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Division of the Department of Medicine,
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***Cardiology Rounds*
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High-density lipoprotein metabolism as a therapeutic target for atherosclerosis

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Objectives: Evaluation of the lipid component of cardiovascular risk should include determination of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, as well as triglycerides. Elevated LDL is a well-known graded predictor of cardiovascular risk. HDL is thought to be protective against atherosclerosis, however, it is an inverse relationship, with lower levels of HDL being associated with greater cardiovascular risks. This issue of *Cardiology Rounds*, by Daniel Rader, M.D., a recognized international expert on lipid metabolism, focuses on HDL, and particularly low HDL, as a contributor to atherosclerosis. This issue will provide physicians with background information regarding low HDL levels, not only as a risk factor, but also in terms of a therapeutic potential that can be addressed by both lifestyle measures and pharmacologic therapies. The reader will gain a better understanding of what has been accomplished with HDL modification therapies, as well as potential mechanisms. New therapeutic approaches that target HDL metabolism are described, including increasing apoA production, promoting cellular cholesterol efflux (the so-called reverse cholesterol transport), and delaying turnover HDL cholesterol. These approaches are discussed in the context of patient care along with current summaries from the National Cholesterol Education Program (NCEP) guidelines regarding HDL cholesterol. Dr. Rader ends the article with common patient scenarios underscoring what is known about statin use and the combination of statins with fibrates. From this strong clinical approach, the reader will gain a firm foundation in some of the current developmental programs that focus on raising HDL cholesterol levels to reduce atherosclerotic cardiovascular disease.

TEST:

1. The inverse association between HDL cholesterol and the incidence of coronary heart disease (lower HDL = greater CV risk) is independent of other known risk factors, including LDL.
True False
2. There is an association between type II diabetes mellitus, end-stage renal disease, hypertriglyceridemia, and the presence of a relatively low HDL cholesterol.
True False

3. Lifestyle measures such as abstaining from cigarette smoking, increasing physical activity, and promoting weight loss can result in mild increases in HDL.

True False

4. Currently, the most effective modality to raise HDL is:

- a) beta-blockers
- b) thiazide diuretics
- c) a very low fat diet
- d) nicotinic acid
- e) androgens

5. Several major randomized controlled clinical trials have clearly demonstrated that pharmacological therapy solely targeting rising HDL levels have resulted in reductions in coronary heart disease events.

True False

6. Tangier disease, which is caused by a rare mutation, is characterized by extremely low HDL cholesterol levels that result in cholesterol accumulation in the liver, spleen, and gastrointestinal tract.

True False

7. Reverse cholesterol transport refers to the process by which HDL promotes the efflux of cholesterol from macrophages in the arterial wall, effectively returning cholesterol to the liver for excretion into bile.

True False

To receive AMA category 1 credit, you must correctly answer 60% of the test questions.

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