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Lipid Goals: Update on their Status

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Target Audience: Pharmacists
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Goal: The goal of this lesson is to discuss current medical management of dyslipidemias, including available agents and goals of therapy, as well as potential future treatment strategies based on recently published literature.

Objectives: At the conclusion of this lesson, successful participants should be able to:
1. Define patient-specific lipid goals based on risk factors.
2. Describe agents used in the treatment of dyslipidemias, including HMG-CoA reductase inhibitors, bile acid sequestrants, cholesterol absorption inhibitors, niacin, fibric acids, and omega-3 fatty acids.
3. Identify the role of each class of agents in lipid management, as recommended by current guidelines and practice.
4. Discuss the impact of recently published literature on current lipid management strategies.

INTRODUCTION

Current guidelines mandate strict low-density lipoprotein (LDL) control in patients with coronary heart disease (CHD) or those at high risk for atherosclerotic disease. LDL cholesterol has been established in several clinical trials as a predictor of coronary atherosclerosis. Further, a reduction in LDL by one percent has been shown to decrease cardiovascular risk by one percent. The breadth of evidence behind reduction in LDL and decreased cardiovascular risk is the driving force behind treating to a target LDL goal.[1]

In 2004, the Adult Treatment Panel III (ATP III) guidelines were updated to include an optional LDL treatment goal of <70 mg/dL in patients at very high risk, particularly those with documented coronary heart disease.[2] Table 1 provides the current ATP III risk stratification used in clinical practice today. Risk factors for increased probability of having a CHD event include age, gender, family history, hypertension, and cigarette smoking. These risk factors can be used to assess the 10 year risk for cardiovascular events.

Although targeting lower LDL is the primary goal of therapy, consideration must be given to other lipoproteins. Triglyceride (TG), very low density lipoprotein (VLDL), and high density lipoprotein (HDL) goals have all been evaluated in clinical trials.[3-4] In response to new literature, the American Heart Association (AHA) published a statement on triglycerides and cardiovascular disease in 2011.[3] Additionally, the lipid research clinic cohort demonstrated a strong correlation between non-HDL cholesterol and cardiovascular mortality, thus making non-HDL targets appropriate for consideration in some patients.[4] Lastly, HDL has long been considered a protective lipoprotein, though no guidelines give specific recommendations for goals of therapy.

The purpose of this review is to discuss agents used to treat dyslipidemias (shown in Table 2), describe current goals of therapy, and discuss the impact of recently published literature on current lipid management strategies.

AGENTS

HMG-CoA Reductase Inhibitors

HMG-CoA reductase inhibitors, or "statins," are considered the most effective LDL-reducing agents currently available.[1] These agents inhibit the conversion of HMG-CoA to mevalonate by the enzyme HMG-CoA reductase, the rate liming step in cholesterol synthesis.[5-11] In addition to decreasing LDL cholesterol, these agents also lead to increases in HDL cholesterol and decreases in triglycerides.

While statins are generally well-tolerated, they may lead to skeletal muscle effects, such as myopathy and/or rhabdomyolysis. Patients may commonly report muscle aches, soreness, and weakness. Myopathies are more common in elderly patients and in patients taking additional myopathy-causing agents. Management of a statin induced myopathy can include a drug holiday, dose decrease, or switching to an alternate statin.[12] Statin-induced myopathies may also lead to an elevation in creatinine kinase, which is most concerning when reaching

greater than ten times the upper limit of normal. These patients are at risk for developing rhabdomyolysis and acute renal failure if statin therapy is not reduced or discontinued.

Statins may also lead to increased hepatic transaminases. This elevation in liver function tests (LFTs) is typically dose-dependent, and a decline in LFTs is usually observed after a statin dose reduction. Those experiencing persistent transaminase elevations at greater than three times the upper limit of normal should discontinue statin therapy.[5-11] Previously, the U. S. Food and Drug Administration (FDA) recommended that patients initiating statin therapy have LFTs checked at baseline, after 12 weeks of therapy, and then periodically thereafter. Recently, the labeling for these medications was updated by the FDA to include new recommendations for LFT monitoring. Current recommendations state that LFTs should be checked prior to initiation and then as needed based on clinical suspicion of liver dysfunction.[13]

Contraindications to statin use include active liver disease, pregnancy or breastfeeding, and sensitivity to statins. Statin use may also be problematic in terms of potential drug interactions, as they are metabolized via the cytochrome P450 (CYP450) isoenzymes. Some of the statins are metabolized via the CYP450 3A4 isoenzyme (see Table 3); therefore, drugs that are strong inhibitors of this isoenzyme should be avoided in patients receiving a statin. Pravastatin and pitavastatin may be beneficial in this regard, as they have been shown to have minimal effects on the CYP450 isoenzymes.

