

FREE

CONTINUING EDUCATION LESSON



APPROVED FOR 1 CEU

Approved for 1 CE unit by the Canadian Council on Continuing Education in Pharmacy. File # 706-0208. Not valid for CE credits after April 3, 2011.

OBJECTIVES

Upon successfully completing this lesson, the pharmacist will be able to:

1. describe the pathophysiology of HDL-C levels in countering atherosclerosis
2. discuss the clinical evidence supporting the role of HDL-C levels in countering atherosclerosis
3. discuss the pharmacologic and nonpharmacologic approaches for increasing HDL
4. discuss the pharmaceuticals prescribed for increasing HDL-C
5. counsel patients on the cautions, side effects and contraindications for niacin use in increasing HDL-C

INSTRUCTIONS

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card or answer online at www.pharmacygateway.ca in the CE Online section, "More CCCEP-Approved" area.
2. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

ANSWERING OPTIONS

- A. For immediate results, answer online at www.pharmacygateway.ca in the CE Online section, "More CCCEP-Approved" area.
- B. Mail or fax the printed answer card to (416) 764-3937. Your reply card will be marked and you will be advised of your results within six to eight weeks in a letter from Rogers Publishing.

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Raising HDL cholesterol: benefits and strategies

By Rhonda Dorren B.Sc.Pharm

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INTRODUCTION

Lipid-management guidelines have incurred increasingly intensive measures for cholesterol lowering. Clinical research and evidence demonstrate that in Western populations, lower blood concentrations of low-density lipoprotein (LDL-C) are associated with lower incidence of cardiovascular disease (CVD), and is presently the primary focus of lipid-lowering therapy for prevention and treatment of coronary heart disease (CHD).¹ Concurrently, the importance of raising high-density lipoprotein (HDL-C) levels has been recognized. In the Framingham Heart Study, the HDL-C level was more potent as a risk factor for CHD than the level of LDL-C.²

The high level of residual risk among treated patients demonstrated in recent coronary prevention studies indicates the need for modification of other major components of the atherogenic lipid profile.³ HDL is a potent, independent risk factor with antiatheroscle-

rotic properties. HDL accelerates cholesterol efflux, and inhibits oxidation and inflammation. Research has begun to focus on drugs that can raise HDL-C and, currently, the most widely prescribed solution to increasing HDL-C is niacin.⁴ Thus, therapeutic intervention aimed at raising HDL-C, to reduce cardiovascular (CV) risk is a recommendation increasingly adopted by international treatment guidelines.⁵

EPIDEMIOLOGY

HDL-C levels are a strong inverse predictor of CV events.⁶ Epidemiological studies have shown that high concentrations of HDL-C (over 60 mg/dL, 1.55 mmol/L) have protective value against CVD such as ischemic stroke and myocardial infarction (MI), and low concentrations of HDL-C (below 40 mg/dL, 1.04 mmol/L for men, and below 50 mg/dL, 1.30 mmol/L for women) are a positive risk factor for these atherosclerotic diseases.

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HDL-C levels < 35.1 mg/dL, 0.90 mmol/L have a fourfold increased risk of CHD when compared to men with HDL-C levels \geq 35.1 mg/dL, 0.90 mmol/L.⁷ An incremental increase of 1.0 mg/dL (0.03 mmol/L), or about 2–3% greater HDL-C level, is associated with a 2–4% reduced risk of CV events independent of LDL-C.^{7,11} A similar inverse relationship between HDL-C and MI is known to be even stronger in women when compared with men.¹² These effects are statistically independent; thus, for moderate lipid changes, they are additive. Thus, a 30% HDL-C increase and a 40% LDL-C reduction would result in an approximately 70% CHD risk reduction, a revolution in CV prevention.^{9,13}

The predictive relationship between HDL-C levels after three months of treatment with statins and the time to the first major CV event has demonstrated that patients in the highest quintile of HDL-C level are at less risk for major CV events than those in the lowest quintile ($p=0.03$).^{6,14} Therefore, new therapies should aim at increasing HDL-C.

STRUCTURE OF HDL

HDL is the smallest lipoprotein and contains the least amount of lipid. It contains a lipid core of cholesteryl esters (CEs) and triglycerides (TGs) surrounded by phospholipids and specialized proteins known as apolipoproteins (apos). Apos are required for the structural integrity of lipoproteins. Moreover, apos direct metabolic interactions of lipoproteins with enzymes, lipid transport proteins and cell-surface receptors. HDL and its major apolipoprotein, apolipoprotein A-I (ApoA-I), are synthesized in both the liver and the intestine. The other primary apolipoprotein, apolipoprotein A-II (ApoA-II), is synthesized only in the liver and its function is unclear.^{15–17}

HDL METABOLISM

The metabolism of HDL is a complex process. HDL particles are formed in the plasma from the coalescence of individual phospholipid-apolipoprotein complexes.¹⁸

Cholesterol synthesized or deposited in peripheral tissues is returned to the liver via reverse cholesterol transport where HDL plays a central role. Reverse cholesterol transport can be divided into three steps: (1) efflux of cholesterol from peripheral cells, (2) intravascular metabolism and remodelling of HDL-C and (3) uptake of cholesterol by the liver. HDL

TABLE 1: 2006 CANADIAN UPDATED GUIDELINES FOR CARDIOVASCULAR RISK CATEGORIES AND LIPID TARGETS

CV risk categories and lipid targets			
Risk level	10-year CAD risk	Recommendations	Grade, level of evidence*
High†	$\geq 20\%$	Treatment target • Primary target: LDL-C <2.0 mmol/L • Secondary target: TC/HDL-C <4.0	Class I, Level A Class IIa, Level A
Moderate	10%–19%	Treat when: • TC/HDL-C ≥ 5.0 or • LDL-C ≥ 3.5 mmol/L	Class I, Level A Class I, Level A
Low	<10%	Treat when: • TC/HDL-C ≥ 6.0 or • LDL-C ≥ 5.0 mmol/L	Class IIa, Level A Class IIa, Level A

*Evidence grading criteria: Class I = evidence and/or general agreement that a given diagnostic procedure or treatment is beneficial, useful and effective; Class IIa = conflicting evidence and/or divergence of opinion about the usefulness and/or efficacy of the treatment; weight of evidence in favour; Level A = data from multiple randomized controlled trials or meta-analyses.

