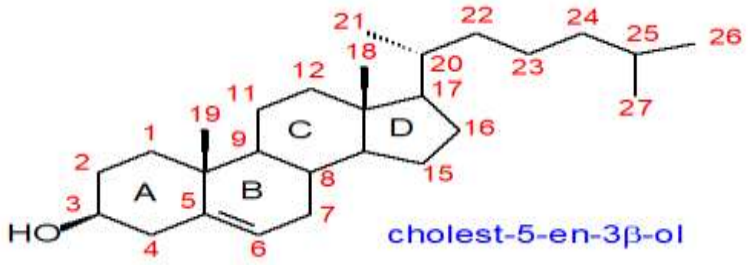
Predominant hypertriglyceridemia

- Familial endogenous hypertriglyceridemia is caused by increased hepatic triglyceride overproduction with increased secretion of VLDL-triglycerides. It may be associated with :

- Obesity.
- Glucose intolerance .
- Decrease in plasma HDL-cholesterol concentration .
- Hyperuricemia .
- Secondary hypertriglyceridemia may be due to :

- Obesity .
- diabetes mellitus .
- Nephrotic syndrome
- -Alcohol
- -Primary hypothyroidism
- -some drugs like pills and estrogen

Steroid hormones



The cortex of the adrenal gland is part of the hypo thalamic-pituitary-adrenal endocrine system ,steroid hormones are derived from cholesterol.

In figure above The side chain on c-17 is the main determinant of the type of hormonal activity.

Adrenal cortex hormones

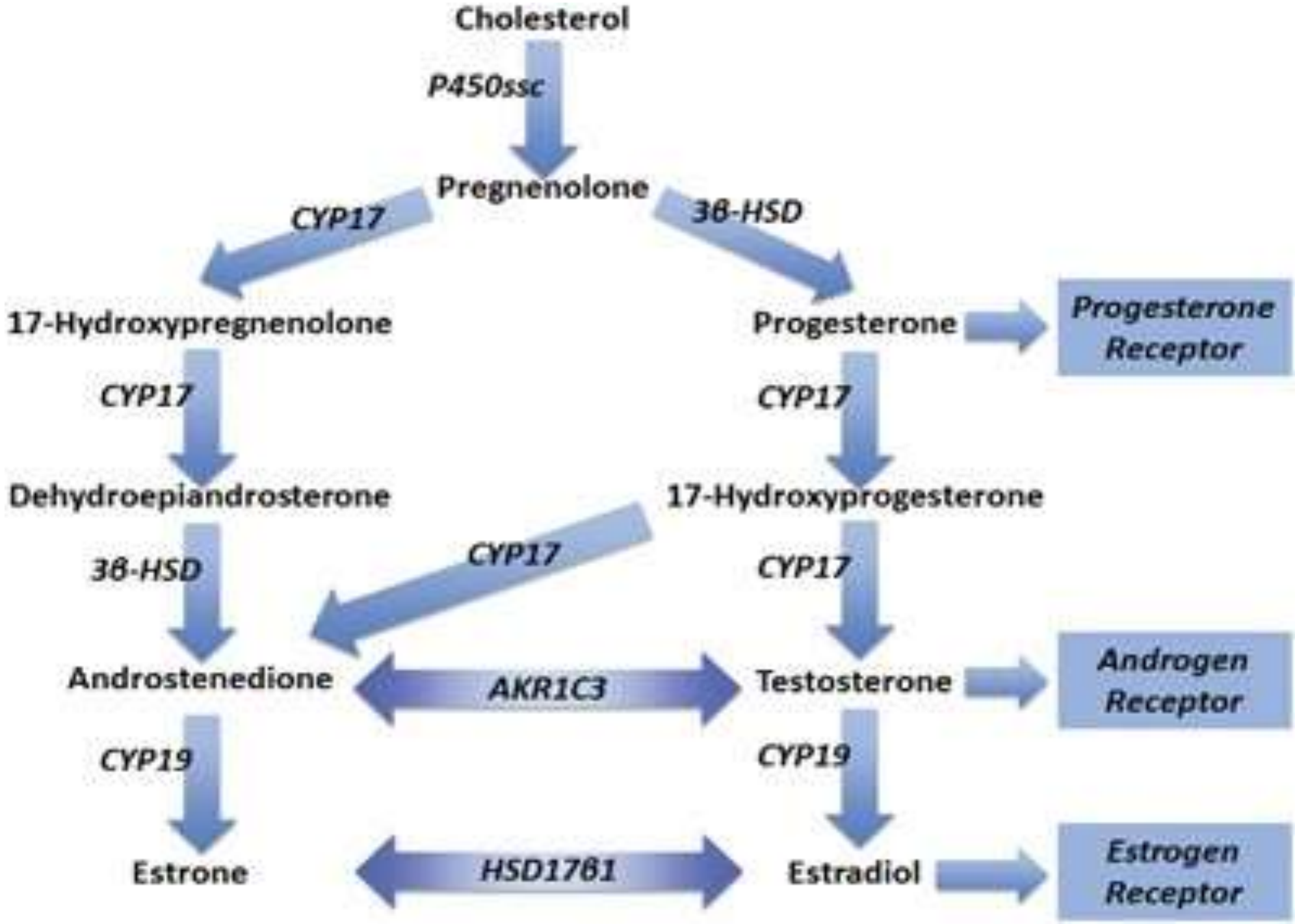
1- Cortisol and corticosterone are naturally occurring glucocorticoids .They stimulate gluconeogenesis and breakdown of protein and fat. therefor they oppose some action of insulin .they maintain the extracellular fluids and normal blood pressure in excess cause glucose intolerance and abnormal adipose tissue distribution .

