Lipid lowering Drugs

Hypercholestrolaemia

- Increased risk of cardiovascular events
- Increased risk of cerebrovascular events

Why use drugs?

- Well known to reduce the complications of elevated lipid levels
- Dietary modification has no major impact on hypercholesterolaemia(1/3)
- Significant reduction of triglycerides can be achieved by diet exercise and weight reduction.

Types of Hyperlipidaemias

- Hypercholesterolaemia
- Hypertriglyceridaemia
- Combined Hyperlipidaemias

Principles in the management

- Treat underlying cause if any
  - Diabetes
  - Obesity(syndrome X)
  - Hypothyroidism
  - Excessive alcohol consumption
  - Cholestatic liver diseases
- Dietary adjustment
- Specific drug therapy

Drugs used in the treatment

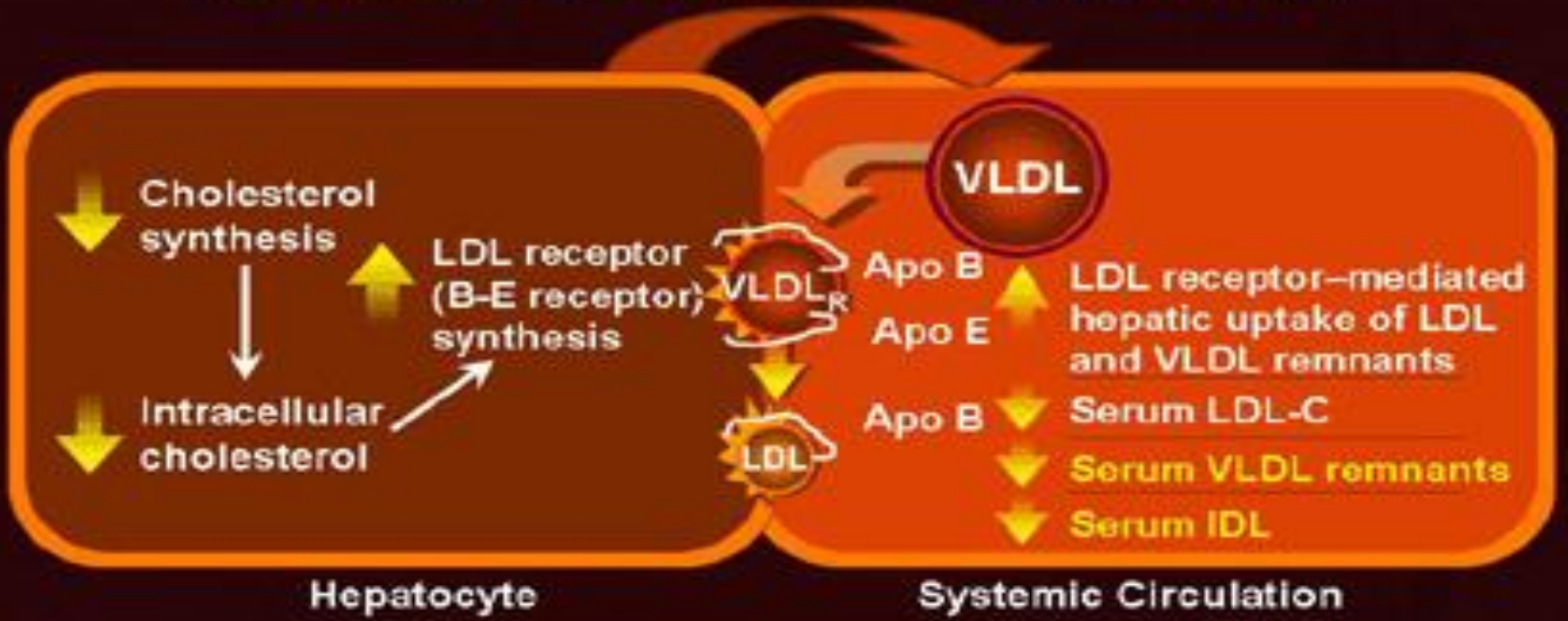
- Statins
- Fibrates
- Anion exchange resins
- Nicotinic acid derivatives
- Ezetimibe
- Others

Statins

Lovastatin,Simvastatin,Pravastatin,Atorvastatin,Rosuvastatin.

- Inhibits the rate limiting step in the endogenous synthesis of cholesterol Inhibits the enzyme HMG CoA reductase
- Increased synthesis of LDL receptors in the liver (up regulation)
- Clears LDL from circulation

Statins: Mechanism of Action



Reduces hepatic cholesterol synthesis, lowering intracellular cholesterol, which stimulates upregulation of LDL receptors and increases the uptake of non-HDL particles from the systemic circulation.

Hardman JG, et al., eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York: McGraw-Hill Professional; 2001.