†High risk includes coronary artery disease, cerebrovascular disease, peripheral arterial disease, and most patients with diabetes. Source: Pearson et al. 2007 guidelines for the management of dyslipidemia and prevention of CV disease by pharmacists; CPJ Nov/Dec 2007;140(6):383-8.

is secreted by the liver or intestine as nascent (in the process of development) particles consisting of phospholipid and apoA-I which interact with peripheral cells (e.g., macrophages) to facilitate (by the ATP-binding cassette protein 1 [ABC1] the removal of excess free cholesterol (FC). HDL is then converted into mature cholesteryl ester (CE)-rich HDL via the plasma cholesterol-esterifying enzyme lecithin:cholesterol acyltransferase (LCAT), activated by apoA-I. CE may be removed by several different pathways, including selective uptake by the liver (e.g., the removal of lipid without the uptake of HDL proteins) mediated by the scavenger receptor class-B, type I (SR-BI). CE derived from HDL contributes to the hepatic-cholesterol pool used for bile acid synthesis. Cholesterol is eventually excreted from the body either as bile acid or as free cholesterol in the bile.^{16,17}

CE can be transferred from HDL to apolipoprotein (apo) B-containing proteins, such as very-low-density lipoproteins (VLDLs) and LDL, by CE transfer protein (CETP). Through uptake of LDL by the liver via hepatic LDL receptors, cholesterol can then be returned to the liver, where it may eventually be excreted as bile.^{16,17}

Rates of reverse cholesterol transport cannot be determined solely by steady-state levels of HDL-C and apoA-I. The development of atherosclerosis may also be affected by genetic defects (e.g., hypoalphalipoproteinemia) in HDL metabolism or therapeutic interventions (e.g., cigarette smoking, obesity [visceral fat]

and certain drugs [beta-blockers, androgenic steroids/progestins]) that alter HDL metabolism.^{16,17,19}

HDL IN CONSENSUS GUIDELINES

With the introduction of well-researched drugs, current lipid therapy often incorporates use of combination therapies. Reduction in major vascular events with statin therapy results in a 33% reduction in risk after the first year with a standard dose of a statin.²⁰

Hyperlipidemia, particularly an elevated LDL-C level and/or elevated total cholesterol (TC) to HDL-C (TC/HDL-C) ratio is recognized as a major independent risk factor for CAD.²¹ Consequently, Canadian national guidelines including pharmacists' guidelines, have been promulgated and regularly updated on the basis of accumulating clinical trial evidence to assist healthcare practitioners with diagnosis and treatment of patients with dyslipidemia (Table 1). In Canada, pharmacists have guidelines identifying their role in the management of dyslipidemia and when they should actively recognize and recommend dyslipidemia screening.^{22,23}

The guidelines advocate the importance of patient awareness and emphasis to patients that cholesterol-lowering therapies are generally well tolerated. Monitoring patient performance and outcomes via a thorough medication history, and an evaluation of patient-specific laboratory data, provides evidence of the efficacy of treatment.^{23,24}

CLINICAL STRATEGIES TO ELEVATE HDL-C

TC/HDL-C ratio

The TC/HDL-C ratio is a key treatment goal in the current Canadian Cholesterol Treatment Guidelines and is detailed on the majority of laboratory lipid profiles. The TC/HDL-C ratio is closely related to the presence and extent of coronary artery narrowing.²³

Once LDL-C targets have been achieved, the following approaches are recommended for achievement of the TC/HDL-C ratio target.²³

- Patients with high TGs (triglycerides): intensify dietary therapy and exercise, focus on weight loss, restrict refined carbohydrates and alcohol, and increase intake of omega-3 fatty acids.
- Patients with low HDL-C: increase aerobic exercise, increase intake of monounsaturated fats, moderate alcohol intake (if TGs are not significantly elevated); weight loss and smoking cessation are beneficial.
- For patients with low HDL-C or mildly high TGs: a further increase in statin dose may achieve the TC/HDL-C ratio target, even if the LDL-C target has been reached.
- For patients with combined dyslipidemia and low HDL-C: the combination of a statin with niacin or a fibrate should be considered.²³

NONPHARMACOLOGIC THERAPY

Antioxidant vitamins

Observational studies suggest that increased dietary intake of antioxidant vitamins may be associated with lower risks of CHD. However, the MRC/BHF Heart Protection Study (n=20,536) demonstrated that the antioxidant vitamins (including 600 mg vitamin E, 250 mg vitamin C and 20 mg beta-carotene daily) did not produce any significant reductions in five-year mortality from, or incidence of, any type of vascular disease, cancer or other major outcome.²⁵

Fish oils (omega-3 fatty acids)

Dietary modification to increase the consumption of cold-water fish (e.g., salmon) rich in polyunsaturated fats may help to raise HDL-C. Patients with familial combined hyperlipidemia (several classes of lipids are elevated), treated with omega-3 fatty acids for eight weeks demonstrated an increase in HDL-C by 8%.²⁶ For patients with moderate

hypertriglyceridemia, the addition of salmon oil (1 g–3 g three times daily) to statin therapy is safe, and may be useful in lowering TG levels and achieving the target TC/HDL-C ratio.²²

Obesity

HDL-C may decline with obesity, and decreases in body mass index have been associated with increases in HDL-C.²⁷

Regular aerobic exercise

Exercise training trials have demonstrated an average increase in HDL-C of 4.6%.^{28–30} The HEalth, RiSk factors, exercise Training, And GENetics (HERITAGE) study, of normolipidemic subjects (n=675) demonstrated an increased HDL-C by 3% among the 299 men and 376 women studied.^{31,32} Canadian guidelines suggest regular physical activity of 60 minutes of light, 30–60 minutes of moderate, or 20–30 minutes of vigorous activity for 4–7 days per week.²²

Diet

For patients with low levels of HDL-C, increased intake of monounsaturated fats, moderate alcohol intake (if TGs are not significantly elevated), and weight loss are beneficial. Moderate alcohol (beer and wine) use is associated with increased HDL-C in a dose-dependent fashion (where “moderate” is defined as 2–3 drinks a day for men, 1–2 drinks a day for women).^{26,33}

