Hyperlipidemia: Should primary care providers
Treat more than LDL?

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The members of the Committee appointed to examine the clinical project of CHRISTY BRIDGET MASTERMAN find it satisfactory and recommend that it be accepted.

[Signatures]
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Hyperlipidemia: Should primary care providers Treat more than LDL?

Abstract

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May 2006

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Purpose: To provide an overview of current recommendations for the treatment of hyperlipidemia and discuss the need for treatment of all aspects of lipids.

Data Sources: Selected clinical research articles and NCEP guidelines.

Conclusions: Evidence-based research supports the aggressive management of lipids. While the treatment of LDL is the standard priority in the treatment of hyperlipidemia, improving LDL size and distribution, decreasing triglycerides, and increasing HDL also decreases mortality in high-risk patients.

Implications for Practice: By incorporating the Health Belief Model, the provider can improve understanding and educational tools needed to manage the patient with hyperlipidemia.

Key Words: hyperlipidemia, metabolic syndrome, Health Belief Model

Journal: Submission of manuscript to the Journal of the American Academy of Nurse Practitioners (JAANP).
**Introduction**

The management of hyperlipidemia has become a major area of research. No longer is the management of cholesterol just the lowering of the total cholesterol or low density lipoprotein (LDL-C). The National Lipid Association is dedicated to the management of lipids. The American Medical Association is now offering certification by the American Board of Clinical Lipidology (www.lipid.org).

The National Cholesterol Education Adult Treatment Panel III (NCEP III) (Grundy, 2004) published an update of its 2001 treatment plan in September of 2004. This update includes results from five additional clinical trials. These trials all advocate aggressive treatment of LDL-C in high-risk and moderately high-risk groups for cardiovascular events. Current recommendations are to achieve an LDL-C of less than 70 mg/dl in a patient with greater than 20% ten-year cardiac risk when using the Framingham Risk Assessment Model. Guidelines (Table 1) for those with 2 or more cardiac risk factors and greater than a 10% ten-year cardiac risk, the treatment goal is a LDL less than 100 mg/dl.

In the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVIT) trial (Dormandy, 2005), a 16% mortality reduction in high-risk cardiac patients was found, when the LDL was treated to an average of 62 mg/dl instead of an LDL of 95 mg/dl. Although this is a significant reduction in mortality, why do cardiovascular events continue to occur? Research has shown that treating the LDL is not enough in high-risk patients. Aspects of hyperlipidemia other than the reduction of LDL need to be evaluated in order to prevent cardiovascular events.
Conceptual Framework

Cardiovascular disease is generally silent during its onset. The risk factors of hypertension, hyperlipidemia, and diabetes are silent in their progression. Preventable risk factors of sedentary lifestyle, diet, and obesity continue to negatively impact the health of a growing population.

The reduction of cardiovascular events with aggressive preventative measures will continue to evolve. The six components to the Health Belief Model (Figure 1) (HBM) include perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy (Tussing & Chapman-Novakofski, 2005). Given that cardiovascular disease is silent until an event occurs; many patients may inappropriately assess their risk factors. The Framingham Risk Calculator and the diagnosis of metabolic syndrome may influence early action in order to prevent events from occurring. A patient’s ability to reduce their risks with both compliance of medication and lifestyle, may better improve cardiovascular health.

Literature Review

An increased low-density lipoprotein raises the risk of atherosclerosis, acute coronary syndrome, and stroke. The Scandinavian Simvastatin Survival Study was a randomized, placebo-controlled trial in coronary heart disease patients with and without insulin resistance (Pyorala et al., 2004). Pyorala (2004) looked at the effect of treating the patient with and without insulin resistance with simvastatin. The subgroup included 3933 nondiabetic patients with established
coronary heart disease, 893 with metabolic syndrome and 3040 without metabolic syndrome. The patients treated with placebos had a higher total mortality including coronary, coronary heart disease, and atherosclerotic events, regardless of having insulin resistance syndrome (metabolic syndrome).