2 Androgens (for example androstenedione) are formed after the removal of the side chain to produce C19 steroids .the main adrenal androgens are dehydroepiandrosterone (DHA), its sulphate(DHAS)and androstenedione.

Testosterone , the most powerful androgen is synthesized mainly in testes and ovaries but not in adrenal gland.

The ovarian steroids are estrogen and progesterone

3-Aldosterone(mineralocorticoids) It stimulates the exchange of sodium for hydrogen and potassium ions across the cell membranes and its renal action is important for sodium and water homeostasis .


Cholesterol
P450ssc
Pregnenolone
CYP17
3β-HSD
17-Hydroxypregnenolone
Progesterone
Progesterone Receptor
CYP17
CYP17
Dehydroepiandrosterone
17-Hydroxyprogesterone
3β-HSD
CYP17
CYP17
Androstenedione
AKR1C3
Testosterone
Androgen Receptor
CYP19
CYP19
Estrone
HSD17β1
Estradiol
Estrogen Receptor

Adrenocortical hyperfunction (Cushing's syndrome)

- It is caused by an excess of circulating cortisol which gives many clinical and biological disturbances :
- Obesity ,
- Impaired glucose tolerance .
- Increased protein catabolism .
- Hypertension.
- Androgen excess --→greasy skin , acne vulgaris ,hirsutism ,menstrual disturbances in women .
- Psychiatric disturbances .

Adrenocortical hypofunction

1. primary (Addison disease)

- Aldosterone deficiency -→ sodium and water depletion .
- Glucocorticoid deficiency → hypotension ,high sensitivity to insulin with hypoglycemia .
- Androgen deficiency --→ no obvious effect .
- Pigmentation .

2-secondary adrenal hypofunction due to impaired function of hypothalamus or pituitary gland by tumor or infarction .

Gonadal hormones (sex hormones)

- hypothalamic hormones
- Gonadotrophin releasing hormone (GTRH) which control release of follicle stimulating hormone (FSH)and luteinizing hormone (LH) .
- Dopamine it is neurotransmitter and control prolactin secretion .
- Pituitary hormones .
- LH stimulate production of hormones by gonads.
- FSH stimulate development of germ cells .
- Testicular hormone -→ testosterone and Inhibin .
- Ovarian hormones --→estrogens ,progesterone and androgens

Investigation of lipids disorders

- Plasma sampling
- Plasma lipid concentrations and lipoprotein patterns are affected by eating , smoking , alcohol intake , stress , and posture .so it is better to take samples under standard conditions .

1. Plasma cholesterol are not significantly affected by fatty meal , but triglycerides concentration are affected , so samples for analysis of both should be collected after 12 hours fast .
2. Normal diet and constant weight , at least 2 weeks before the test .
3. Unless treatment to be monitored ,then patient should not on any antihyperlipidemic drugs
4. Avoid venous stasis ,and the patient should be in comfortable posture . avoid stress , and the test should be delayed 3 months after myocardial infarction , and any sever illness .
5. The sample should not heparinized , and plasma separated as soon as possible

Indication for measuring plasma lipids

- Plasma cholesterols and fasting triglycerides (lipid profile) should be measured if there

1. Is a clinical indications :

- arterial disease in young patient .

- corneal arcus in a patient under 40 .

-xanthelasma or tendinous xanthomata .

2- is a family history of arterial disease .

3 - are risk factors of coronary disease (diabetic or hypertensive patient).

4-lipemic appearance of plasma is noticed by chance

Secondary causes of hyperlipidemia should be identified and treated, such as:

- High fat diet .
- Diabetes mellitus .
- Hypothyroidism .
- Excessive alcohol intake .

Notice : if plasma appears turbid , that means it is lipemic and mostly it is hypertriglyceridemia ,in this case we leave the sample stand for 18 h. at 4 C , if it is chylomicron it will form creamy layer which can be removed if still turbid it may be VLDL