Statins are typically dosed once daily. Because of increased LDL-lowering effects during the night, statins should generally be administered in the evening. Statins with relatively longer half-lives (atorvastatin, pitavastatin, pravastatin, rosuvastatin), however, can be administered at any time of the day.

Bile Acid Sequestrants

Bile acid sequestrants work by binding to bile acids in the gastrointestinal tract, which leads to decreased enterohepatic recycling and subsequent increased bile acid excretion in the feces.[14-16] Because cholesterol is a major prescursor of bile acids, removal in the feces leads to increased removal of cholesterol from the serum to form new bile acids.

Due to the lack of absorption in the GI tract, bile acid sequestrants have minimal systemic adverse effects. They are capable, however, of causing severe gastrointestinal side effects, the most common being constipation. Bile acid sequestrants may also lead to nausea, vomiting, diarrhea, and abdominal pain or discomfort. These effects are dose-dependent and are seen less often with low to moderate doses.

Bile acid sequestrants may also lead to increased triglycerides by stimulating triglyceride production and promoting triglyceride-rich VLDL secretion. As a result, bile acid sequestrants are contraindicated in patients with serum triglycerides greater than 500 mg/dL and in patients with a history of pancreatitis caused by hypertriglyceridemia.

Bile acid sequestrants may also have significant drug-drug interactions due to their role in altering the absorption of other medications. To avoid this potential interaction, other medications should be taken at least one hour before or at least four hours after administration of a bile acid sequestrant. Colesevelam may not alter absorption of other medications as much as the other agents in this class and can be administered concomitantly with other medications.

Bile acid sequestrants are dosed once or twice daily and are administered with meals. Cholestyramine and colesevelam are commercially available in powder form. These agents should be mixed with water or other liquid, including juices and soups. Colestipol and colesevelam are available in tablet forms.

Current guidelines highlight the additive LDL-lowering effects of bile acid sequestrants when combined with other agents such as statins.

Cholesterol Absorption Inhibitors

Ezetimibe is the only currently available agent in the cholesterol absorption inhibitor class. It works at the brush border of the small intestine to inhibit cholesterol absorption in the gastrointestinal tract.[17] This unique mechanism of action allows ezetimibe to be added to other therapies for LDL reduction.

Ezetimibe has been associated with an increased incidence of myopathies and rhabdomyolysis. While the majority of these reported cases have been in patients also taking a statin, myopathies have occurred in patients receiving ezetimibe monotherapy. If patients present with myopathy, including creatinine kinase greater than 10 times the upper limit of normal, ezetimibe should be discontinued. Ezetimibe may also cause increased hepatic transaminases, especially when co-administered with a statin. If patients present with LFTs greater than 3 times the upper limit of normal, ezetimibe should be discontinued.

Ezetimibe is contraindicated in patients with active liver disease, pregnancy and breastfeeding, and hypersensitivity to any part of the formulation. This agent does not contribute to significant drug-drug interactions.

Ezetimibe is typically dosed once daily and can be taken without regard to meals.

Niacin

Niacin, or nicotinic acid, works by inhibiting free fatty acid release from adipose tissue, increasing lipoprotein lipase activity, and increasing triglyceride removal from plasma by chylomicrons.[1,18] Niacin is beneficial in reducing LDL cholesterol and triglycerides while also increasing HDL

cholesterol.

Niacin therapy can be difficult for patients to tolerate, with the most common side effect being flushing. While flushing typically subsides with continued use, measures can be taken to reduce the incidence. Pre-treating with aspirin prior to niacin administration, administering niacin with a meal, and taking niacin in the evening are all beneficial recommendations to reduce the incidence of flushing. Additionally, the branded product Niaspan® is an extended-release formulation that has demonstrated less flushing than immediate-release niacin.[19]

Other adverse effects of niacin include gastrointestinal effects such as nausea, vomiting, diarrhea, and dyspepsia. Hepatotoxicity is a severe adverse reaction associated with niacin use; this risk appears to be increased in patients using sustained or extended-release niacin formulations. Niacin can also lead to glucose dysregulation and hyperuricemia.