Patients who had a history of an acute coronary event were put into double blind categories (de Lemos et al., 2004). One category (n=2265) was given simvastatin 40 mg a day for 30 days, then an increased dose of 80 mg for the rest of the study. The second category (n=2232) was given a placebo for four months and then simvastatin 20 mg every day, thereafter. If the patient's LDL was greater than 130 mg/dl six weeks into the study, the patient was taken out of the study and put on an open label statin therapy regimen. The initial four months found no difference between groups in the reduction of cardiovascular death, nonfatal myocardial infarction, readmission for acute coronary syndrome (ACS), and stroke (HR, 1.01; 95%, 0.60-0.95; P=.02). There was a significant reduction in all cardiovascular events and death in the group treated immediately after an ACS event. This reduction was seen after the initial four months until the end of the four year study (HR, 0.75; 95% CI, 0.60-0.95; p=.02). From this study, long-term mortality reduction could be seen by immediately treating a patient with statins after a cardiovascular event.

The study which was phase Z in the “A to Z trial” (2004), as well as two other studies named PROVE IT and Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL), “support a strategy of aggressive LDL cholesterol lowering following ACS to prevent death and major
cardiovascular events.” Each study put emphasis on safety of the regimen with monitoring adverse reactions (de Lemos et al., 2004).

The Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI22) trial showed the importance of aggressive management of LDL-C. The PROVE IT trial compared moderate versus aggressive treatment of LDL-C for patients with recent cardiovascular events in a randomized controlled study. The PROVE IT trial was stopped early due to the significant reduction in mortality of patients managed with aggressive lipid lowering. Aggressive management was defined as LDL <70 in high-risk and an LDL <100 in moderate to moderate high-risk patients. Atorvastatin (Lipitor) was used in order to achieve these aggressive LDL goals. Conventional therapy was defined as LDL<100 mg/dl and attained with pravastatin (Pravachol). Aggressive LDL reduction was found to reduce cardiovascular mortality by 16% in high-risk patients over conventional treatment of a LDL<100 (HR, 0.16; CI 95%, 0.5-0.26; p=.005) (Cannon, 2004).

**Lipid Monitoring**

With the advent of more aggressive cholesterol treatments comes advanced lipid testing. The stringent guidelines for aggressive cholesterol management cause difficulty in testing LDL with standard lipid testing. Advanced lipid testing is a more accurate testing option in the treatment of LDL-C. Standard lipid testing uses the Friedewald equation (LDL=total cholesterol - HDL – Triglycerides/6). This equation was developed in 1972 and is highly dependent on the accuracy triglycerides. If a patient did not fast, LDL levels may
be falsely low due to a falsely elevated triglyceride level. Also, if triglycerides are greater than 400 mg/dl, the LDL will be falsely low. Lindsey (2004) suggested that triglycerides, as low as 200 mg/dl may cause, as much as 19% lower estimated LDL, than direct LDL. Advanced lipid panel measurements give a direct, rather than calculated measurement of LDL-C.

LDL-C is just one of four types of atherogenic lipoproteins. Atherogenic lipoproteins deposit cholesterol on the arterial wall. The four types are very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and lipoprotein (a) (McGovern, 2005).

Standard lipid panels include total cholesterol, estimated LDL, HDL and triglycerides. The LDL in a standard lipid panel is a calculated number representing a combination of LDL, IDL, and lipoprotein (a) in one number. HDL is a direct measurement combining both HDL-2 and HDL-3.

Three advanced lipid panels have been developed to directly measure LDL-C, as well as breakdown the standard lipid panel in order to individualize treatment. The panel differentiates HDL-2 from HDL-3 and gives an actual VLDL instead of an estimated VLDL. VLDL is traditionally estimated by dividing triglycerides by 5. Advanced lipid panels also differentiate types of atherogenic cholesterol in order to better recognize high-risk lipid profiles.

