

**Harvard Medical School Department of  
Continuing Education and the Cardiovascular  
Division of the Department of Medicine,  
Brigham and Women's Hospital**



***Cardiology Rounds***  
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**The Pleiotropic Effects of Statins: Fact or Fantasy?**

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**Objectives:**

- To describe the potential mechanisms of lipid-dependent and lipid-independent effects of statin therapy on atherosclerosis
- To discuss the implications and limitations of the lipid-independent effects of statins and their potential clinical benefits

**Questions: Only one response is correct.**

1. The plaque regression trials have shown that statin therapy:
  - a. reduces plaque size by 50%-80%
  - b. reduces plaque to a greater extent in intravascular ultrasound (IVUS) trials than angiographic trials
  - c. highlights the importance of tight stenoses in causing cardiac events
  - d. decreases arterial lumen diameter or plaque by about 2%-3%
2. Intensive reduction of low-density lipoprotein (LDL) cholesterol by dietary or non-statin therapies:
  - a. has no effect on inflammation in animals with atherosclerosis
  - b. improves endothelial function in human studies
  - c. has few pleiotropic effects on vascular function
  - d. decreases collagen density in the plaque of animals with atherosclerosis
3. Pleiotropic effects of statins that may be LDL-independent include:
  - a. decreased high-density lipoprotein (HDL) cholesterol
  - b. decreased activation of nitric oxide synthase
  - c. reduction in isoprenoid-mediated pathways of inflammation
  - d. increases in oxidant stress
4. LDL-independent effects of statins in cell culture studies:
  - a. include activation of nitric oxide by inhibition of caveolin production
  - b. include interference of Rho pathways
  - c. may be modulated by LDL or oxidized LDL
  - d. all of the above

5. Blood cholesterol levels in humans are:
  - a. related to the extent of carotid atherosclerosis on non-invasive ultrasound
  - b. consistently related to hemorrhagic stroke
  - c. unrelated to the reduction in stroke risk in patients on statin therapy
  - d. unrelated to the risk of ischemic stroke (infarction/embolic stroke)
  
6. Meta-analysis of major statin randomized controlled trials have shown a relationship between the degree of LDL lowering and:
  - a. reduction in coronary heart disease risk
  - b. development of diabetes
  - c. incidence of cancer
  - d. incidence of rhabdomyolysis
  
7. Pleiotropic, LDL-independent effects of statins:
  - a. are necessary for their benefit in humans
  - b. may help us discover new therapies that have adjunctive benefits to statins
  - c. are proven in clinical trials by statistical modeling
  - d. are only theoretical at this stage

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