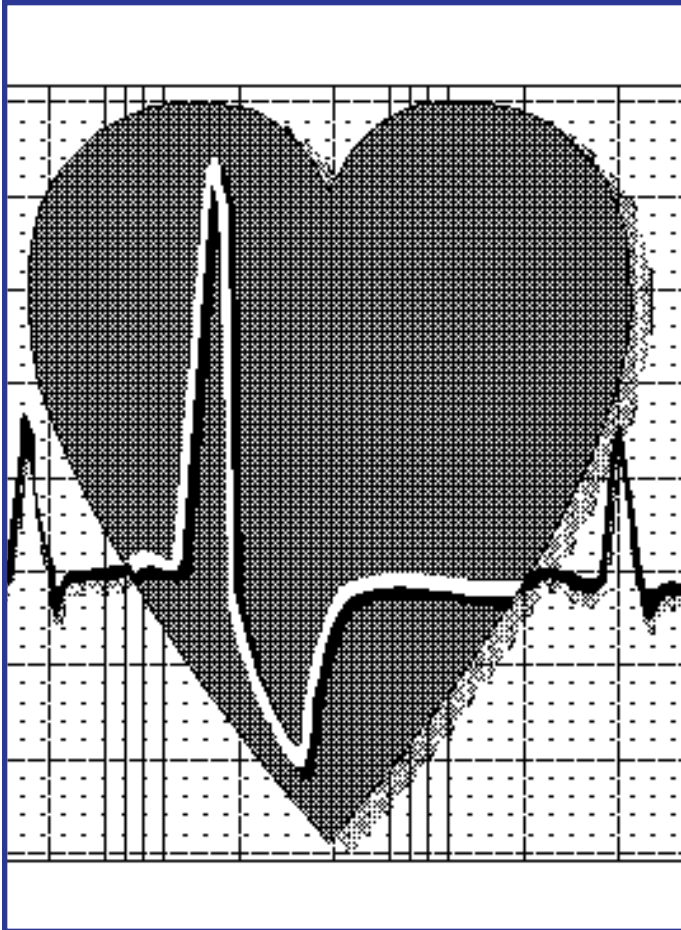


Recognition and Management of Hyperlipidemia: A Guide for Clinicians

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LIPIDS SERIES, P1



- Hyperlipidemia is a risk factor for coronary artery disease (CAD). A goal of LDL<100 is recommended if patient has history of CAD (secondary prevention of CAD), or LDL<130-160 if no history of CAD exists (primary prevention of CAD).
- CAD causes 500,000 deaths per year in the United States.
- Controlling hyperlipidemia by diet and drugs have prolonged survival in more than 50% of patients.
- This brochure is based on the published guidelines of the National Cholesterol Education Program (NCEP) and the American Heart Association.

SCREENING BASED ON NCEP GUIDELINES

1. Recommend Step 1 Diet, weight control, and physical activity for all adults.
2. Order non-fasting total cholesterol and HDL every 0-5 years or post Coronary Artery Disease (CAD):
Total Cholesterol (TC): _____ mg/dl
LDL: _____ mg/dl
3. Interview patient to identify risk factors for CAD:

Age (Men > 45, Women > 55)	Yes	No
Family History of CAD	Yes	No

(MI or sudden death in father or brother < 55)		
(MI or sudden death in mother or sister < 65)		
Smoking	Yes	No
Diabetes	Yes	No
Hypertension	Yes	No
HDL<35mg/dl	Yes	No
(If HDL>60, subtract one risk factor)		

Number Yes _____

4. Identify patients eligible for secondary prevention post-coronary artery or atherosclerotic disease:

MI	Yes	No
Angina	Yes	No
Coronary Artery Angioplasty	Yes	No
Peripheral Arterial Disease	Yes	No
Abdominal Aortic Aneurysm	Yes	No
Symptomatic Carotid Artery Disease	Yes	No
Coronary Artery Bypass Graft	Yes	No

Number Yes _____

5. Order a fasting lipid panel (cholesterol, HDL, TG, LDL) if any of the following exist:

- Total cholesterol>240 (primary prevention)
- HDL<35 (primary prevention)
- More than 1 risk factor for CAD (primary prevention)
- Known CAD or other ASCVD (secondary prevention)

LDL = TC - HDL - TG/5. (Invalid if TG>400. In this case, order a fasting lipid profile measured by ultracentrifugation technique.)