There are three methods (Table 2) of directly measuring LDL-C. Arthrotec’s VAP and Liposcience’s NMR are both comparable in cost to traditional lipid testing with calculated LDL. The Berkeley Heart Test is the most accurate, but also twice as expensive and has limited data.
The question now is why cardiovascular events continue to occur even when a patient’s LDL is less than 70. In the PROVE-IT trial, patients continued to have cardiac events and death with a median LDL of 62 mg/dl. Although the reduction of total LDL is effective in reducing cardiac risk, a greater understanding of the components of cholesterol, as well as aggressive treatment may further decrease cardiac events.

Pathophysiology

In order to understand the need for testing different components of cholesterol, one must understand their interrelationship. As previously mentioned, the measurement of LDL has the components of LDL, IDL and lipoprotein (a). VLDL works on the same pathway as LDL, but is not included in the LDL measurement. All atherogenic cholesterol contains apolipoprotein B 100 (McGovern, 2005).

VLDL-IDL-LDL work in a pathway. VLDL is produced in the liver and regulated by both diet and hormones (Figure 2, Figure 3). VLDL carries most of the triglycerides in the fasting state, when secreted by the liver. VLDL is then catabolized by lipoprotein lipase, shedding triglycerides. The lipoprotein is converted to IDL and eventually to LDL (Dipiro, 2002).

Lipoprotein (a) (Lp(a)) is an LDL-like substance with apolipoprotein B100 linked to another large protein, the apolipoprotein (a). This has a similar structure due to a common descent with plasminogen of the fibrinolytic system. Plasma levels do not change with environmental factors, but vary from person to person. For this reason lipoprotein (a) is thought to be genetically linked (Peltier,
Lipoprotein (a) "is a significant risk factor for atherothrombogenesis in both diabetic and nondiabetic subjects" (Song, 2005, p. 1719).

HDL (Figure 4) increases the efflux of cholesterol from the intimal arterial wall reducing the formation of foam cells. HDL cholesterol decreases atherosclerosis by protecting LDL from oxidation. LDL is oxidized in the intimal wall of the artery. Once LDL is oxidized, LDL is taken up by the macrophage scavenger receptor resulting in the formation of foam cells from macrophages (Brewer, 2004). Foam cells promote cell proliferation and matrix degradation in the intimal wall. HDL prevents LDL oxidation, as well as promotes cholesterol removal out of the intima reducing the atherogenic effects of LDL (Ross, 1999). Without the presence of foam cells, macrophages may accumulate, but do not lead to inflammation associated with atherosclerosis.

HDL is made up of two major components, HDL2 and HDL3. HDL2 is a larger more mature HDL particle. HDL2 is active in the reuptake of LDL cholesterol in the liver. Ziajka's (2005) describes HDL3 as a "hockey puck" due to its smaller, denser nature. For this reason, HDL2 is more cardioprotective, than HDL3.

The role of advanced lipid testing is three-fold. The tests show LDL distribution, Lp(a), and accurately estimate HDL protection. Reviewing these values may show a need for treatment that may not be seen on a standard lipid profile.

**Current Recommendations for Primary Treatment**

The use of statin drugs for patients with acute coronary syndrome is
widely accepted. With the enormous health implications of having not only a high LDL, but also a low HDL, statins should be considered a preventive measure for diabetes, cardiovascular disease, and stroke. Although these drugs have many side effects, the benefit of the use of statins outweighs the side effects on most patients.

Choosing a statin for therapy may be guided by the patient’s current medications. Atorvastatin (Lipitor) and simvastatin (Zocor) inhibit the CYP450 3A4 enzyme. This is the same enzyme used to activate clopidogrel (Plavix) causing patients taking Lipitor or Zocor to have decreased effects of Plavix. Given the same patient population frequently requires these categories of medications; Rosuvastatin (Crestor) may be an alternative. Rosuvastatin works though the CYP450 2C9 isoenzyme. Although Plavix is not affected by rosvastatin, the INR may be increased with patients on warfarin. CYP450 interactions should be reviewed and the need for each medication assessed (Leonard, 2004). Although Rosuvastatin (Crestor) may avoid CYP 450 3A4 interactions, the FDA issued an advisory due increased serious muscle toxicity, especially at maximum dosage, 40mg per day (FDA Public Health Advisory, 2004).