Niacin is typically dosed once or twice daily. It is commercially available as both over-the-counter and prescription-only formulations. When switching from an immediate-release form of niacin to an extended-release product, equivalent doses should not be given; extended-release niacin should be restarted at a low dose and titrated to response.

Fibric Acid Derivatives

Fibric acid derivatives, or "fibrates," work as agonists at the peroxisome proliferator activated receptor α (PPARα), leading to overall increased lipolysis and removal of triglycerides from the plasma. Hence, these agents are most beneficial in reducing triglycerides.[20-21]

Fibrates are generally well tolerated by patients.[1] The most common adverse effects are gastrointestinal in nature (nausea, constipation, etc.). These agents have been linked to an increased risk of gallstone development. Fibrates

may also lead to an increased serum creatinine, so renal function should be monitored in patients at risk for renal impairment. Additional caution should be used in patients receiving nephrotoxic agents.

Patients taking fibrates should be regularly monitored for the development of myopathies (especially when using a concomitant statin agent) and for increases in LFTs.

Fibrates should be avoided in patients with pre-existing renal, hepatic, or gallbladder dysfunction. Fibrates may have significant drug-drug interactions due to a strong affinity to albumin. Fibrates bind to albumin and may lead to displacement of other albumin-bound drugs, such as warfarin.

Fibrates are typically dosed once daily. The majority of commercially available agents can be administered without regard to meals; however, some formulations must be taken with food.

Omega-3 Fatty Acids

Omega-3 fatty acids (EPA and DHA) are primarily used to decrease triglycerides.[1] These agents have several proposed mechanisms of action including increased hepatic oxidation, decreased hepatic synthesis of triglycerides, and increased lipoprotein lipase activity in the plasma.

The most common side effects associated with omega-3 fatty acids include belching, dyspepsia, and taste disturbances. These agents may also lead to increased LFTs; these should be routinely monitored, especially in patients with pre-existing hepatic dysfunction. Omega-3 fatty acids may also increase LDL cholesterol.

Omega-3 fatty acids should be used with caution in patients with an allergy to fish or shellfish, as they are derived from fish sources.

Few drug interactions exist with omega-3 fatty acids. These agents may,

however, lead to prolonged bleeding time. Use of omega-3 fatty acids with other anticoagulant or antiplatelet agents should be monitored closely.

Omega-3 fatty acids are commercially available as both over-the-counter fish oil and a prescription-only formulation (Lovaza®).[22] Unlike Lovaza®, the quality and efficacy of over-the-counter products are not regulated by the FDA and may provide inconsistent reductions in triglycerides.[23] Lovaza® should be dosed one to two times per day and can be administered without regard to food.

LIPID GOALS

Released in 2001, the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) identifies serum LDL cholesterol as a major cause of coronary heart disease (CHD) and thus the primary target for lipid-lowering therapy.[1] LDL goals are based on number of CHD risk factors and calculation of 10-year risk using the Framingham risk score. Current LDL goals and treatment recommendations are found in Table 1.

One exception to LDL-lowering as the primary therapeutic goal exists. When a patient presents with triglycerides greater than 500 mg/dL, lowering triglycerides to less than 500 mg/dL becomes a priority, in effort to reduce the risk of pancreatitis secondary to hypertriglyceridemia.[1] Once triglycerides have been decreased to less than 500 mg/dL, the focus returns to LDL-lowering. After the LDL goal is achieved, ATP III recommends further goals depending on other lipid levels. For patients with triglycerides ≥ 200 mg/dL, lowering non-HDL cholesterol to a target 30 mg/dL higher than the LDL goal should be the secondary focus. When triglycerides are normal or borderline high (< 200 mg/dL) and HDL is low (< 40 mg/dL), the addition of a medication to increase HDL can be considered, particularly in patients with significant CHD risk. The currently

accepted classifications of LDL, triglyceride, and HDL levels are listed in Table 4.