Treatment decisions are based on two LDL measurements. If they differ by >30, a third measurement may be done and the average should be used. Low HDL should be determined by the average of two measurements.

6. Based on the current LDL level, start treating the following patient population (Step II Diet with or without medications) to achieve the goal LDL level:

<u>Patient Category</u>	<u>LDL Goal</u>	<u>Diet if</u>	<u>Drug if</u>
With CAD	<100 mg/dL	>100	>130
Without CAD:			
>1 risk factor	<130 mg/dL	>130	>160
0-1 risk factor	<160 mg/dL	>160	>190

7. The choice of drug therapy is based on the current levels of tryglycerides (TG) and LDL. See the “Treatment Based on the NCEP Guidelines” section.

TREATMENT BASED ON NCEP GUIDELINES

Recommend Step I and II Diets as tolerated, then drug therapy based on TG and LDL levels.

Dietary Therapy

	<u>Step I Diet</u>	<u>Step II Diet</u>
Saturated Fat	<8-10% of total calories	<7% of total calories
Cholesterol	<300 mg	<200 mg
Total Fat	<30% of total calories	<30% of total calories
Carbohydrate	>55% of total calories	>55% of total calories
Protein	15% of total calories	15% of total calories

Monitoring:

- Identify potential reasons for elevated cholesterol, LDL or TG (i.e., food elements, alcohol consumption).
- **Step I:**
Monitor total cholesterol at 4-6 weeks and again in 3 months. You may ask your patient to continue the diet for 3 additional months or advance to Step II. When the therapeutic goal is reached, check total cholesterol at 4-6 months and annually thereafter.
- **Step II:**
Initiate if patient adheres to Step I and there is no decrease in cholesterol, or if LDL>220. Monitor total cholesterol and LDL at 3-4 weeks, 3 months, and 6 months. If cholesterol goal is not reached, consider drug therapy.

DRUG THERAPY

1. Elevated LDL and TG<500:

Start with statin therapy if the patient has active peptic ulcer disease; otherwise, start with niacin unless contraindicated. If there is no response to maximally tolerated niacin dose, bile acid sequestrant or statin therapy may be initiated.

2. Elevated LDL and ITG>500:

Start with niacin unless contraindicated. If there is no response to maximally tolerated niacin dose, gemfibrozil therapy may be initiated in the case of primary prevention of CAD, or statin therapy may be initiated in the case of secondary prevention of CAD.

3. Normal LDL and TG>1000:

Start with niacin unless contraindicated. If no response to maximally tolerated niacin dose, gemfibrozil therapy may be initiated.

If there is no response to diet and maximal therapeutic medication regimens, an endocrinologist may need to be consulted.

If there is a satisfactory response, check total cholesterol every 6 months and fasting lipid panel annually.

Inadequate Response To Diet:

- Poor adherence to diet and intensive and repetitive counseling.
- Consider role of stress-induced eating and binge eating, and provide counseling.
- Modification of eating habits may require a long period of time.
- Elevated LDL may be resistant to or insufficiently reduced by dietary modification.

Inadequate Response to Single Drug Therapy

- Should have utilized maximum therapeutic dose.
- Should have allowed a minimum of 4-6 weeks on the same dose to observe maximum effect.
- If no response to single drug therapy, combination drug therapy may be used.
- Combination therapy has an additive effect and may produce less toxicity. However, the combination of a statin and gemfibrozil needs close monitoring for myopathy. It may require CK monitoring and patient education.