Numerous side effects are related to lipid lowering medications. Statins have numerous side effects. Nausea, diarrhea, constipation, and muscle aching are the most common. Statins can also increase liver enzymes and cause hepatotoxicity without symptoms. For this reason, liver function tests must be done prior to, as well as periodically during therapy. Patients may be counseled
to reduce their alcohol intake. Statins also may increase myoglobin breakdown leading to kidney failure or rhabdomyolysis. Consequently, a patient complaining about muscle pain or tenderness may either need dose adjustments, switched to another statin, or be taken off the medication completely.

Ezetimibe (Zetia) was approved by the FDA in 2002 and may augment the effects of statin for LDL reduction. Ezetimibe is not a statin. Instead it works by inhibiting the absorption of cholesterol from the intestine. There are no CYP450 interactions. Ezetimibe may be added for a relatively safe combination therapy, if statin monotherapy does not achieve therapeutic goals. There is considerable monetary cost in the addition of ezetimibe as an individual medication, which may be prohibitive to some patients (Coleman, 2004). Ezetimibe/simvastatin (Vytorin) is comparable in cost to atorvastatin (Lipitor). As a combination of simvastatin (Zocor) and ezetimibe (Zetia), Vytorin can give a patient two synergistic hyperlipidemia medications for the price of one.

Statin therapy is the primary treatment for elevated LDL-C. It also has protective qualities for diabetics, although it only minimally raises HDL. In the West Scotland Coronary Prevention Study, 5974 men ages 45 to 65 were analyzed for the development of new onset diabetes mellitus. With 139 subjects becoming diabetic during the course of the study, Freeman (2001) reported that the use of pravastatin (Pravachol) therapy found a 30% reduction in the development of diabetes.

The reduction in diabetes can be explained three ways. The first is that one of the major risk factors for diabetes is a high-density lipoprotein (HDL) level
less than 35 mg/dl, in addition to elevated LDL and triglyceride levels. By lowering these levels, there is a reduced risk of the development of insulin resistance and eventually diabetes mellitus.

The second explanation is that cytokines IL-6 and TNF-a are derived from adipose tissue. With the reduction of these cytokines, central obesity will not evolve into insulin resistance.

The third explanation is the improvement of endothelial function. "Impaired endothelial function has recently been shown to result in diminished capillary recruitment function and in turn correlates with the degree of insulin resistance" (Freeman et al, 2001, p. 360). In reducing the development of insulin resistance and diabetes, the macrovascular risks involved with being a diabetic may be prevented. Unfortunately, statins do not lower Lp(a) or improve LDL distribution. For this reason, patients with diabetes or metabolic syndrome may need individualized treatment of the hyperlipidemia.

Metabolic syndrome causes adults to be a high-risk population. In 2002, an estimated 22% of adults in the United States had metabolic syndrome. With 47 million US residents having metabolic syndrome, management of this condition is crucial (Ford, 2002). The American Heart Association and the National Heart, Lung, and Blood institute released a scientific statement on the diagnosis of metabolic syndrome. The diagnostic criterion for metabolic syndrome is the inclusion of three of the five risk factors (Table 3) (Grundy, p.5).
Patients with metabolic syndrome should first attain LDL goals appropriate for their risk factors. After the LDL goal has been reached, other treatment modalities must be considered. The primary treatment for metabolic syndrome is dietary changes, exercise, and weight loss. A full understanding of the risks involved with the diagnosis of metabolic syndrome can increase a patient’s perceived susceptibility of diabetes and cardiovascular risk. Although this can be effective, treatment options for hypertriglyceridemia and decreased HDL include fenofibrates (Tricor), omega-3 fatty acids (fish oil), and nicotinic acid (niacin) (Grundy, 2005; Kris-Etherton, 2002). Patients with diabetic mellitus Type II may use thiazolidinediones (TZDs) for blood glucose control, as well as reduction of triglycerides and an increase in HDL.

