SECONDARY DYSLIPIDEMIA

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- ***Definition:***

Dyslipidemia caused by some underlying etiology rather than a primary disorder of lipid metabolism.

- ***Prevalence:***

  - Secondary dyslipidemia represents 28%of cases of dyslipidemia in US.
  - The most common conditions that were felt to be contributing to dyslipidemia were excessive alcohol consumption and uncontrolled DM, renal disorders and obstructive liver disease

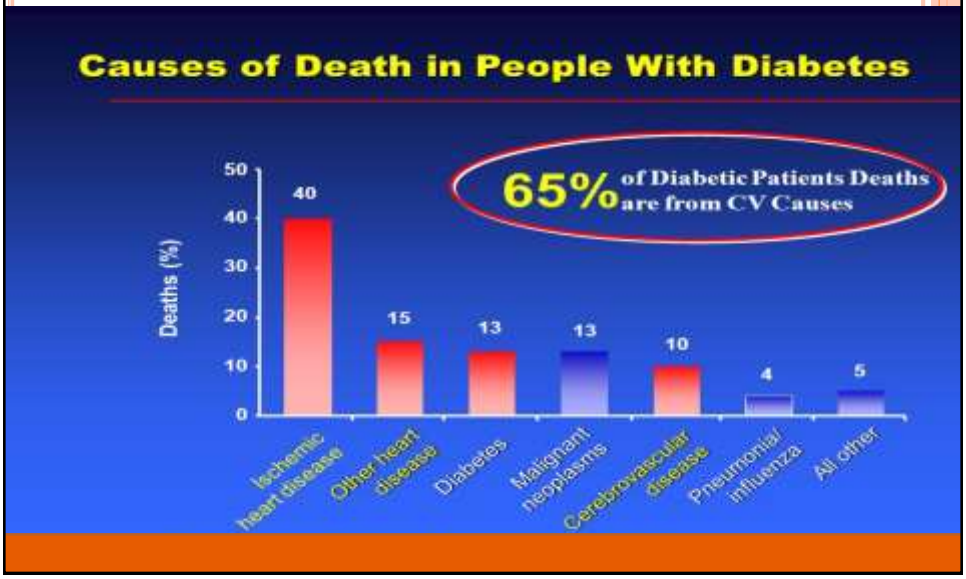
CAUSES

Diseases	Drugs
Uncontrolled DM	Thiazide Diuretics
Obesity and IR	Non-selective BB
Hypothyroidisms	Estrogens
Nephrotic syndrome & CKD	Cigarette smoking
Pregnancy and polycystic ovary	Steroids
Obstructive liver disease	Cyclosporine , cyclophosphamide
Alcoholism	Antipsychotics (colazpin)
HIV infection	Ticlopidine

SECONDARY DYSLIPIDEMIA

↑ LDL cholesterol	↑ Triglycerides	↓ HDL cholesterol
Diabetes mellitus	Alcoholism	Cigarette smoking
Hypothyroidism	Diabetes mellitus	Diabetes mellitus
Nephrotic syndrome	Hypothyroidism	
Obstructive liver	Obesity	Menopause
disease	Renal insufficiency	Obesity
Drugs	Drugs	
Anabolic steroids	Beta blockers	Uraemia
Progestins	Bile acid resins	Drugs
Beta blockers	Estrogens	Anabolic steroids
Thiazides	Ticlopidine	Beta blockers

DIABETIC DYSLIPIDEMIA



LIPID ABNORMALITIES COMMONLY PRESENT IN TYPE 2 DM

- Hypertriglyceridemia & low (HDL)
- (LDL) is converted to smaller more atherogenic small dens LDL
- Elevated levels of VLDL

- In type 2 DM these lipid abnormalities not fully corrected with glycemic control because they are related to IR not hyperglycemic state alone