Smoking

Smoking has been associated with low HDL-C as well as increased oxidative stress, endothelial injury and a range of vascular and other adverse sequelae. Conversely, smoking cessation has been associated with significant increases in HDL-C.³⁴

PHARMACOLOGIC THERAPY

Four different therapeutic approaches for increasing HDL-C may be beneficial: fibrate, niacin (nicotinic acid), statin and direct injection of HDL-like particles in patients with acute coronary syndrome. Several drugs raise HDL levels: statins 5%–10%, niacin 15%–35%, and fibrates 10%–15%.¹⁶

Cholesteryl ester transfer protein (CETP) inhibitors

The ILLUMINATE (Investigation of Lipid

Level Management to Understand its Impact in Atherosclerotic Events) trial investigating the CETP inhibitor torcetrapib was terminated because of an imbalance of mortality and CV events and therefore has no role in therapy at this time.³⁵

Statins

One-third of dyslipidemic patients treated with statins display low HDL-C levels; however, statins can also produce increases in HDL levels.³⁶ The extent of this effect, an increase of 5–11%, depends on the molecule and the dose.³⁷ The STELLAR study which assessed statin lipid-modifying effects demonstrated that rosuvastatin 10–40 mg was capable of achieving the highest increase in HDL-C levels (6–12%) over its dose range compared with atorvastatin 10–80 mg (2%–8%), simvastatin 10–80 mg (5%–7%), and pravastatin 10–40 mg (3%–6%).³⁸ The clinical significance of this statin-related increase in HDL is poorly known.

Fibrates

All fibrate derivatives share common hypolipidemic effects characterized by a reduction in LDL-C, a marked reduction in plasma triglyceride levels and an elevation in HDL-C levels.³⁹ Similarly, all fibrates, with the exception of clofibrate, increase HDL-C concentration by 4.1 mg/dL (0.11 mmol/L) or 10%. Different fibrates, such as bezafibrate (11%), gemfibrozil (11%) and fenofibrate (10%) demonstrate similar increases in HDL-C levels, an effect that is more pronounced in patients with combined hyperlipidemia and/or hypercholesterolemia (11%–16%).

Only the Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT) and the Helsinki Heart Study (HHS) showed statistically significant reductions in major coronary events. The Veterans Affairs High-Density Lipoprotein Intervention Trial confirmed the efficacy of gemfibrozil (1200 mg) in a distinct population of patients (n=2,531) selected on the basis of a low HDL-C. It was shown that the changes in HDL-C drove the demonstrated benefit observed of a significant 22% reduction for CV events of all types.^{40,42} In summary, evidence from the fibrate trials has shown that they reduce risk in the range of 15%–20% for CHD and CVD and reduce risk of major coronary events by 25%.^{41–43}

Combination fibrate and statin

Fibrates are also recommended as adjunct therapy for patients receiving statins whose LDL-C is not reduced to goal levels. The SAFARI trial demonstrated marked lowering of triglycerides, VLDL cholesterol, an additional reduction in LDL-C, and a striking rise in HDL-C.⁴⁴ The combination of a statin and a fibrate may, however, raise the risk of myopathy and rhabdomyolysis. There is a possibility of benefit from combination therapy with simvastatin and simvastatin plus fenofibrate, which is not associated with an inhibition of statin metabolism and may explain the lower incidence of myopathy.

Fibrates alone may be used with caution at low doses in cases of mild renal impairment.⁴³ Gemfibrozil is associated with a higher risk of myotoxicity and should not be used in combination therapy with statins.²²

Niacin

Therapy with niacin (nicotinic acid), a water-soluble B vitamin, is the most effective HDL-raising agent currently available. It significantly reduces LDL-C, TG, and lipoprotein(a) (Lp-a) levels, and increases HDL-C, producing significant improvements in both CAD and clinical outcomes.⁴⁵⁻⁴⁷ The average increase of HDL-C with niacin is almost twice (7%–23%), the increase observed with fibrates while the effect on triglycerides and LDL-C is similar.^{48,49} Niacin has been shown to have CV benefit when used alone or in combination with statins in several clinical trials.⁵⁰ The addition of niacin (nicotinic acid) to primary statin therapy is a logical approach to dyslipidemia management, given their complementary mechanism of action.

Benefits of niacin are observed long after (nearly a decade) its discontinuation. The long-term efficacy and safety of five lipid-influencing drugs, niacin, clofibrate, dextrothyroxine and conjugated equine estrogens in men (n=8,341, aged 30–64 years) with previous MI in patients given nicotinic acid 3 g/day or below, over a five- to seven-year follow-up, demonstrated that treatment with niacin reduced all-cause mortality by 11% ($p=0.0004$) compared with placebo.^{50,51}

Placebo-controlled studies have been conducted to establish the efficacy and safety of extended-release niacin (Niaspan[®]) tablets dosed once daily at bedtime. Hypercholesterolemic patients (n=120) demonstrated a sig-

TABLE 2: MONITORING OF VARIOUS LIPID-LOWERING DRUGS*

Parameter	Lipid-lowering therapies in which parameters should be monitored	Signs and symptoms that may accompany parameter	Drug-drug combinations that increased likelihood of adverse event
AST/ALT	Statins Fibrates Niacin IR and SR Ezetimibe	Abdominal pain, jaundice, dark urine, malaise, fatigue	Statin + fibrate [†] Statin + ezetimibe Statin + niacin
CK	Statins Ezetimibe ¹²	Muscle aches, pains, cramps, weakness, absent reflexes, fatigue	Statin + ezetimibe Statin + fibrate Statin + niacin
Glucose	Niacin IR and SR	Asymptomatic	
Uric acid	Niacin IR and SR	Asymptomatic; may develop gout	
TSH	Statins Niacin IR and SR	Muscle aches, pains, cramps, weakness, fatigue	
Gastrointestinal upset	Bile acid resins Fibrates Statins Niacin	Abdominal bloating/pain, belching, flatulence, nausea, constipation, GERD	