Thiazolidinediones, most notably pioglitizone (Actos), are effective in the treatment of lipids, as well as lowering blood glucose levels. Dormandy et al. (2005) published the results of the prospective pioglitazone clinical trial (PROactive) on the prevention of cardiovascular event. Pioglitazone (Actos) (n=2605) or placebo (n=2633) was added to type 2 diabetics medication regimen. Although pioglitazone (Actos) did not show a significant reduction in macrovascular events, it did improve the “metabolic profile in terms of glucose, HDL cholesterol, and triglyceride concentrations, and provided a better blood-pressure profile at the end of the study than at the beginning” (HR 0.90; CI 0.80-1.02, p=0.095) (Dormandy, 2005).

Pankaj et al. (2005) noted that although HDL levels increase with both rosiglitazone (Avandia) and pioglitazone (Actos), rosiglitazone may raise LDL.
"LDL cholesterol levels remain unchanged with pioglitazone monotherapy or a combination of pioglitazones with other oral hypoglycemic agents or insulin. In contrast, LDL cholesterol levels increase with rosiglitazone monotherapy or combination therapy. Although pioglitazone has been associated with a decrease in triglyceride levels, the effects of rosiglitazone on triglycerides have been variable, ranging from a 2% increase to a 19% decrease" (p.344). Therefore, use within the class of thiazolidinediones may not be interchangeable.

Thiazolidinediones are another class of medications that need to be closely monitored in specific patient populations. One of thiazolidinediones (TZDs) most significant side effect is weight gain. An average person can expect to gain 0.9 kg to 5.4 kg in a 26-week period. Weight gain is dose dependent for both rosiglitazone (Avandia) and pioglitazone (Actos). Weight gain also increases when used in combination therapy. The most significant weight gain has been seen in combination with insulin. Associated with weight gain is peripheral edema and fluid retention. For this reason certain considerations should be made in prescribing TZDs. Patients with known cardiac disease, shortness of breath, and taking medications associated with fluid retention should be monitored and taught the symptoms of heart failure. TZDs should be used cautiously in patients with class I or II New York Heart Association Congestive Heart Failure (NYHA CHF) categories and are not recommended for class III and IV NYHA CHF categories (Nesto, 2004).

Involving the patient in the treatment plan is imperative. An assessment of barriers and benefits and addressing concerns can help increase patient
compliance. The Health Belief Model can aid in an assessment of these barriers.

**The Use of the Advanced Lipid Profile in Primary Practice**

The lower the density of a cholesterol particle, the greater the cardiovascular risk. Both the Quebec Cardiovascular Study and Familial Atherosclerosis Treatment Study (FATS) have discussed patterns of LDL-C. The Quebec Cardiovascular Study concluded that small LDL particles are an independent risk factor for ischemic heart disease. FATS then concluded that therapies facilitating conversion of small, dense LDL (IDL) to LDL reduced the risk of ischemic heart disease (Lamarche, 1997; Zambon, 1999). These patterns of LDL are currently referred to as pattern A and pattern B. Pattern A represents a normal pattern of the LDL cholesterol. Pattern B signifies a small, dense pattern of LDL-C that presents a significantly higher risk for a cardiovascular event (Zambon, 1999). If statins have little effect on LDL distribution (Table 4), reducing the total LDL to 62 mg/dl may not have been enough in the PROVE IT trial.