DRUG THERAPIES

Nicotinic Acid (Niacin)

Dosage and Expected Effects

Dose Range (immediate release): 1-5 g daily

Indications: Type IIb, IIb, IV and V hyperlipidemia

Percent Lipid Change from Baseline

<u>DOSE</u>	<u>TG</u>	<u>HCL-C</u>	<u>LDL-C</u>
1.5G	-20	+15	-15
3.0G	-30	+20	-20
4.5G	-40	+25	-25

Before Prescribing Niacin:

1. Order baseline LFTs, glucose, uric acid, and lipid profile. Active liver disease is an absolute contraindication to niacin use. Relative contraindications include diabetes, active gout, peptic ulcer disease, and severe gastritis. If the patient is diabetic, there is a greater than 50% chance of poor glycemic control with niacin. If patient has active gout or peptic ulcer disease, treat the gout or ulcer first, then wait 6 months before starting niacin.
2. Advise patients about expected/probable side effects and how to manage them. The patient must be cooperative to withstand the initiation of niacin therapy. To minimize the transient cutaneous side effects, start at a lower dose, recommend that niacin be taken with meals, and premedicate with aspirin.

Ask the patient to report any side effects to you, especially rash and poor glucose control. A follow-up visit with labs (lipid profile, LF, glucose, and uric acid) should be scheduled in 4-6 weeks.

After Prescribing Niacin:

1. At first follow-up, re-evaluate lipid profile, LFT, glucose, and uric acid.
2. Evaluate any reported adverse effects. Flushing, pruritis, rash/urticaria, and acanthosis nigricans are not serious. However, hepatitis, gastritis/GI bleeding, hyperglycemia, gout, myalgias, and myositis are potentially serious.
3. Schedule appointment in 3 months to evaluate lipid profile and see if LDL goal is achieved. If the maximum tolerated dose has been reached without satisfactory response, another agent should be tried.

Bile Acid Sequestrants

Dosage and Expected Effects:

Cholestyramine (Questran®) 1 scoop = 4 g daily
Colestipol (Colestid®) 1 scoop = 5 g daily

Dose Range: 2 to 5 scoops daily (2 scoops q PM or BID [with meals])

Indications: Type IIa hyperlipidemia

Percent Lipid Change from Baseline			
<u>DOSE</u>	<u>TG</u>	<u>HCL-C</u>	<u>LDL-C</u>
2 scoops	+8	+3	-15
4 scoops	+12	+4	-20
6 scoops	+20	+5	-25

Before Prescribing Bile Acid Sequestrants:

1. Order baseline lipid profile. Contraindications include hypertriglyceridemia. Triglycerides will worsen by 10-50% with sequestrants. Lower triglycerides to below 200 ml/dl before using sequestrants. If the patient has failed previous sequestrant treatment, you might try a different sequestrant preparation (i.e., Questran Light® instead of Questran®).
2. Advise patients about expected/probable side effects and how to manage them. Suggest low doses (2 scoops q PM) or different preparations to improve tolerance. If constipation becomes a problem, suggest stool softeners, fiber, or mineral oil. The patient should be urged to maintain an adequate water intake during the treatment period. If patient is taking other medications, recommend a proper dosing schedule to avoid drug interactions with the bile acid sequestrant. Ask patient to report any unusual side effects to you. A follow-up visit with lipid profile should be scheduled in 4-6 weeks.

After Prescribing Sequestrant:

1. At first follow-up, re-evaluate lipid profile.

- Evaluate any reported adverse effects. Sandy taste, constipation, abdominal gas, and cramping are not serious.
- Schedule appointment in 3 months to evaluate lipid profile.

The Statins

Dosage and Expected Effects:

Simvastatin (Zocor®)	10-40 mg daily
Lovastatin (Mevacor®)	20-80 mg daily
Pravastatin (Pravachol®)	10-40 mg daily
Atorvastatin (Lipitor®)	10-80 mg daily
Fluvastatin (Lescol®)	20-40 mg daily

Indications: Type IIa and IIb hyperlipidemia

Percent Lipid Change from Baseline (Simvastatin [Zocor])

<u>DOSE</u>	<u>TG</u>	<u>HCL-C</u>	<u>LDL-C</u>
20-40 mg	-11	+7	-37

The use of simvastatin reduced total mortality by 42%, CHD death by 55%, hospitalization cost by 34% and total hospitalization by 37%.⁴ Its long-term safety has been established.