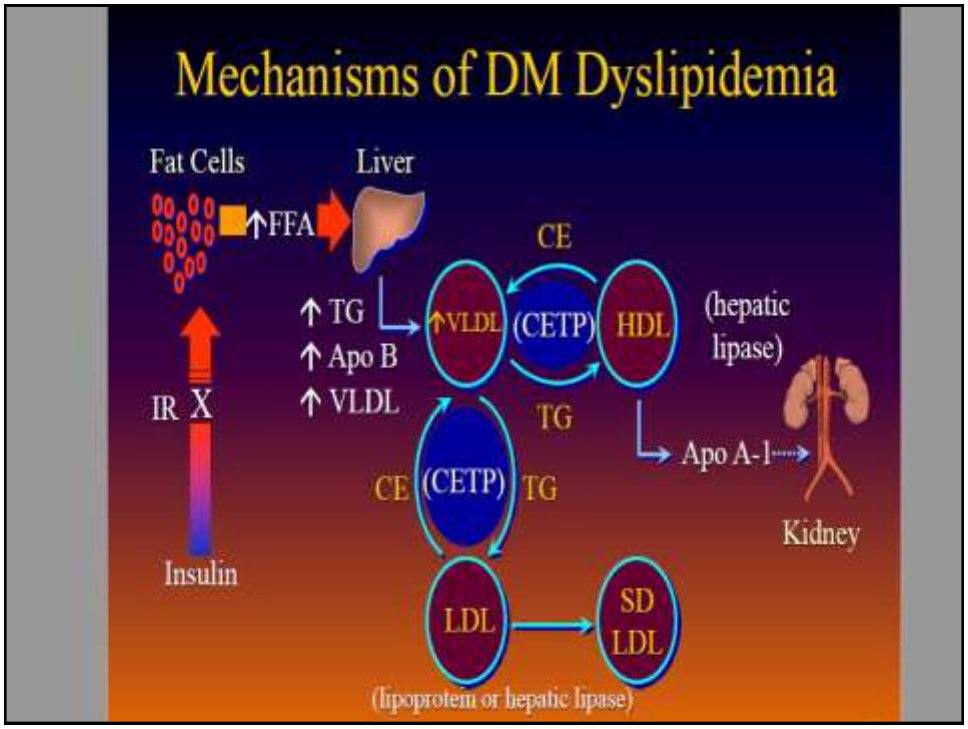
- In support of this hypothesis, in some studies drugs improving insulin actions on peripheral tissues lead to a greater improvement in lipid profiles than seen with other glucose-reducing agents

SPECIFIC LIPID ABNORMALITIES

Postprandial hyperlipemia

- Patients with type 2 DM have a slower clearance of chylomicrons from the blood after dietary fat

- There is decreased activity of LPL in diabetics resulting in increase in the TG rich chylomicrons & VLDL



SPECIFIC LIPID ABNORMALITIES

- ***Increased plasma VLDL***

  - Return of more FA to liver due to increased actions of (HSL) in adipose tissue prevents the degradation of newly synthesized apoB and lead to increased lipoprotein production.

  - VLDL, like chylomicrons, requires LpL for its catabolism, leading to the production of LDL

SPECIFIC LIPID ABNORMALITIES

- ***Increased small dense LDL***

  - A decrease in the size and an increase in density of LDL are characteristic of most hypertriglyceridemia in DM
  - Small dense LDL can be oxidized more easily, the particles do not interact with LDL receptors in liver as well
  - Although LDL production is reduced but is compensated by down regulation of LDL receptors and increased LDL oxidation in DM increasing its atherogenicity

SPECIFIC LIPID ABNORMALITIES

- ***Reduced HDL level***

  - Increased VLDL drive the exchange of triglyceride from VLDL for the cholesteryl esters found in HDL. This well results in hypertriglyceridemia and reduced HDL production

SPECIFIC LIPID ABNORMALITIES

- A false numerical not actual decrease in LDL with hypertriglycidemia is this equation.

$$\text{LDL} = \text{Total cholesterol} - \text{HDL} - \frac{\text{Triglycerides}}{5}$$

- So calculation of non-HDL cholesterol is more accurate for risk assessment and targets in cases of severe hypertiglycidemia.

DYSLIPIDEMIAS IN RENAL DISEASE

- Dyslipidemia is associated with a faster rate of CKD progression: in one study of 4483 apparently healthy males with baseline creatinine <1.5 mg/dl high cholesterol levels were associated with elevated creatinine and reduced GFR over an average 14 years of follow-up compared to non-dyslipidemics.

