CHOLESTEROL LOWERING DRUGS

Fat (lipids) are combinations (esters) of fatty acids plus an alcohol. The two main fats in the body are triglycerides (TGs) and cholesterol:

- **Triglycerides** (glycerol esterified with 3 fatty acids), normal level is **< 150 mg/dL (1.69 mmol/L).**
- **Cholesterol** (cholesterol alcohol esterified with fatty acids), normal value is **< 200 mg/dL (5.17 mmol/L).**
- Cholesterol, triglycerides, and phospholipids are transported as complexes of lipids and specialized proteins (apolipoproteins) known as lipoproteins.
- **Chylomicrons** are large lipoprotein particles that are created by the absorptive cells of the small intestine. Chylomicrons transport lipids to adipose tissue where they are broken down by lipoprotein lipase.
- **Very Low Density Lipoprotein (VLDL)** is a lipoprotein subclass. It is assembled in the liver from cholesterol and apolipoproteins. It is converted in the bloodstream to low density lipoprotein (LDL). VLDL is prone to **accelerate atherosclerosis**, and is elevated in a number of diseases and metabolic states. Target value is **> 60 mg/dL.**
- **Low-density lipoprotein (LDL)** refers to a class and range of lipoprotein particles, which carry cholesterol in the blood and around the body, for use by cells. It is the final stage of VLDL. Normal value is **< 100 mg/dL.**
- **High-density lipoprotein (HDL)** is "**bad cholesterol**". HDLs are the smallest of the lipoproteins. Low concentrations of HDL (**below 40 mg/dL or 1 .03 mmol/L for men**, **below 50 mg/dL for women**) are a positive risk factor for these atherosclerotic diseases.

Nonpharmacological treatment:

- Smoking cessation
- Take antioxidant vitamins (A, C, E). Long term, high doses may slow atherogenesis.
- Diet modifications (reduction in fats, proteins and carbohydrates), eat homemade food if possible
- Moderate exercise 30 minutes 5 times per week or 10000 steps per day.
- Avoid alcohol
- Fish oils are rich in **omega 3 polyunsaturated fatty acids (linolenic acid)**. They decrease the synthesis and enhance clearance of VLDL. These are as effective as **vegetable oils (omega 6 fatty acids)** in controlling lipids (TGs).

Drug Therapy

Statins**: inhibit HMG – CoA reductase, interrupting the conversion of HMG – CoA to mevalonate involved in liver cholesterol biosynthesis.**

Name and Dose	Efficacy	Adverse Effects	Interactions	Precautions/Comments/Monitoring
Atorvastatin (Lipitor) **10 – 80 mg po QD** Lovastatin (Mevacor) **20 – 80 mg po QD with food** Simvastatin (Zocor) **10 – 40 mg po qhs** Fluvastatin (Lescol) **20 – 80 mg po qhs** Rosuvastatin (Crestor) **10 – 40 mg po qd** Pravastatin (Pravachol) **10 – 40 mg po qhs**	Most effective Greatest effect on **lowering LDL (40%)** and **TC (30%)** Modest (**15%) increase in HDL** **Atrovastatin** has **greatest decrease** in LDL and is **most effective** in decreasing TGs Increasing dose will not provide much increasing effect **Lovastatin** and **simvastatin are prodrugs** and require liver hydrolysis Stabilize plaques in MI patients Effects are seen after 14 days of therapy	GI effects **Myositis** Skin rash **Elevated LFTs** Constipation occurs in fewer patients	**Metabolized by 3A4**: Atorvastatin Simvastatin Lovastatin **Potent 2C9 inhibitor**: Fluvastatin Rosuvavstatin Fluvastatin interacts with warfarin, digoxin, H2 RA	**Absolute contraindicated in pregnancy** and **lactation** **Active liver disease** Adjust dose in severe renal impairment **Can be used with bile acid resins** Pravastatin is least protein bound Atorvastatin and rosuvastatin can be taken at any time while the rest at evening time or bed time **Grape fruit juice** should be spaced 1 hour before or 3 hours after with atorvastatin, simvastatin and lovastatin. **LFTs q 3 months** and **CPK** Limit alcohol consumption

Cholesterol Absorption Inhibitor**: inhibits intestinal absorption of cholesterol and related phytosterols**.