AST = aspartate aminotransferase; ALT = alanine aminotransferase; CK = creatinine kinase; TSH = thyroid-stimulating hormone; GERD = gastroesophageal reflux disease.
**The bile acid sequestrants (e.g., cholestyramine) do not require laboratory monitoring.*
[†]Gemfibrozil appears to confer a greater risk when used in combination with statins compared to bezafibrate or fenofibrate.
Source: Pearson et al. 2007 guidelines for the management of dyslipidemia and prevention of CV disease by pharmacists; CPJ Nov/Dec 2007;140(6):383-8.

nificant rise in HDL-C levels, estimated to be 17% at 1000 mg/day and 23% at 2000 mg/day doses.⁵² After eight weeks, hypercholesterolemic adult men and women (n=223) receiving extended-release niacin (niacin ER) versus plain niacin demonstrated comparable efficacy-raising HDL-C (20%/17%), respectively ($p<=0.5$ in all instances).⁵³ Patients (n=87 extended-release niacin; n=44 placebo) treated for 25 weeks demonstrated significant increases from baseline in levels of HDL-C at 500 mg/day reaching 30% at 3000 mg/day ($p<=0.05$).⁵⁴ Adverse effects were most commonly flushing and gastrointestinal disturbance in all studies, and although the incidence of flushing was significant, these episodes were generally well tolerated.

Niacin may be administered successfully to patients with diabetes and peripheral arterial disease who do not tolerate statins or fibrates.⁵⁵ Patients receiving immediate-release niacin up to 3 g daily for 48 weeks have demonstrated increases of 29% in HDL-C; glucose levels rose moderately but significantly, by 8.7 mg/dL (0.48 mmol/L) in men with diabetes and 6.3 mg/dL (0.35 mmol/L) in those without diabetes.

Niacin ER and immediate-release niacin

(IR) have demonstrated comparable efficacy at equivalent doses. Lp-a was significantly lower with niacin ER than niacin IR ($p<0.05$). High Lp-a in blood is a risk factor for CHD, CVD, atherosclerosis, thrombosis and stroke.⁵³

Combination statin and niacin

When combining a statin with niacin, dramatic improvement of primary endpoints of major coronary events (90% reduction) has been demonstrated and has also been shown to raise HDL-C, and further lower triglycerides.⁴⁹

The ARBITER 2 study demonstrated a slowdown in the progression of the rate of carotid artery intima-media thickness (CIMT) after a combined therapy of statins plus ER (1 g/day). Patients (n=167) with known CHD (mean age 67 years) and moderately low levels of HDL-C, receiving once-daily niacin ER (1000 mg) or placebo in combination with statin therapy for one year demonstrated that CIMT progression was 68% slower, and was statistically unchanged from baseline (0.014 mm/year), in the niacin group.⁵⁰ The ARBITER-3 study (n=130) demonstrated that extended-release niacin added to statin therapy significantly increased HDL-C and induced atherosclerosis

regression measured by CIMT over 24 months.⁵⁶

The HDL Atherosclerosis Treatment Study (HATS) demonstrated that patients with CAD (normal LDL-C levels and low HDL-C) had marked clinical and angiographically measurable benefits when treated with a combined therapy of simvastatin plus niacin. Antioxidant vitamins in combination with simvastatin plus niacin slowed coronary progression but had a suppressive effect on the increase in total HDL-C and no effect on clinical events. Antioxidant vitamins alone had no benefit on progression or on clinical events, providing no justification for their use in CHD prevention. Patients (n=160, average age 53 years) were given combined low-dose simvastatin (10–20 mg/day) and high-dose niacin (slow-release or immediate-release, 2–4 g/day) with and without antioxidants, or antioxidants alone. This trial demonstrates the use of combination lipid-altering drugs with complementary actions may not only provide superior effects on multiple lipid parameters as compared with either agent alone, but may also improve CHD outcomes.

Simvastatin and niacin significantly reduced LDL-C and triglycerides by an average of 42% and 36%, respectively, while increasing HDL-C by 26%. The addition of antioxidants resulted in similar decreases in LDL-C and triglycerides but blunted the HDL-C increase, resulting in a +18% change for simvastatin plus niacin plus antioxidant vitamins.^{57,58}

Doses of 1000 mg of extended-release niacin (Niaspan[®]) added to varying doses and types of statin therapy: atorvastatin (n=44), simvastatin (n=13), pravastatin and fluvastatin (n=1) were found to be safe and highly effective in improving lipid parameters.⁵⁹ Outcome measures were associated with an approximate 30% increase in HDL-C, and an approximate decrease of 28% in triglycerides and 8% in LDL-C.

Atorvastatin demonstrated a preferred LDL-C effect, and niacin had a preferred HDL-C effect in a study of patients with dyslipidemia randomly assigned to atorvastatin 10 mg or immediate-release niacin 3000 mg daily for 12 weeks following a low-fat diet stabilization period.⁶⁰

Although monotherapy with niacin or fibrates has been shown to prevent CVD events, there is currently insufficient evidence for statin plus niacin and evidence is lacking

for fibrate plus niacin combinations to reduce CV risk in patients with diabetes. For high-risk individuals who have a persistent elevation of TC/HDL-C despite achieving the primary LDL-C target of <2.0 mmol/L, niacin or fibrates can be added to statin therapy at the physician's discretion.⁶¹

Combination regimens of statins with niacin, ezetrol

The COMPELL study demonstrated low to moderate-dose combination therapy with a statin and niacin ER provided broad control of lipids and lipoproteins independently associated with CHD. In this open-label, multicentre, 12-week study (n=292, 50% women), patients with known CHD risk factors were randomized to four parallel arms: atorvastatin/niacin ER, rosuvastatin/niacin ER, simvastatin/ezetimibe, or rosuvastatin alone. Statin/niacin ER combination regimens increased HDL-C and large HDL (HDL2) and lowered triglycerides and Lp-a significantly more than other regimens.⁶²

MONITORING OF LIPID-LOWERING DRUGS

Table 2 outlines the parameters for lipid-lowering therapies that require monitoring.²² For comprehensive prescribing information consult product monographs.