While the ATP III recommendations remain the gold-standard for cholesterol management, a growing body of evidence and recommendations exist supporting the consideration of triglycerides, non-HDL, and HDL when initiating and titrating medications for lipid management.

Triglycerides

Whether plasma triglyceride concentrations represent an independent risk factor for CHD has been a subject of research and debate for decades, and the evidence remains conflicting.[3] Data from the Framingham Heart Study support hypertriglyceridemia as an independent risk factor in women 50 to 69 years of age.[24] Similarly, a relationship between triglycerides and coronary artery disease (CAD) in patients with Type II diabetes mellitus was established by the Paris Prospective Study.[25] In other prospective trials, the association between triglycerides and cardiovascular risk has been dampened when other established risk factors were taken into account.[26] This effect was demonstrated in a meta-analysis of seventeen studies completed between 1959 and 1991.[27] When considered independently, patients with elevated triglycerides were found to have a significantly increased relative risk of cardiovascular events (RR 1.32 for males, 1.76 for females). When adjusted for other risk factors, the values maintained statistical significance but were decreased to 1.14 for males and 1.37 for females.

A more convincing evidence base supports hypertriglyceridemia as a CAD risk factor when found in combination with other risk factors. The Helsinki Heart Study was a randomized, double-blind, placebo-controlled trial originally designed to study the effects of gemfibrozil on the incidence of CHD in men aged 40-55 years with dyslipidemia at baseline.[28] A post hoc analysis was performed on the data collected during the 5-year study period to determine the combined effect of baseline triglyceride, LDL, and HDL concentrations on cardiac outcomes. Results of this secondary analysis suggest that middle-aged men with elevated plasma triglycerides along with low HDL cholesterol and high LDL cholesterol are at increased CHD risk and may significantly benefit from long-term lipid-lowering therapy with gemfibrozil.

In 2011, the American Heart Association (AHA) published a statement on triglycerides and cardiovascular disease.[3] After reviewing the role of triglycerides in lipid metabolism and atherogenesis, as well as the available evidence related to potential complications of hypertriglyceridemia, the AHA suggests an optimal fasting triglyceride level of less than 100 mg/dL (less than 200 mg/dL non-fasting). Intensive therapeutic lifestyle modifications are strongly encouraged and may be effective in achieving triglyceride goals. The combination of weight reduction, limitation of dietary fat, and an increase in physical activity has the potential to achieve a 50% reduction in triglycerides.

Non-HDL

The role of apolipoprotein B (apoB), and thus apoB-containing lipoproteins, in the process of atherogenesis has been increasingly highlighted in the last few years.[3] Non-HDL cholesterol represents all apolipoprotein B containing lipoproteins, including LDL and VLDL. Some evidence exists suggesting a stronger link between CHD risk and non-HDL than with LDL.

A recent meta-analysis published by Boekholdt and colleagues looked at the relationship between various lipid markers and the risk of cardiovascular events in patients receiving statin therapy.[29] Criteria for inclusion in the meta-analysis consisted of randomization of at least one study group to statin therapy; measurement of total cholesterol, LDL, HDL, triglycerides, and apolipoproteins at baseline and at some point during therapy; mean follow up of at least 2 years; and at least 1000 participants. The authors identified eight randomized controlled trials meeting these criteria and acquired individual patient data from each. The primary outcome was defined as time to first major cardiovascular event, which included a composite of fatal and nonfatal events.

A statistically significant relationship was found between all studied lipid markers and cardiovascular risk. Interestingly, patients treated with statins who achieved their non-HDL goal (130 mg/dL) but not their LDL goal (100 mg/dL) had a similar risk of cardiovascular event as those reaching both targets, but patients who achieved their LDL goal but not their non-HDL goal were at increased risk. Thus, the authors concluded that non-HDL cholesterol was more strongly associated with cardiovascular risk than LDL. Based on these and previous results, non-HDL may have clinical utility as a target for initiating and titrating statin therapy.

HDL

HDL has long been considered a protective lipoprotein, with a strong inverse relationship identified between HDL levels and CHD. Based on results from the Framingham Heart Study, ATP III recognizes an HDL of ≥ 60 mg/dL as a "negative" risk factor for CHD.[1] However, no current guidelines outline specific recommendations for target HDL levels. Within the last two years, new literature has become available regarding the effectiveness of targeting HDL goals in patients who have been treated to their LDL goals.

