Perhaps I don’t watch enough television because only last week I saw for the first time this commercial: “You may have lowered your LDL cholesterol but if the good HDL is low and your triglycerides are high you still might be at risk for a heart attack...” Finally, a television commercial directed at the public on the role of lipid components and cardiovascular risk. This message was timely and necessary. Focusing on just LDL and ignoring the other two lipids seems akin to sitting on a one-legged stool. Even if you manage to do it somehow, sooner or later you are going to fall.

Most physicians know the goals for LDL-C, HDL-C and triglycerides but managing the lipids to those goals can be difficult, especially in patients with type 2 diabetes.

And just to recap, what are those goals? LDL-C ≤ 100 mg/dL or ≤ 70 mg/dL if cardiovascular disease, stroke or peripheral disease are present. Alternatively, a 40% reduction from baseline is indicated if all interventions fail to reach these values.

- HDL-C ≥ 40 mg/dL
- Triglycerides < 150 mg/dL
- LDL-C < 100 mg/dL

We have effective interventions but the health problem with which we are dealing is multifactorial and successful treatment requires that the patients actively participate in the management of their hyperlipidemia. So, where do we start to practice best current management?

People with diabetes need to have an annual fasting lipid profile. If the fasting lipids are abnormal, the first step is not a prescription for a statin, resin, fibrate or niacin, or anything else like that. The necessary first step is to rule out secondary causes of the hyperlipidemia.

The most common causes are alcohol and uncontrolled diabetes. Other causes include hypothyroidism, hepatic disease, chronic renal failure, nephrotic syndrome, corticosteroids and anabolic steroids and estrogen. Thus, the first step for lipid management in people with diabetes is to obtain good glycemic control and initiate lifestyle changes.

The A1C goal should be ≤ 6% only if this can be done without hypoglycemia. Otherwise the A1C goal is ≤ 6.5%-7%. In older patients with cardiovascular disease, an A1C of ≤ 8% may be acceptable. Underlying conditions should be aggressively treated and fasting lipids reanalyzed. LDL-C is the primary target of therapy unless the triglycerides are ≥ 400 mg/dL. The 400 mg/dL cutpoint is used because at higher concentrations the calculated values become inaccurate.

**Lifestyle changes**

Lifestyle changes are the cornerstones of therapy for all lipid disorders. Lifestyle changes include diet, exercise, weight loss and smoking cessation.

There are many opinions on what constitutes a proper diet for people with diabetes and hyperlipidemia. A good case can be made for what’s called a Mediterranean diet. Boiled down to the basics, it appears to be a common sense approach to nutrition: Eat fruits and vegetables, more fish, less red meat and avoid saturated fats. No doughnuts, pies, cakes or “power grazing” between dinner and bedtime.

Regular exercise is at least walking 30 minutes each day. Weight loss is essential in overweight patients. Physical trainers teach that eating less is the prerequisite to losing weight and exercise is the tool to maintain weight loss.

Smoking cessation is mandatory. K. Maeda and colleagues analyzed available studies and concluded that the increase in HDL-C, after smoking was discontinued, translated into an approximate 10% to 12% decrease in cardiovascular events.

Medications are added, if necessary, to lifestyle modifications to target specific lipid abnormalities. But remember, any medication regimen can be defeated if the patient does not actively participate in changing his or her behavior. Certified diabetes educators or registered dieticians can be effective educating patients about lifestyle changes. Referrals to these people are recommended.

**Current best management**

The best current management of hyperlipidemia can be divided into three main categories:

1. Isolated low HDL-C
2. Elevated triglycerides
3. Elevated LDL-C

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Management of isolated low HDL-C hinges on lifestyle modifications. The management can then be optimized by adding a fibrate, niacin, fish oil or a statin.\textsuperscript{7,8}

Management of elevated triglycerides is stratified by the degree of hypertriglyceridemia.\textsuperscript{9}

- Levels of 150 mg/dL to 199 mg/dL do not require medications. The patient needs to participate with the cornerstones of therapy.
- Triglycerides of 200 mg/dL to 399 mg/dL require lifestyle changes and the addition of a fibrate, niacin and/or fish oil.
- If the triglycerides are $\geqslant 400$ mg/dL, the above intervention is used and LDL-C is reevaluated when the triglyceride is $< 400$ mg/dL. If the LDL-C is above goal, a statin is added.