COUNSELLING ON THE USE OF NIACIN

“Flush-free” niacin preparations are ineffective because they contain little bioavailable niacin.⁶³ Inositol hexaniacinate (inositol nicotinate or no-flush niacin), has very limited data available. No-flush niacin may not be effective for the management of dyslipidemia at lower doses, and doses of >2400 mg/day may be necessary to provide any added benefit for dyslipidemia management, but this remains unestablished. The safety profile of inositol hexaniacinate is not well understood.^{64,65}

Niacin is available in three formulations (immediate and extended release, and long-acting), which differ with respect to their safety and, in some cases, efficacy profiles.⁶⁶ All niacin formulations are associated with flushing. Crystalline niacin (immediate-release niacin) is taken three times daily and is associated with elevations in blood glucose levels. Long-acting niacin is taken once daily and is associated with significantly reduced flushing, but its metabolism increases the risk

of hepatotoxic effects. Extended-release niacin, also given once daily, has an absorption rate intermediate between the other formulations and is associated with fewer flushing and gastrointestinal symptoms without increasing hepatotoxic risk.⁶⁶

Extended-release niacin (Niaspan[®]), taken once daily at bedtime, has a better tolerability profile than immediate-release or long-acting niacin, and is the only Health Canada-approved niacin indicated for the treatment of mixed dyslipidemia.^{22,67}

ADVERSE REACTIONS OF NIACIN

Widespread use of niacin for dyslipidemia has been limited by symptoms of flushing.⁴⁹ Administration of cyclooxygenase (COX) inhibitors (e.g., aspirin) or NSAIDs (e.g., ibuprofen) before ingestion of niacin can attenuate the niacin-induced cutaneous reactions in most patients. For best results, non-enteric coated ASA is recommended.^{68,69}

DOSING OF NIACIN

For dosing instructions see Table 3.

WARNINGS AND PRECAUTIONS OF NIACIN

Niacin ER preparations should not be substituted for equivalent doses of immediate-release (crystalline) niacin or nicotinic acid. For patients switching from immediate-release niacin or nicotinic acid to niacin ER, therapy should be initiated with low doses and the niacin ER should then be titrated to the desired therapeutic response.⁶⁹

CONTRAINDICATIONS OF NIACIN

Niacin ER is contraindicated in patients with active liver disease or unexplained persistent elevations of serum transaminases, active peptic ulcer or active bleeding.⁶⁹

Immediate-release niacin is contraindicated in patients with active liver disease, peptic ulcer disease, hyperuricemia with history of gouty arthritis, controlled hyperglycemia or severe hypertension.⁶⁹

PHARMACIST'S ROLE

Pharmacists can take an active role in, and responsibility for, medication management and health outcomes in patients with dyslipidemia. The 2006 Canadian Cardiovascular Society (CCS) position statement, “Recommendations for the Diagnosis and Treatment

TABLE 3: NIACIN DOSING

Take non-enteric coated ASA (or NSAID e.g., ibuprofen) 30 minutes prior to taking niacin. Avoid alcohol, spicy foods and hot beverages near the time of taking niacin.

Extended-release niacin dosing

Titration schedule	Weeks	Daily dose
Initial titration schedule	1 to 4 5 to 8	500 mg 1000 mg
Further titration schedule*	After week 8	1500 mg 2000 mg

Take at bedtime after a low-fat snack, minimizes daytime flushing. After Week 8, titrate patient response and tolerance. If response to 1000 mg daily is inadequate, increase dose to 1500 mg daily; may subsequently increase dose to 2000 mg daily. Daily dose should not be increased more than 500 mg in a four-week period, and doses above 2000 mg daily are not recommended.

Immediate-release niacin dosing

Titration schedule	Double dose every 5 days	Daily dose
Initial titration schedule	1–5	50 mg three times daily
Further titration schedule	5–10	100 mg three times daily
Further titration schedule	10–15	4.0 g/day maximum daily dose

Take on a full stomach to help reduce gastrointestinal distress. Starting at a low dose and titrating slowly may reduce potential adverse reactions and achieve treatment goals by improving adherence to the regimen.

Source: CPS 2007. Monograph. Niaspan, Niacin

of Dyslipidemia and Prevention of Cardiovascular Disease,” has been adapted and expanded, emphasizing where the knowledge and skills of pharmacists should be applied in the management of patients with dyslipidemia. The Canadian pharmacist-practice guidelines are a part of the continuing national effort to recognize and advance “the responsible and patient-centred role of the pharmacist” in chronic disease management.^{61,70}

All clinicians should be aware that HDL-C is one of the single strongest predictors of CHD and, therefore, needs to be measured in all patients at risk for CHD.¹⁸ In subjects with low HDL-C, look for specific causes and give advice to change inappropriate lifestyle components associated with low HDL-C, such as smoking, lack of physical exercise and being overweight. Patients with very low HDL-C need a thorough evaluation by specialist physicians.

CONCLUSION

A large number of high-risk individuals have reduced HDL-C levels, resulting in increased residual risk for CVD. Niacin is the most effective agent currently available for raising HDL-C; however, it has limited tolerability and compliance.

REFERENCES

- Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002 Jul 6;360(9326):7-22.
- Kannel WB. The Framingham Study: Its 50-year legacy and future promise. *J Atheroscler Thromb* 2000;6(2):60-66; *Am J Hypertens*. 2000;13:3s10s.
- Koro CE, Bowlin SJ, Stump TE, et al. The independent correlation between high-density lipoprotein cholesterol and subsequent major adverse coronary events. *Am Heart J* 2006;151(3):755.e1-755.e6.
- Brooks L. Raising low high-density lipoprotein (HDL) cholesterol. *AHA* 2006: New Approaches to Treating Dyslipidemia. Medscape Pharmacists. Available at www.medscape.com, accessed January 10, 2008.
- Chapman MJ, Assmann G, Fruchart JC, et al. Raising high-density lipoprotein cholesterol with reduction of CV risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C. *Curr Med Res Opin* 2004 Aug;20(8):1253-68.
- Barter P, Gotto AM, LaRosa JC, et al. HDL Cholesterol, very low levels of LDL cholesterol, and CV events. *N Engl J Med* 2007 Sep 27;357(13):1301-10.
- Assmann G, Schulte H, von Eckardstein A, et al. High-density lipoprotein cholesterol as a predictor of coronary heart disease risk: the PROCAM experience and pathophysiological implications for reverse cholesterol transport. *Atherosclerosis* 1996;124(Suppl.):S11-20.
- Wilson PW, Anderson KM, Castelli WP. Twelve-year incidence of coronary heart disease in middle-aged adults during the era of hypertensive therapy: the Framingham offspring study. *Am J Med* 1991 Jan;90(1):11-6.
- Brown BG, Stukovsky KH, Zhao X. Simultaneous low-density lipoprotein-C lowering and high-density lipoprotein-C elevation for optimum CV disease prevention with various drug classes, and their combinations: a meta-analysis of 23 randomized lipid trials. *Curr Opin Lipidol* 2006;17:631-6.
- Assmann G, Cullen P, Schulte H. The Munster Heart Study (PROCAM): results of follow-up at 8 years. *Eur Heart J* 1998; 19 (Suppl A):A2-A11.