Nicotinic acid (niacin) combination trials have had some exciting, although preliminary results. The HDL-Atherosclerosis Treatment Study (HATS) was a relatively small trial using statin and niacin combination therapy on patients with a low HDL (averaging 31 mg/dl) and LDL (averaging 125 mg/dl). The enrollment included 160 men (<63 years of age) and women (<70 years of age) with previous coronary disease and at least three vessels stenosed greater than 30% or one vessel stenosed greater than 50%. This was a double blind study attempting to compare the use of antioxidant vitamins (vitamin E 800 IU, vitamin
C 1000 mg, beta carotene 25 mg, and selenium 100 mcg daily) with and without a combination of niacin and simvastatin against placebo. The combination therapy of niacin and simvastatin found a reduction of major coronary events by 60-90%, 60% being the research group taking the antioxidant vitamins. Unfortunately, the size of the trial hinders its significance, but this study could have huge implications on treatment modalities (Brown, 2001).

Niacin’s “primary action is to inhibit the mobilization of free fatty acids, thereby reducing hepatic synthesis of triglycerides and secretion of VLDL” (Knopp, 1999, p. 505). At maximum dose, nicotinic acid is able to increase serum HDL concentrations by up to 30%. This exceeds all other medications. Nicotinic acid also shifts LDL from small dense particles into large, buoyant, less atherogenic particles. These shifts from IDL to LDL can be seen when monitoring a patient’s Vertical Auto Profile (VAP). Lipoprotein (a) concentrations are lowered approximately 30% by nicotinic acid (Knopp, 1999).

Nicotinic acid is a treatment option for decreased HDL levels. It is effective in lowering both LDL-C, as well as its components IDL and Lipoprotein (a). It also reduces VLDL cholesterol and raises HDL. Unfortunately, patients have difficulty tolerating niacin. Niacin causes flushing, itching, and headache. The use of controlled release niacin can significantly reduce flushing episodes. Taking aspirin 30-60 minutes before taking the niacin dose, increasing the dose at monthly intervals of 500-1000 mg per day, encouraging niacin to be taken after a meal, and using fiber supplementation can aid in the tolerability of the drug (Knopp, 1999). Niacin Extended Release (Niaspan) is more tolerated, than
immediate release. Although Niacin is Vitamin B3, in high doses, hepatitis is more common than with statins. Due to this, liver function tests should be done every six to twelve weeks for one year after the initiation of therapy.

Currently, in Stage III clinical trials is a medication called torcetrapib. A partial cholesteryl ester transfer protein (CETP) inhibitor, torcetrapib reduces the reuptake of HDL. After four weeks of therapy on daily dosed monotherapy, HDL was increased by 46% and increased 61% in combination with 20 mg of atorvastatin (Lipitor). At this time no significant side effects have been found (Brewer, 2004).

Monitoring advanced lipid profiles can aid in more effective management of lipids. These profiles can provide information about patients in greater risk for cardiovascular events.

Education is greatly important in treating hyperlipidemia without classic elevated cholesterol. Most patients understand “bad cholesterol” and “good cholesterol,” but treating patients using the new ATP III treatment guidelines may find some resistance. The first point of issue is the side effects of statins, thiazolidinediones, and nicotinic acid.

Challenges

“Findings from the National Health and Nutrition Examination survey report that only 11 million of the 36 million Americans eligible to receive statin therapy are being treated with statins” (Hughes, et al., 2004). The reasons for so few being treated are multifaceted. Non-compliance to asymptomatic conditions that require long-term therapy is commonplace.
Jackevicius (2002) found that approximately 30% of Canadian elderly on a statin for prevention without acute coronary syndrome (ACS) discontinued their regimen within two years, a substantial number of this population stopping therapy within six months. In the United States this number would be even higher due to higher cost for medication.

In giving a pill to lower cholesterol, patients may feel diet and exercise are not important. Instead a patient needs to be self-efficacious in their treatment regimen. A low fat, high fiber diet should be highly recommended. Teaching a patient how to introduce this diet into their lifestyle may be difficult. Giving alternatives, such as cooking in olive oil, can be helpful. Thirty minutes of walking most days or other physical activities should also be emphasized. Although dietary changes are important, with new treatment guidelines, diet and exercise are generally not enough, especially for high-risk cardiac patients (Grundy, 2004).