Before prescribing a statin:

- Order baseline lipid profile, LFT, serum creatinine and CK (if symptoms develop or it used with high risk medications). Active liver disease or unexplained persistent elevations of serum transaminases are absolute contraindications to statin use. The kidney clears statin metabolites; severe renal impairment heightens the risk of rhabdomyolysis. Relative contraindications include renal disease, and other medications, e.g., gemfibrozil, cyclosporine (and other immunosuppressives), erythromycin, and mibefradil (Posicor®) may potentiate rhabdomyolysis. Lower triglycerides to below 300 mg/dl before using a statin. Although statins do lower triglycerides by 10-30%, this generally holds true only when they are not initially elevated.
- Advise patients about expected/probable side effects and how to handle them. A follow-up visit with lipid profile, LFT, serum creatinine and CK should be scheduled in 4-6 weeks. Please advise patients on the following: Zocor and Mevacor are better absorbed when taken with food; Pravachol and Lescol are better absorbed when taken at bedtime; and Lipitor may be taken without regard to meals.
- Schedule appointment in 3 months to evaluate lipid profile, LFT, serum creatinine and CK.

Gemfibrozil (Lopid®)

Dosage and Expected Effects:

Dose: 600-1200 mg daily

Indications: Type IIb, IV and V hyperlipidemia

Response Depends Upon Triglyceride Level

A. Response to gemfibrozil in hypertriglyceridemia

Percent Lipid Change from Baseline			
<u>DOSE</u>	<u>TG</u>	<u>HCL-C</u>	<u>LDL-C</u>
1200 mg	-50	+15	-2

B. Response to gemfibrozil with TG<200 mg/dl.

Percent Lipid Change from Baseline			
<u>DOSE</u>	<u>TG</u>	<u>HCL-C</u>	<u>LDL-C</u>
1200 mg	-30	+10	-15

Before Prescribing Gemfibrozil:

1. Order baseline lipid profile, CBC, LFT, and serum creatinine. Relative contraindications include hepatic or severe renal disease, gallstones, or current therapy with a statin. Gemfibrozil is catabolized primarily by the kidneys. Toxicity is much more likely if creatinine clearance is less than 50 ml/min. Gemfibrozil is indicated primarily when triglycerides are elevated. If fasting triglycerides are below 250 mg/dl, reevaluate whether gemfibrozil is really needed since it will *NOT* reduce LDL. Be prepared to add an additional lipid lowering drug if LDL remains elevated.
2. Advise patients about expected/probable side effects and how to manage them. Epigastric discomfort, dyspepsia and abdominal pain are not serious. Cholelithiasis, myopathy, hepatitis and neutropenia are potentially serious. A follow-up visit with lipid profile, CBC, LFT, and serum creatinine should be scheduled in 4-6 weeks.

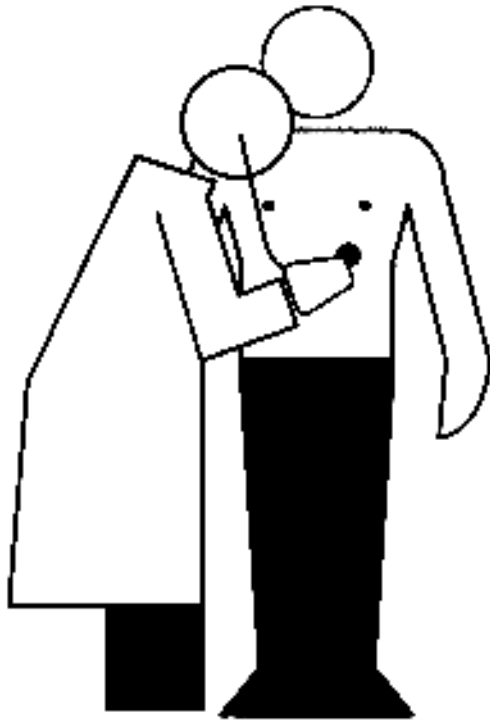
After Prescribing Gemfibrozil:

1. Order another CBC shortly after starting drug.
2. At first follow-up, re-evaluate lipid profile, CBC, LFT and serum creatinine.
3. Evaluate any reported adverse effects. Epigastric discomfort, dyspepsia, and abdominal pain are not serious. Cholelithiasis, myopathy, hepatitis and neutropenia are potentially serious.
4. Schedule appointment in 3 months to evaluate lipid profile, serum creatinine, and CBC.

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INTERNET LINKS: American Heart Association, ClinPharm International, Virtual Pharmacy, PharmWeb.



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