Name and Dose	Efficacy	Adverse Effects	Interactions	Precautions/Comments/Monitoring
Ezitimibe (ezetrol) **10 mg po QD**	Well tolerated and can be taken any time Can be used with statins	Diarrhea fatigue	Not significant	Should be taken 2 hr before or 4 hours after antacids

Bile acid resins**: bind to bile acids in the intestinal lumen interrupting the enterohepatic circulation of bile acids, which decreases the bile acid pool size and stimulates hepatic synthesis of bile acids from cholesterol.**

Name	Dose and Efficacy	Adverse Effects	Interactions	Precautions/Comments/Monitoring
Cholestyramine (Questran) Colestipol (Colestid) Colesevelam	Cholestyramine: 4 – 24 g/d 1 – 2 hour before meals Colestipol: 5 – 30 g/d **20% reduction in LDL and TC** **no effect on HDL** can be used with statins and fibrates and in increase TGs Peak effects are seen after 3 weeks.	Flatulence Bloating, Nausea Constipation No absorption	**Decreases absorption of fat soluble vits (A, D,E, K)** A lot of interactions with many drugs and decrease absorption mainly by adsorption	**Safe in pregnancy** **Take 1 hr before or 4 hours after any other medication** The gritty texture and bulk may be minimized by mixing the powder with orange juice or drink and drink immediately **High fiber diet is recommended to decrease constipation** Colestipol is tasteless and odourless Tab form has better palatability Vitamin A, D, E, K supplement may be required on long term

Fibric acids (Fibrates): act on VLDL, decrease hepatic cholesterol synthesis and increase LDL catabolism

Name and Dose	Efficacy	Adverse Effects	Interactions	Precautions/Comments/Monitoring
Bezafibrate (Bezalip SR) **200 mg po TID with meals**	Second line to statins Have **greatest effect on lowering TGs (45%)** **Good for diabetics** First gen. (gemfibrozil) cause an increase in mortality and LDL Modest increase in HDL (15%) **Bezfibrate and fenofibrate are most effective**	Nausea **Abdominal pain** **Flatulence** Rash Insomnia **Myalgia** **Rhabdomylosis**	**Statins** Warfarin Oral coagulants level increases	**Gemfibrozil increase stone formation** Clofibrate is obsolete now **Contraindicated in pregnancy and lactation** Precaution in renal failure Ok in hepatic failure
Fenofibrate **100 mg po BID – QID with meals**				
Fenofibrate microcoated (Lipid supra) **160 – 200 mg po QD with main meal**				
Fenfibrate micronized (Lipidil micro) **200 mg po QD with main meal**				
Gemfibrozil (Lopid) **600 mg BID 30 mins. ac meal**				

Niacin**: reduces the hepatic synthesis of VLDL, cause a reduction in the synthesis of LDL** and **increases HDL by reducing its catabolism.**

Name	Dose and Efficacy	Adverse Effects	Interactions	Precautions/Comments/Monitoring

Niacin	Adult: 250 – 1500 mg po BID with food **20 % reduction in LDL** and **TC** Provides **greatest increase in HDL (20%)** Good **decrease in TGs (40%)** Absorption is rapid and extensive. Extensive first pass effect.	**PG mediated facial flushing and rash** Orthostatic hypotension Hyperuricemia (inhibits uric acid excretion) **Myopathy** GI intolerance	Increases effects of hypoglycemia With statins / fibrates cause more myopathy	Cutaneous flushing and itching can be prevented by taking ASA 325 mg 30 minutes before niacin Titrate dose slowly upward **Blood glucose, LFTs**, pretreatment and every 6 – 12 weeks for first year then periodically. Lipid profile periodically. **Concomitant use of alcohol and hot drinks may magnify pruritus** Caution in **liver disease, diabetes** and **gout.**