The AIM-HIGH investigators published the results of a study evaluating the effect on cardiovascular events when extended-release niacin was added to aggressive statin therapy.[30] The study was, in part, a response to data from a post hoc analysis of the Treating to New Targets (TNT) trial which showed fewer cardiovascular events in patients with higher HDL levels, compared to those

with lower HDL levels, when patients were treated to an LDL goal of less than 70 mg/dL.[31] Patients included in the AIM-HIGH study had established cardiovascular disease along with low HDL and high triglycerides at baseline. All subjects received simvastatin with or without ezetimibe to treat to an LDL of 40 to 80 mg/dL, while the study group also received niacin at a dose of 1500 to 2000 mg per day. Of note, approximately 94% of patients were taking a statin prior to enrollment in the study, and the median LDL at baseline was 71 mg/dL for this group.

While the addition of niacin was associated with increases in HDL and decreases in triglycerides, no significant difference was seen in the primary cardiovascular endpoint (death from CHD, nonfatal myocardial infarction, ischemic stroke, hospitalization for acute coronary syndrome, or symptom- driven coronary or cerebral revascularization). Thus, the authors concluded that increasing HDL and decreasing triglycerides adds no clinical benefit to intensive LDL control in patients with pre-existing cardiovascular disease.

Much discussion was sparked in the medical community with the release of the AIM-HIGH results. Criticism of the study included its inadequate statistical power, the small absolute difference in HDL between treatment and placebo groups, and the continued titration of other LDL-lowering therapies (simvastatin and ezetimibe) throughout the study.[32] Additionally, the discrepancy between results of the AIM-HIGH trial and the TNT trial may be at least partially explained by the observation that patients in the AIM-HIGH trial achieved a mean HDL of 44 mg/dL, while subjects in the highest HDL quintile in the TNT trial had a mean HDL of 61.5 mg/dL at baseline.[30-31]

Based on the results of AIM-HIGH, it is unclear whether raising HDL, and in particular the use of niacin to accomplish this, is a beneficial target in clinical practice. The HPS2-THRIVE study is currently being conducted to further evaluate the effects of increasing HDL with a niacin-based regimen on cardiovascular outcomes.[33] It is hoped that, with a larger study population and less controversial methodology, the THRIVE study will produce results that clarify the role of niacin and HDL in lipid management.

CONCLUSIONS

Interest in cholesterol management is ever increasing, as management within recommended goals has been linked to various health benefits, including decreased cardiovascular disease. Many treatment options currently exist to help manage patients with dyslipidemia according to ATP III guidelines. While LDL-lowering remains the primary goal of therapy at this time, a building body of evidence supports consideration of other lipid goals to minimize cardiovascular risk. As further research is completed and practice guidelines are updated, an increased emphasis may be placed on lowering triglycerides and non-HDL cholesterol.

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TABLE 1:

Risk Category	Treatment Goal	Recommended Treatment Strategy
High Risk CHD or CHD risk equivalents CHD Risk Equivalents: Framingham >20% Diabetes mellitus	LDL < 100mg/dL Optional LDL goal <70mg/dL	LDL > 100mg/dL Initiate lifestyle modifications LDL > 130mg/dL Initiate drug therapy
Moderate Risk 2+ risk factors AND Framingham 10% to 20%	LDL < 130mg/dL	LDL > 130mg/dL Initiate lifestyle modifications LDL > 160mg/dL Initiate drug therapy
Low Risk 0 to 1 risk factor Framingham < 10%	LDL < 160mg/dL	LDL > 160mg/dL Initiate lifestyle modifications LDL > 190mg/dL Initiate drug therapy

TABLE 2:

Agents Used in the Treatment of Dyslipidemia						
Agent	Brand Name(s)	Total Daily Dose Range	Effect on LDL	Effect on TG	Effect on HDL	Approximate Cost for 30-Day Supply
HMG-CoA Reductase Inhibitors						
Atorvastatin	Lipitor ®	10 – 80 mg	↓ 39 – 60%	↓ 19 –37%	↑ 5 – 9%	+++*
Fluvastatin	Lescol ®; Lescol XL	20 – 80 mg	↓ 22 – 36%	↓12 –25%	↑ 3 – 11%	+++
Lovastatin	Mevacor ®; Altoprev ®	20 – 60 mg	↓ 21 – 32%	↑9 – ↓10%	↑ 2 – 8%	+*
Pitavastatin	Livalo ®	1 – 4 mg	↓ 32 – 43%	↓ 15 –18%	↑ 5 – 8%	+++
Pravastatin	Pravachol ®	10 – 80 mg	↓ 22 – 37%	↓ 11 –24%	↑ 2 – 12%	+*
Rosuvastatin	Crestor ®	5 – 40 mg	↓ 45 – 63%	↓ 10 –35%	↑ 8 – 14%	++++
Simvastatin	Zocor ®	5 – 80 mg	↓26 – 47%	↓ 12 –33%	↑ 8 – 16%	+*
Bile Acid Sequestrants						
Cholestyramine	Prevalite ®; Questran ®; Questran Light®	4 – 24 g	↓10 – 20%	↑ 5%	Little effect	+++
Colesevelam		3.75 g	↓15 – 18%	↑ 9%	↑ 3%	
Colestipol	Colestid ®	5 – 30 g	↓10 – 20%	↑ 5%	Little effect	+*
Cholesterol Absorption Inhibitors						
Ezetimibe	Zetia ®	10 mg	↓18%	↓8%	↑ 1%	+++
Niacin						
Niacin	Niacor®; Niaspan®; Slo-Niacin®	1 – 3 g	↓7 – 16%	↓16 – 38%	↑ 14 – 22%	+++
Fibric Acid Derivatives						
Fenofibrate	Antara®; Fenoglide®; Lipofen®; Lofibra®; TriCor®; Triglide®	40 – 200 mg	↓21%	↓29%	↑ 11%	+*
Gemfibrozil	Lopid ®	1200 mg	↓ 10-15%	↓ 35-50%	↑ 5-20%	+*
Omega – 3 Fatty Acids (EPA and DHA)						
Omega-3-acid ethyl esters	Lovaza ®	4 g	↑ 45%	↓45%	↑ 9%	++++
+ = $1 – 50 ++ = $51 – 100 +++ = $101 – 150 ++++ = $151 = 200 * = includes generic drug pricing						

TABLE 3:

Differences in Statin Metabolism via CYP450 3A4	
CYP3A4 Involvement/ Lipophilic Agents	No CYP 3A4 Involvement / Hydrophilic Agents
Lovastatin	Fluvastatin
Simvastatin	Pravastatin
Atorvastatin	Rosuvastatin

* Pitavastatin is a lipophilic statin that has no CYP 3A4 involvement

TABLE 4:

LDL (mg/dL)	
<100	Optimal
100-129	Above or near optimal
130-159	Borderline high
160-189	High
>190	Very high
Triglycerides (mg/dL)	
<150	Normal
150-199	Borderline high
200-499	High
>500	Very high
HDL (mg/dL)	
<40	Low
>60	High

Test name: 2012 Article #8: Lipid Goals - Update on their Status

This test is worth: 10 points

INSTRUCTIONS: This page is intended to help participants REVIEW the quiz questions prior to submitting their answers online. Please take the quiz online using the link in the MEMBERS section of the website.

Question 1 of 19

Did the article help you achieve EACH of the stated objectives? If not, describe in the comment box at the end of this section. Refer to the article for the list of learning objectives.

- [ ] **A)** Yes
- [ ] **B)** No

Question 2 of 19

Quality of the written material/content?

- [ ] **A)** Very Good Quality
- [ ] **B)** Good Quality
- [ ] **C)** Neutral
- [ ] **D)** Poor Quality
- [ ] **E)** Very Poor Quality

Question 3 of 19

Overall evaluation of this article?

- [ ] **A)** Very Good
- [ ] **B)** Good
- [ ] **C)** Neutral
- [ ] **D)** Poor
- [ ] **E)** Very Poor

Question 4 of 19

How much time was required to complete this article?

- [ ] **A)** 0.5 hours
- [ ] **B)** 1.0 hours
- [ ] **C)** 1.5 hours
- [ ] **D)** 2.0 hours
- [ ] **E)** 2.5 hours

Question 5 of 19

The learning activities (e.g. case studies, quiz) were effective?