- Gordon DJ, Probstfield JL, Garrison RJ et al. High-density lipoprotein cholesterol and CV disease: four prospective American studies. *Circulation* 1989;79:8-15.
- Gordon T, Castelli WP, Hjortland MC, et al. High-density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. *Am J Med* 1977;62:707-14.
- Phillips NR, Waters D, Havel RJ. Plasma lipoproteins and progression of coronary artery disease evaluated by angiography and clinical events. *Circulation* 1993 Dec;88(6):2762-70.
- Waters DD, LaRosa JC, Barter P, et al. Effects of high-dose atorvastatin on cerebrovascular events in patients with stable coronary disease in the TNT (treating to new targets) study. *J Am Coll Cardiol* 2006 Nov 7;48(9):1793-9. Epub 2006 Oct 17.
- Shah PK, Kaul S, Nilsson J, et al. Exploiting the vascular protective effects of high-density lipoprotein and its apolipoproteins: an idea whose time for testing is coming, part II. *Circulation* 2001;104:2498-502.
- Rader DJ. Toward a higher standard: raising HDL in clinical practice. *Medscape Cardiology* 8(1),2004. Available at www.medscape.com, Date accessed January 10th, 2008.
- Rader DJ. Physiology and Pathophysiology of HDL metabolism. *Lipids Online*. Available at www.lipidsonline.org, accessed January 18, 2008.
- Bruckert E, Hansel B. HDL-C is a powerful lipid predictor of CV diseases. *Int J Clin Pract* 2007;61(11):1905-13.
- Francis GA, Perry RJ. Targeting HDL-mediated cellular cholesterol efflux for the treatment and prevention of atherosclerosis. *Clin Chim Acta* 1999 Aug;286(1-2):219-30.
- Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005 Oct 8;366(9493):1267-78. Epub 2005 Sep 27.
- Yusuf S, Hawken S, Öunpuu S, et al., on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364(9438):937-52.
- McPherson R, Frohlich J, Fodor G, et al. Canadian CV Society position statement—recommendations for the diagnosis and treatment of dyslipidemia and prevention of CV disease. *Can J Cardiol* 2006 Sep;22(11):913-27.
- Pearson GJ, Thompson AE, Semchuk W. 2007 guidelines for the management of dyslipidemia and prevention of CV disease by pharmacists. *CJPM* 2007;140(6):386-88.
- Thompson PD, Clarkson PM, Rosenson RS. An assessment of statin safety by muscle experts. *Am J Cardiol* 2006;97[suppl]:69C-76C.
- Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002 Jul 6;360(9326):23-33.
- Calabresi L, Villa B, Canavesi M, et al. An omega-3 polyunsaturated fatty acid concentrate increases plasma high-density lipoprotein 2 cholesterol and paraoxonase levels in patients with familial combined hyperlipidemia. *Metabolism* 2004;53:153-8.
- Wilsgaard T, Arnesen E. Change in serum lipids and body mass index by age, sex, and smoking status: the Tromsø study 1986-1995. *Ann Epidemiol* 2004;14:265-73.
- Thompson PD, Buchner D, Pina IL, et al. Exercise and physical activity in the prevention and treatment of atherosclerotic CV disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation and Prevention) and the Council on Nutrition, Physical Activity and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003 Jun 24;107(24):3109-16.
- Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc* 2001 Jun;33(6 Suppl):S502-15;discussion S528-9.
- Leon AS, Sanchez O. Meta-analysis of the effects of aerobic exercise training on blood lipids. *Circulation* 2001;104(suppl II):II-414-II-415.
- Leon AS, Rice T, Mandel S, et al. Blood lipid response to 20 weeks of supervised exercise in a large biracial population: the HERITAGE Family Study. *Metabolism* 2000;49:513-20.