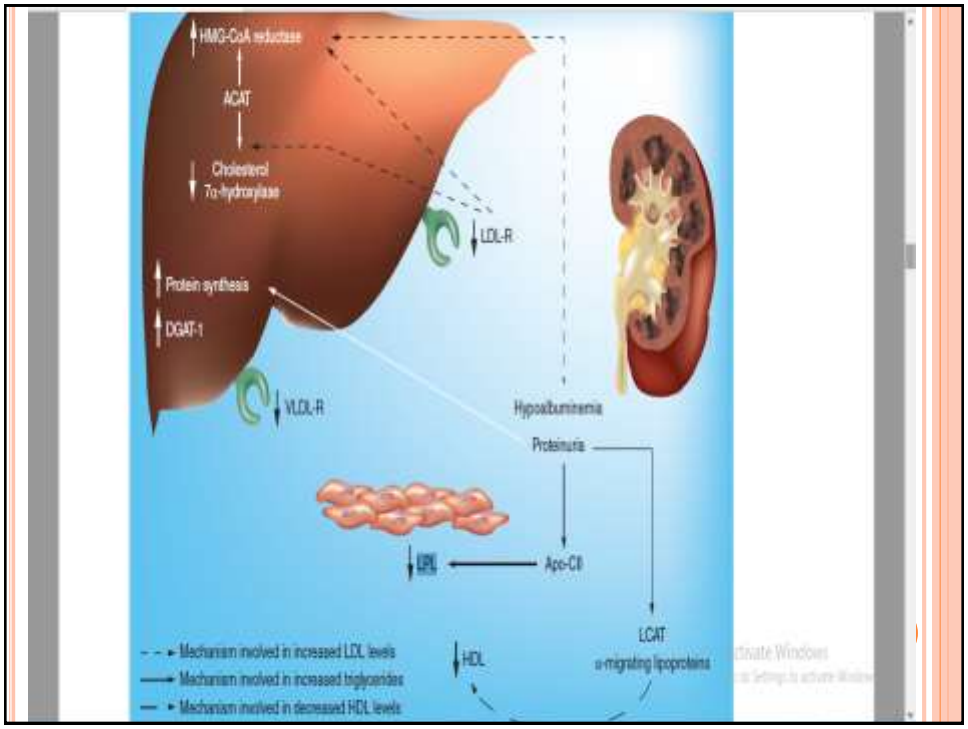
- Low (HDL) & elevated non-HDL cholesterol are linked to a 2 fold risk of renal insufficiency after adjustment for other risk factors

SPECIFIC LIPID ABNORMALITIES IN NS

- Upregulation of HMG-CoA reductase is stimulated by hypoalbumineamia due to decreased level of free hepatic colesterol due to upregulation of acylCo-A cholesterol acyltransferase.
- Elevated LDL cholesterol levels seem to be mainly due to decreased LDL catabolism
- Pathogenetic role of decreased LDL catabolism, due to a downregulation of cholesterol 7α-hydroxylase,
  with downregulation of LDL receptors

SPECIFIC LIPID ABNORMALITIES IN NS

- increased VLDL production secondary to a nonspecific increase in hepatic protein synthesis in order to compensate proteinuria and subsequent hypoalbuminemia
- Also VLDL clearance is impaired during NS due to reduced LPL action, which because of the urinary loss of apoC-II, which is a LPL activator
- The third characteristic of dyslipidemia reduced HDL, LCAT loss into urine



DYSLIPIDEMIA OF ADVANCED CKD

- ***MAINLY INCREASE TG DUE TO***

- LPLdepletion caused by a down-regulation of *LPL* gene expression
- Increased levels of apo C-III, a potent LPL inhibitor
- CKD can cause hepatic lipase deficiency with defective conversion of IDL to LDL
- Down-regulation of VLDL encoding gene and LDL receptor related protein (LRP), causing an increase in chylomicron remnants

DYSLIPIDEMIA OF ADVANCED CKD

- **REDUCED LEVEL OF HDL**

- Hypo-α-lipoproteinemia with a reduced plasma concentration of apoA-I and apoA-II, the main HDL components due to decreased there genes expression and there loss in urine

DYSLIPIDEMIA IN DIALYSIS PATIENT & IN RENAL TRANSPLANTATION

- Dyslipidemia of patients on dialysis characterized by hypertriglyceridemia.

- Heparin releases LPL from endothelium and thus its recurrent use for anticoagulation may lead to an LPL depletion, which in turn causes an increase of triglyceride levels

DYSLIPIDEMIA IN DIALYSIS PATIENT & IN RENAL TRANSPLANTATION

- Dyslipidemia is commonly found after renal transplantation 44% of patients with renal transplantation show increased LDL levels
- Immunosuppressive agents particularly corticosteroids, cyclosporine are the main causes.

TAKE HOME MASSAGE

- Many drugs and diseases can cause alteration in lipid profile
- In patients with high CV risk pay attention to your prescribed drugs in order not to increase there CV risk
- Your treatment strategies of patients with Dyslipidemia should focus on secondary causes and correct them if possible
- In condition with hyper-TG non-HDL should be the target of treatment not LDL

TAKE HOME MASSAGE

- The dyslipidemia in type II diabetics should include drugs that improve insulin sensitivity and weight reduction as there dyslipidemia not only due to hyperglycemia alone but due to IR and normalizing blood glucose alone may not revert the atherogenic effects of IR
- In patients with CKD attention should be paid to there lipid profile as there dyslipidemia worsens there renal function and increases there CV risk

Thanks