Before beginning a patient on statin drugs, assessing a patient’s ability to be compliant is very important. For thirty tablets of Lipitor 40 mg, the Target pharmacy charges $107. As discussed earlier, long-term statin use may not be feasible for the low-risk cardiac population with no prescription coverage. The perceived barriers to the statins may cause a decrease in compliance. Although the cost in the long term may be higher by hospitalization, convincing an asymptomatic patient of taking a $107 a month prescription seems challenging.

For those with prescription coverage, compliance may also be a factor. As evidenced by the study of Canadian elderly, only 70% had a compliance rate after
two year. This figure is even bleaker in Leonard’s study which states, “more than 70% of patients currently on statins fail to continue drug therapy beyond a year” (p.11). The benefits of taking statins should be reiterated many times. The need for lipid testing should be explained. Blood tests are not only to check for side effects, but to see progress in controlling cholesterol.

The health belief model can help a practitioner understand matters of compliance. Education of treatment may allow the patient to take control of their health. Addressing and validating a patient’s concerns of side effects and cost, as well as discussing a patient’s susceptibility of a cardiovascular event may improve compliance of both diet and medication regimen.

Statins have proven efficacy in patients with acute coronary syndrome. Treating hyperlipidemia aggressively as a preventive measure, may prevent the need for angioplasty or bypass surgery due to a reduction in cardiovascular events. To obtain therapeutic cholesterol levels, statin therapy, as well as diet and exercise should be emphasized. Treatment options such as nicotinic acid should be considered and advanced lipid profiles utilized. In the United States heart disease is the number one cause of death, mentioned previously. Elevated cholesterol and triglyceride levels have too many negative health implications to not aggressively treat.

Application to Nurse Practitioner Practice

Although lowering LDL-C to goal, smoking cessation, and blood pressure management are the primary targets in reducing the cardiovascular events, secondary management strategies can further reduce mortality. Two patients may
have similar standard lipid profiles, but have very different risks based on how cholesterol levels are broken down into different components. Effective teaching about the appropriate management of lipid may increase compliance. Nurse practitioners may also participate in future research on this much studied topic.

Summary

The assessment and management of hyperlipidemia continues to evolve. As LDL levels decrease due to more aggressive treatment a reduction in cardiovascular events has followed. Unfortunately, events continue to happen to patients with normal standard lipid profiles. LDL’s are normal in 40% of patients presenting with cardiovascular events (Ziajka, 2005). With better tools to monitor and a greater understanding of lipids, cardiovascular events will continue to decrease. Treating LDL is not enough, especially in high-risk patients. LDL size and density, as well as HDL and lipoprotein (a) should be monitored especially in patient having CHD with normal lipid profiles.
References


### Cardiac Risk Factors

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<td>CHD risk equivalents</td>
<td>Noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease, diabetes)</td>
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<td>Risk factors</td>
<td>Cigarette smoking, hypertension (&gt;(140/90) or on antihypertension medication), low HDL cholesterol (&lt;40 mg/dl), family history of premature CHD (male first-degree relative &lt;55 years of age; CHD in female first-degree relative &lt;65 years of age) and age (men &gt;45 year; women &gt;(=55) years)</td>
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<td>resonance spectroscopy)</td>
<td></td>
<td></td>
<td>Direct HDL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Direct VLDL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Direct triglycerides</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Non-HDL cholesterol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IDL cholesterol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Real LDL cholesterol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Real LDL-C size</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pattern (A or B)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Remnant lipoproteins</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(IDL+VLDL3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HDL-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HDL-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>VLDL-3</td>
</tr>
<tr>
<td>Berkeley Heart</td>
<td>Gradient Gel Electrophoresis</td>
<td>$290</td>
<td>Lipid profile</td>
</tr>
<tr>
<td>Test</td>
<td></td>
<td></td>
<td>Direct LDL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Direct HDL</td>
</tr>
</tbody>
</table>