Statins Cont-

- well tolerated orally
- abnormal liver function tests- Test LFTs
- elevated CPK levels
  - Myopathy
- Contraindicated in pregnancy and breast feeding

Statins cont-

Statins have other beneficial effects in MI/IHD

- Decreased oxidative stress
- Effects on endothelial dysfunction
- Atherosclerotic plaque stabilization

Statins Cont

- Reduces LDL cholesterol by 30%
- Reduces triglycerides
- Used in Hypercholeasterolaemia and combined hyperlipidaemias resistent to diet
- Used in STEMI NSTEMI, Primary and secondary prevention of IHD

Statins adverse effects

- Asymptomatic elevation of liver enzymes
- Hepatitis
- Myositis

Statins & liver

- Asymptomatic elevation of transaminases are recognized.
- Considered not due to liver damage
- True liver damage is rare. Stop if bilirubin is rising
- Safe in NASH(Non alcoholic steatohepatitis)
- Avoid in active liver disease
- Safe in early cirrhosis, PBC

Fibrates

Gemfibrosil, Fenofibrate

- Reduces hepatic lipid synthesis
- Reduces serum triglyceride by 20-30%
- Reduces serum cholesterol by 10-15%
- Are the drugs of choice for mixed hyperlipidaemias

Fibrates cont

- Raises HDL cholesterol
- Commoly used in Diabetic hyperlipidaemias
- Extensively protein bound
- CI in alcoholism, Liver disease, Breast feeding and pregnancy
- Elevated CPK and myopathy is a concern especially in combination with statin

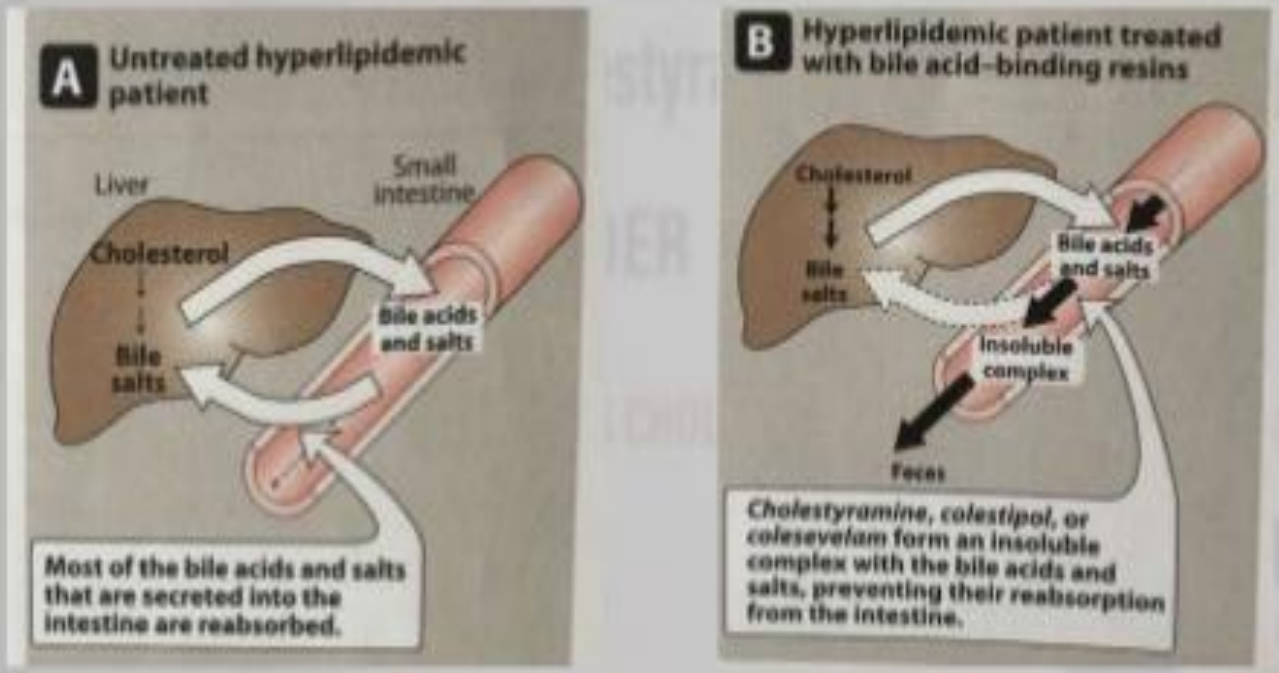
Anion exchange resins(Bile acid sequestrants)

Cholestyramine

- Binds bile acids in the intestines
- Bile acids are formed from cholesterol in the liver
- Aggravates Triglyceridaemia
- Dyspepsia is common.