- [ ] **A)** Strongly Agree
- [ ] **B)** Agree
- [ ] **C)** Neutral
- [ ] **D)** Disagree
- [ ] **E)** Strongly Disagree

Question 6 of 19

The information in this article will help assist and reinforce my practice/treatment habits?

- [ ] **A)** Strongly Agree
- [ ] **B)** Agree
- [ ] **C)** Neutral
- [ ] **D)** Disagree
- [ ] **E)** Strongly Disagree

Question 7 of 19

The author(s) did NOT appear to be promoting a product or company? Please use COMMENT box at end of evaluation to explain or provide comment.

- [ ] **A)** Strongly Agree
- [ ] **B)** Agree
- [ ] **C)** Neutral
- [ ] **D)** Disagree
- [ ] **E)** Strongly Disagree

Question 8 of 19

Author(s) communicated material clearly?

- [ ] **A)** Strongly Agree
- [ ] **B)** Agree
- [ ] **C)** Neutral
- [ ] **D)** Disagree
- [ ] **E)** Strongly Disagree

Question 9 of 19

Comments. Please use this space to provide comments related to any of the above questions.

If NO COMMENT, please write " NONE " in the box below.

Question 10 of 19

SN is a 48-year-old female with a past medical of asthma, type 2 diabetes mellitus, hypertension, and migraines. She has no family history of coronary heart disease. She does not have a history of cigarette smoking. Her most recent HDL = 55 mg/dL. **Based on her risk factors, what is SE's LDL goal?**

A) < 160 mg/dL

B) < 145 mg/dL

C) < 130 mg/dL

D) < 100 mg/dL

Question 11 of 19

KA is a 52 year old male with no significant past medical history; however, his mother had a myocardial infarction at the age of 56 years old. He is a non-smoker, and his most recent HDL = 45 mg/dL. **What is his LDL goal?**

A) < 160 mg/dL

B) < 130 mg/dL

C) < 100 mg/dL

D) < 70 mg/dL

Question 12 of 19

Which of the following represents an appropriate recommendation regarding timing of liver function test (LFT) monitoring?

A) Prior to initiating a statin, then only as clinically indicated.

B) Prior to initiating a statin, then every 12 weeks as long as the statin is continued.

C) Prior to initiating a statin, then annually as long as the statin is continued.

D) LFTs do not need to be monitored in patients taking statins.

Question 13 of 19

Which of the following agents results in drug-drug interactions that would warrant separating administration of other medications (given at least one hour before or two hours after)?

A) Fluvastatin

B) Cholestyramine

C) Gemfibrozil

D) Ezetimibe

Question 14 of 19

What percentage decrease in LDL would be expected with ezetimibe 10 mg by mouth daily?

A) 8%

B) 11%

C) 18%

D) 28%

All of the following are potential adverse reactions associated with niacin EXCEPT:

- A) Hyperuricemia
- B) Glucose dysregulation
- C) Flushing
- D) Gallstone formation

Which of the following is the most appropriate first line agent for a patient with an LDL of 182 mg/dL, HDL of 46 mg/dL, and triglycerides of 529 mg/dL?

- A) Colestipol
- B) Ezetimibe
- C) Fenofibrate
- D) Pitavastatin

Which of the following is NOT true of omega-3 fatty acids?

- A) Have favorable effects on LDL, triglycerides, and HDL
- B) Available as prescription and over-the-counter formulations
- C) May lead to prolonged bleeding time
- D) Should not be used in patients with a shellfish allergy

Which of the following is true regarding non-HDL goals?

- A) Current guidelines recommend targeting non-HDL goals prior to achieving other cholesterol goals
- B) Non-HDL goals are typically 30 mg/dL lower than the LDL goal.
- C) Non-HDL has been suggested to be more strongly related to cardiovascular risk than LDL.
- D) All of the above are true.

Which of the following is true regarding HDL goals?

- A) Current guidelines recognize HDL ≥ 70 mg/dL as a negative risk factor for CHD.
- B) TNT showed fewer cardiovascular events in patients with higher HDL levels, regardless of the LDL achieved with therapy.
- C) AIM-HIGH found that increasing HDL and decreasing triglycerides lead to significant differences in the primary cardiovascular endpoint.
- D) Discrepancies in TNT and AIM-HIGH study conclusions may be attributed to differences in mean HDL achieved during the course of each study.