Table 2

Advanced Lipid Monitoring
<table>
<thead>
<tr>
<th>Standard lipid panel</th>
<th>Estimated LDL</th>
<th>$50</th>
<th>Direct VLDL Direct triglycerides Non-HDL cholesterol Lp(a) IDL cholesterol Real LDL cholesterol Real LDL-C size Remnant lipoproteins Apo B</th>
</tr>
</thead>
</table>

### Table 3

** Metabolic Syndrome Diagnostic Criteria **

<table>
<thead>
<tr>
<th>Metabolic Syndrome Criterion</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated waist circumference</td>
<td>Men $\geq 102$ cm; Women $\geq 88$ cm</td>
</tr>
<tr>
<td>Elevated triglyceride</td>
<td>$&gt;150$ mg/dL OR medication therapy for hypertriglyceridemia</td>
</tr>
<tr>
<td>Reduced HDL-C</td>
<td>men $&lt; 40$ mg/dL; women $&lt; 50$ mg/dL OR On drug treatment for reduced HDL</td>
</tr>
<tr>
<td>Elevated blood pressure</td>
<td>$\geq 130$ systolic blood pressure OR $\geq 85$ diastolic blood pressure OR On antihypertensive drug treatment in a patient with a history of hypertension</td>
</tr>
<tr>
<td>Elevated fasting glucose</td>
<td>$\geq 100$ mg/dL OR On drug treatment for elevated glucose</td>
</tr>
</tbody>
</table>

Table 4

Changing LDL Distribution

<table>
<thead>
<tr>
<th>Improve LDL distribution</th>
<th>Impair LDL distribution</th>
<th>Minimal effect on LDL distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>High fat diets</td>
<td>Statins</td>
</tr>
<tr>
<td>Exercise</td>
<td>Beta blockers</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>Niacin</td>
<td>Weight gain</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>Fibrates</td>
<td>Sedentary lifestyle</td>
<td>Thiazides</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Hypothyroidism</td>
<td>Garlic</td>
</tr>
<tr>
<td>Alpha blockers</td>
<td>Poor diabetic control</td>
<td>Fiber</td>
</tr>
<tr>
<td>Thiazolidinediones (TZDs)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 1.

Health Belief Model

**Perceived Susceptibility**
One’s belief regarding the chance of getting a condition.
- Describe the risk of developing cardiovascular disease with hyperlipidemia
- Explain the need for treatment to start at an early age
- Use the Framingham risk calculator to quantify risk of CV events

**Perceived Severity**
One’s belief about how serious a condition and its sequelae are.
- Discuss the mortality related to the first myocardial infarction
- The long-term consequence of a myocardial infarction
- The long-term consequence of a cerebrovascular accident

**Cues to Action**
Strategies to activate one’s “readiness.”
- Family history of CV Disease
- CV event
- Education by provider
- Advanced lipid profile showing high risk LDL distribution
- Framingham risk calculator showing a high-risk

**Perceived Benefits**
One’s belief in the efficacy of the advised action to reduce the risk or seriousness of impact.
- Patient may understand that improving lipid profile reduce the risk of cardiovascular events
- Understanding that improved outcomes by prevention are difficult to see

**Perceived Barriers**
One’s belief about the tangible and psychological costs of the advised action.
- Adherence to cardiac diet
- Taking medication with no symptomatology
- Misconceptions of safety of medications
- Expense of medications
- Does not fully understand disease state

**Self-Efficacy**
One’s confidence in one’s ability to take action.
- Patient understands that prevention cannot occur without compliance
- Avoids disease progression or occurrence of cardiovascular events
- Lipid profile improves

Insulin Resistance causes a decreased conversion of VLDL and IDL into LDL
Figure 3.

**Improved LDL Distribution**

- VLDL → IDL → LDL

**Improved Insulin Sensitivity** allows Shifting of Atherogenic Cholesterol to Less Atherogenic Cholesterol