4.Bile acid-Sequestrants

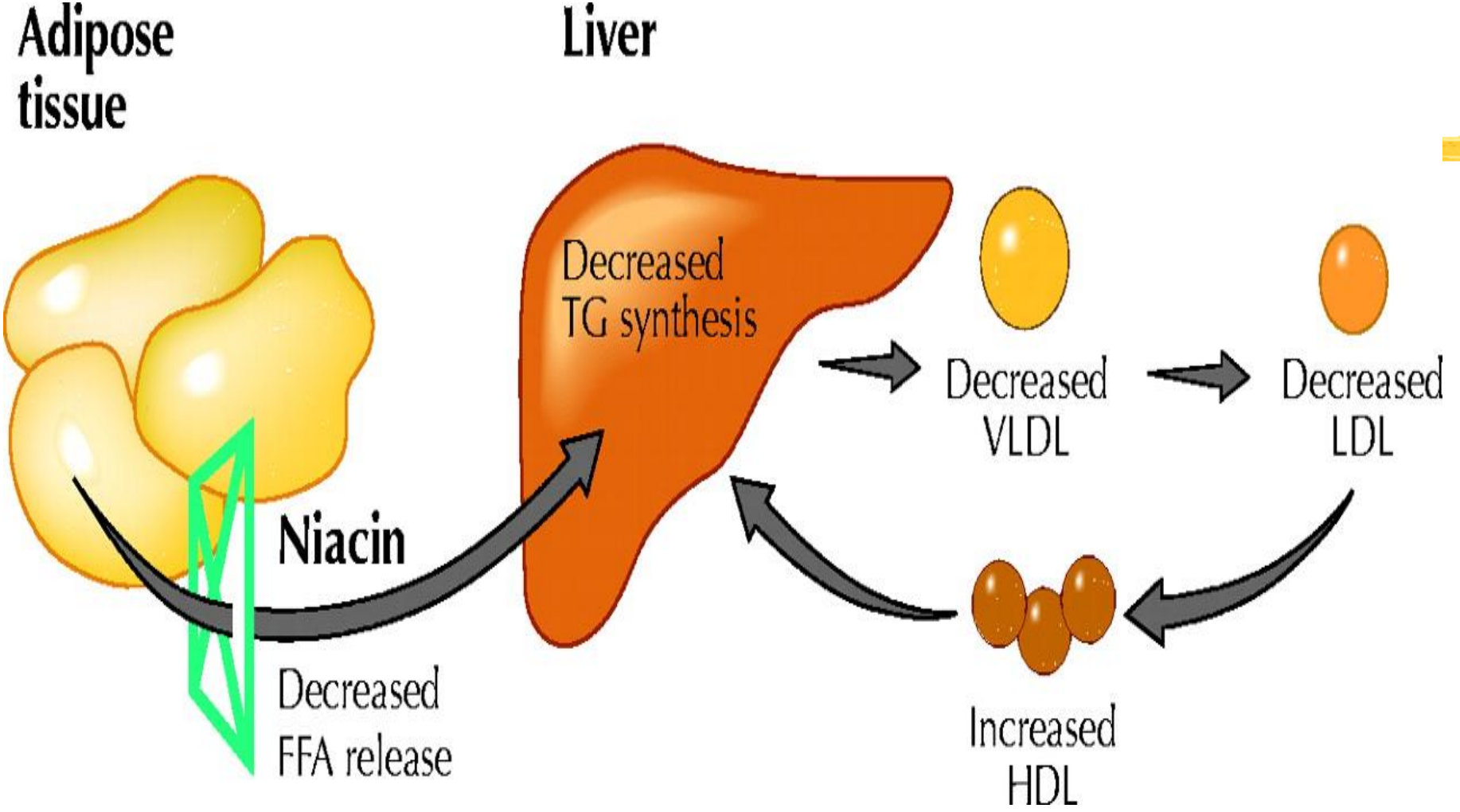
Mechanism of Action : Colestipol and cholestyramine are anion exchange resins.



Lowered Bile acid concentration= Hepatocyte conversion of cholesterol to bile acid increased.

Nicotinic Acid derivatives

- Lowers plasma triglyceride and cholesterol concentrations
- Use is limited by side effects- Flushing


Adipose tissue
Liver
Decreased TG synthesis
Decreased VLDL
Decreased LDL
Niacin
Decreased FFA release
Increased HDL

Ezetimibe

- Lowers LDL cholesterol levels
- Long term benefits not yet recognized
- Inhibits intestinal sterol absorption
- Adverse effects not common

Omega 3 marine triglycerides(fish oils)

- Reduces serum triglyceride levels

Lipid reduction in specific illnesses

- IHD
- Diabetes
- Inflammatory arthritis

Both conditions require a LDL concentration of <100mg/dl

Lipid abnormalities in children

Consider drug therapy in children ≥**10 y of age** (usually wait until menarche for females) and after a 6- to 12m trial of fat- and cholesterol-restricted dietary management.
Consider drug therapy if
LDL level remains ≥4.90 mmol/L (190 mg/dL) or
LDL remains >4.10 mmol/L (160 mg/dL) and
there is a positive family history of premature cardiovascular disease