32. Couillard C, Despres JP, Lamarche B, et al. Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arterioscler Thromb Vasc Biol* 2001; 21:1226-32.
33. Ashen MD, Blumenthal RS. Clinical practice. Low HDL cholesterol levels. *N Engl J Med* 2005 Sep 22;353(12):1252-60.
34. Maeda K, Noguchi Y, Fukui T. The effects of cessation from cigarette smoking on the lipid and lipoprotein profiles: a meta-analysis. *Prev Med* 2003;37:283-90.
35. In interests of patient safety, Pfizer stops all torcetrapib clinical trials; company has notified FDA and is in the process of notifying all clinical investigators and other regulatory authorities. December 2, 2006. Available at: www.pfizer.com. Accessed January 10, 2008.
36. Bruckert E, Baccara-Dinet M, McCoy F, Chapman J. High prevalence of low HDL-cholesterol in a pan-European survey of 8,545 dyslipidaemic patients. *Curr Med Res Opin* 2005;21:1927-34.
37. Deedwania PC, Hunninghake DB, Bays HE, et al. STELAR Study Group. Effects of rosuvastatin, atorvastatin, simvastatin, and pravastatin on atherogenic dyslipidemia in patients with characteristics of the metabolic syndrome. *Am J Cardiol* 2005;95:360-6.
38. Nissen SE, Nicholls SJ, Sipahi I, et al. ASTEROID Investigators. Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial. *JAMA* 2006;295:1556-65.
39. Birjmohun RS, Hutten BA, Kastelein JPD, et al. Efficacy and safety of high-density lipoprotein cholesterol-increasing compounds: a meta-analysis of randomized controlled trials. *J Am Coll Cardiol* 2005;45:185-97.
40. Robins SJ. Targeting low high-density lipoprotein cholesterol for therapy: lessons from the Veterans Affairs High-density Lipoprotein Intervention Trial. *Am J Cardiol* 2001;88:19N-23N.
41. Wierzbicki AS. FIELDS of dreams, fields of tears: a perspective on the fibrate trials. *Int J Clin Pract* 2006;60:442-9.
42. Otvos JD, Collins D, Freedman DS et al. Low-density lipoprotein and high-density lipoprotein particle subclasses predict coronary events and are favorably changed by gemfibrozil therapy in the Veterans Affairs High-Density Lipoprotein Intervention Trial. *Circulation* 2006;113:1556-63.
43. Keech A, Simes RJ, Barter P, et al. Effects of long-term fenofibrate therapy on CV events in 9,795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet* 2005; 366: 1849-61.
44. Grundy SM, Vega GL, Yuan Z, et al. Effectiveness and tolerability of simvastatin plus fenofibrate for combined hyperlipidemia (the SAFARI trial). *Am J Cardiol* 2005;95:452-8.
45. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Circulation* 2002;106:3143-421.
46. Kamanna VS, Kashyap ML. Mechanism of action of niacin on lipoprotein metabolism. *Curr Atheroscler Rep* 2000 Jan;2(1):36-46.
47. Carlson LA. Nicotinic acid: the broad-spectrum lipid drug. A 50th anniversary review. *J Int Med* 2005;258:94-114.
48. McCormack PL, Keating GL. Prolonged-release nicotinic acid: a review of its use in the treatment of dyslipidaemia. *Drugs* 2005;65:2719-40.
49. The Coronary Drug Project Research Group. Clofibrate and niacin in coronary heart disease. *JAMA* 1975;231:360-81.
50. Taylor AJ, Sullenberger LE, Lee HJ, et al. Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) 2: a double-blind, placebo-controlled study of extended-release niacin on atherosclerosis progression in secondary prevention patients treated with statins. *Circulation* 2004 Dec 7;110(23):3512-17. Epub 2004 Nov 10.
51. Canner PL, Berge KG, Wenger NK, et al. Fifteen-year mortality in Coronary Drug Project patients: long-term benefit with niacin. *J Am Coll Cardiol* 1986;8:1245-55.
52. Morgan JM, Capuzzi DM, Guyton JR, et al. Treatment Effect of Niaspan, a Controlled-release Niacin, in Patients With Hypercholesterolemia: a placebo-controlled Trial. *J Cardiovasc Pharmacol Ther* 1996 Jul;1(3):195-202.
53. Knopp RH et al. Equivalent efficacy of a time-release form of niacin (Niaspan) given once-a-night versus plain niacin in the management of hyperlipidemia. *Metabolism*. 1998 Sept;47(9):1097-104.
54. Goldberg A, Alagona P Jr, Capuzzi DM, et al. Multiple-dose efficacy and safety of an extended-release form of niacin in the management of hyperlipidemia. *Am J Cardiol* 2000 May 1;85(9):1100-05.
55. Elam MB, Hunninghake DB, Davis KB, et al. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: a randomized trial. *Arterial Disease Multiple Intervention Trial*. *JAMA* 2000;284:1263-70.
56. Taylor AJ, Lee HJ, Sullenberger LE. The effect of 24 months of combination statin and extended-release niacin on carotid intima-media thickness: ARBITER 3 trial. *Curr Med Res Opin* 2006 Nov;22(11):2243-50.
57. Brown GC, Zhao Z-Q, Chait A, et al. Simvastatin and Niacin, Antioxidant Vitamins, or the Combination for the Prevention of Coronary Disease. *N Engl J Med* 2001;345:1583-92.
58. Zhao XQ, Morse JS, Dowdy AA, et al. Safety and tolerability of simvastatin plus niacin in patients with coronary artery disease and low high-density lipoprotein cholesterol (The HDL Atherosclerosis Treatment Study). *Am J Cardiol*. 2004 Feb 1;93(3):307-12.
59. Wolfe ML, Vartanian SF, Ross JL, et al. Safety and effectiveness of Niaspan when added sequentially to a statin for treatment of dyslipidemia. *Am J Cardiol* 2001;87:476-9.
60. McKenney JM, McCormick LS, Schaefer EJ, et al. Effect of niacin and atorvastatin on lipoprotein subclasses in patients with atherogenic dyslipidemia. *Am J Cardiol* 2001 Aug 1;88(3):270-4.
61. Canadian Diabetes Assoc. Clinical Practice Guidelines Expert Committee. Dyslipidemia in Adults with Diabetes. *CJD* 2006;30(3):230-40.
62. McKenney JM, Jones PH, Bays HE, et al. Comparative effects on lipid levels of combination therapy with a statin and extended-release niacin or ezetimibe versus a statin alone (the COMPELL study). *Atherosclerosis* 2007 Jun;192(2):432-7. Epub 2007 Jan 19.
63. Meyers CD, Carr MC, Park S, et al. Varying cost and free nicotinic acid content in over-the-counter niacin preparations for dyslipidemia. *Ann Intern Med* 2003 Dec 16;139(12):996-1002.
64. No authors listed. Inositol hexaniacinate. *Altern Med Rev* 1998;3:222-3.
65. Taheri R. No-Flush Niacin for the Treatment of Hyperlipidemia. Expert Viewpoint. Medscape Pharmacists. Available at <http://www.medscape.com/viewarticle/447528>, accessed January 15, 2008.
66. McKenney J. New perspectives on the use of niacin in the treatment of lipid disorders. *Arch Intern Med* 2004 Apr 12;164(7):697-705.
67. McKenney JM, Proctor JD, Harris S, et al. A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. *JAMA* 1994 Mar 2;271(9):672-7.
68. Cheng K, Wu T, Wu KK, et al. Antagonism of the prostaglandin D2 receptor 1 suppresses nicotinic acid-induced vasodilation in mice and humans. *Proc Natl Acad Sci USA* 2006 April 25;103(17):6682-7.
69. Compendium of Pharmaceuticals and Specialties (CPS) 2007. Monographs: Niacin, Niaspan. Canadian Pharmacists Association.
70. Tsuyuki RT. CPJ as an agent of change (editorial). *Can Pharm J* 2007;140:10. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Dyslipidemia in adults with diabetes. *Can J Diabetes* 2006;30(3):230-40.