Management of elevated LDL-C begins with lifestyle changes and a statin. If the LDL-C remains above goal or the patient does not tolerate a statin, then add a bile acid resin, ezetimibe, niacin or orlistat.\textsuperscript{5,10}

Effective therapy requires adherence by the patient, but medication regimens might generate a new set of complications for that patient in the process.

Here are some recommendations for dealing with adverse drug reactions:

- Niacin is very effective, but few people tolerate it because it causes flushing. To diminish this problem, use a slow-release form of niacin. The main reason that patients stop niacin therapy is that concrete instructions are not given on how to take the drug. For review, the recommended approach is to teach the patient to take aspirin 30 minutes before taking niacin. Further, niacin should not be taken on an empty stomach. We suggest eating apple sauce (or another fiber source) to further delay its absorption. The starting dose is 500 mg at bedtime. The dose is increased by 500 mg each month to a final dose of 2000 mg per day. Additional aspirin, if tolerated and not contraindicated, may be needed.

- Statin therapy may be complicated by elevations in liver enzymes or the development of myalgias. Oftentimes these problems can be corrected by changing to another statin. For example, if the patient does not tolerate the drug, one can empirically change from a hydrophobic (simvastatin, lovastatin, atorvastatin) to a hydrophilic (pravastatin, fluvastatin, rosuvastatin) statin.\textsuperscript{11}

- Combination therapy with a statin is often needed. Several studies have evaluated the effects of a fibrate and a statin and have demonstrated efficacy over monotherapy. If this approach is adopted, use one of the fenofibrates. Do not use gemfibrozil in combination with a statin because there is an increased risk of myositis and rhabdomyolysis.\textsuperscript{12}

- Combining niacin with a statin was shown to be effective in the HDL-Atherosclerosis Treatment Study (HATS) for lowering cardiovascular risk in persons with type 2 diabetes.\textsuperscript{13} The same strategy for introducing niacin should be used as previously discussed.

### Lipid Control
Placing a strong emphasis on lipid control in people with diabetes really is important. Years ago, the 4S,\textsuperscript{14} CARE,\textsuperscript{15} LIPID\textsuperscript{16} and AFCAPS/TexCAPS\textsuperscript{17} studies demonstrated the value of LDL-C reduction. Each study contained a small subset of participants who were discovered to have diabetes. The degree of cardiovascular risk reduction was about the same as for the participants without diabetes—overall, approximately 25% to 35% reduction in cardiovascular events occurred in both secondary prevention (4S, CARE, LIPID) and primary prevention (AFCAPS/TexCAPS).

Subsequent studies specifically aimed at lowering lipid levels in people with type 2 diabetes demonstrated the effectiveness of lipid therapy. The UK Heart Protection Study (HPS) showed a 24% decrease in vascular events and 13% decrease in all-cause mortality in participants treated with simvastatin.\textsuperscript{18}

The results from the HPS formed the basis for the recommendation that all people with diabetes should be considered for statin therapy, regardless of the initial lipid concentration.

The Collaborative Atorvastatin Diabetes Study (CARDS)\textsuperscript{19} was halted 3.3 years into the five-year trial with atorvastatin because the interim analysis showed a “substantial and highly significant benefit of treatment.”

The ASTEROID study demonstrated that statins reduced atheroma volume in diabetic persons.\textsuperscript{20}

The VA HDL Intervention Trial (VA-HIT) demonstrated that therapy with fenofibrate decreased vascular events\textsuperscript{21} although this was not con-
firmed in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.9

HATS reported a significant decrease in cardiovascular event in patients treated with a statin plus niacin compared to the statin alone.10 Data evaluating statin plus fibrates11 and ezetimibe plus simvastatin12 therapy on cardiovascular event rates in diabetics are due in 2009 and 2012, respectively. Given the weight of evidence for treating dyslipidemic patients with diabetics, and considering that about 50% to 65% of people with diabetes die from cardiovascular events,13 aggressive lipid management must be considered a best current management strategy.

References

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