QUESTIONS - Answer online at [pharmacygateway.ca](http://www.pharmacygateway.ca), CE section, "More CCCEP-approved" dept.

1. Which percentage in changes in the following lipid values could result in a 70% CHD reduction (increase in HDL-C and decrease in LDL-C)?

- a) 10% HDL-C and 40% LDL-C
- b) 30% HDL-C and 40% LDL-C
- c) 20% HDL-C and 10% LDL-C
- d) 20% HDL-C and 20% LDL-C

2. A major component of HDL is:

- a) lecithin:cholesterol acyltransferase (LCAT)
- b) low-density lipoprotein (LDL)
- c) apolipoprotein A-I (ApoA-I)
- d) cholesteryl ester transfer protein (CETP)

3. Where is HDL secreted from?

- a) intestine
- b) macrophages
- c) kidney
- d) pancreas

4. HDL metabolism may be altered by:

- a) LDL metabolism
- b) apolipoprotein A-II (Apo-AII)
- c) cigarette smoking
- d) plasma protein

5. Reverse cholesterol transport is a process wherein cholesterol:

- a) from peripheral tissues is returned to the liver

- b) is transported from plasma to peripheral tissues
- c) is transported to the kidneys for excretion
- d) from peripheral tissues is transported to the intestine

6. Thirty minutes prior to taking a dose of niacin for lipid lowering, patients are advised to:

- a) Consume a moderate amount of alcohol.
- b) Take an enteric coated ASA.
- c) Take acetaminophen.
- d) Take non-enteric coated ASA.

7. The TC/HDL-C ratio is:

- a) a primary lipid treatment target and LDL-C is the secondary target
- b) related to coronary artery narrowing
- c) rarely measured in laboratory lipid profiles
- d) not a key target in the Canadian Cholesterol Treatment Guidelines

8. Patient R.M. presents with lipid levels of LDL-C and triglycerides in the normal range but needs to raise his HDL-C. Moderate intake of alcohol may be suggested. True or false?

- a) True
- b) False

9. Patient P.L. presents with LDL-C levels in the normal range, high TGs and needs improvement in the TC/HDL-C ratio. Which answer offers the most helpful suggestion?

- a) Increase refined carbohydrates.
- b) Decrease intake of omega-3 fatty acids.
- c) moderate alcohol consumption
- d) dietary therapy, exercise

10. Patient T.K. has combined dyslipidemia (elevated LDL-C, high TGs) and low HDL-C. Which combination therapy may be most beneficial?

- a) fibrate with niacin
- b) statin with niacin
- c) statin and ASA
- d) fibrate and ASA

11. Patients B.N. presents with normal range LDL-C, low HDL-C, and mildly high TGs. An additional increase in the statin dose may help achieve the target TC/HDL-C ratio. True or false?

- a) True
- b) False

12. Patient N.Y. has moderate hypertriglyceridemia and a high TC/HDL-C ratio. What dose of salmon oil may help improve these lipid targets?

- a) 1 g-3 g three times daily
- b) 1 g-3 g daily
- c) 10 g-30 g three times daily
- d) 10 g-30 g daily

13. Patient R.S. has been instructed by his attending physician to increase her physical exercise to help increase her HDL-C levels. What exercise routine is suggested?

- a) 60 minutes vigorous, 4-7 days per week
- b) 30-60 minutes moderate, 4-7 days per week
- c) 60 minutes vigorous, 3 days per week
- d) 20 minutes regular, 3 days per week

14. Patients taking 1200 mg of gemfibrozil with low HDL-C have demonstrated what percentage improvement for CV events?

- a) 38%
- b) 33%
- c) 22%
- d) 12%

15. Patient S.R. has CAD, low HDL-C, normal range LDL-C levels and is taking simvastatin daily. Evidence has demonstrated antioxidants such as vitamins E and C, and beta-carotene, and are suggested in such patients. True or false?

- a) True
- b) False

16. The most correct answer describing the most common adverse effect observed with niacin is:

- a) peripheral numbness
- b) flushing

- c) dizziness
- d) dry mouth

17. The addition of antioxidants to low-dose simvastatin (10-20 mg/day) and high-dose niacin (2 to 4 g/day) has what effect on HDL-C?

- a) significantly enhances the effect of HDL-C increase
- b) marginally enhances the effect of HDL-C increase
- c) blunts the effect of HDL-C increase
- d) no effect

18. For patients with low HDL-C, pharmacists can give advice on:

- a) appropriate lifestyle components
- b) vitamin B levels
- c) reduction in daily protein consumption
- d) relaxation therapy

19. Extended-release niacin preparations may be substituted for equivalent doses of immediate-release (crystalline) niacin or nicotinic acid. True or false?

- a) True
- b) False

20. When titrating extended-release niacin it is important that:

- a) dosing begin at 2000 mg per day
- b) extended-release niacin is taken on an empty stomach
- c) the daily dose not be increased more than 500 mg in a four-week period
- d) dosing increases at 1000 mg per week

FACULTY: Raising HDL cholesterol: benefits and strategies

About the author

Rhonda Dorren has an extensive background in various capacities directly related to the practice of pharmacy. Rhonda has extensive practical experience and training with herbs, botanicals, nutraceuticals, nutritional supplements, homeopathy, homotoxicology and functional medicine. Rhonda is the author of numerous published articles and continuing education courses for medical practitioners and pharmacists.

Reviewers

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

Continuing Education Project Manager

Sheila McGovern, Toronto, Ont.

This lesson is valid until April 3, 2011. Information about raising HDL cholesterol may change over the course of this time.

Readers are responsible for determining the most current aspects of this topic.

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Mayra Ramos

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Fax: (416) 764-3937

Email: mayra.ramos@rci.rogers.com

Francine Beauchamp

Quebec Pharmacie and L'actualite Pharmaceutique

Fax: (514) 843-2183

Email: francine.beauchamp@rci.rogers.com