Stroke and Cholesterol: Weakness of Risk Versus Strength of Therapy
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This is one of the most tortured issues yet debated by our team of experts. Each of our protagonists has identified the key points, but naturally has selectively cited those more likely to advance their argument. Let us review the facts, as we see them.

1. Cholesterol is a very weak risk factor for ischemic stroke, in contrast to coronary artery disease.
2. Cholesterol reduction with diet and nonstatin drugs is not effective in stroke prevention, although reductions in levels of cholesterol are modest.
3. Statins have potent treatment effects in stroke prevention, although most of the evidence to date is in patients with coronary artery disease.
4. There is some evidence that statins are also effective in secondary stroke prevention,1 with pivotal trial results awaited.2

Because of the systemic nature of atherosclerosis, it may at first seem counterintuitive that cholesterol is not a potent risk factor for stroke, as it is for coronary artery disease. An obvious explanation for this difference is the heterogeneous nature of stroke, although even when homogenous cohorts of ischemic stroke have been studied, the association remains weak. Thrift argues that cholesterol cannot be unequivocally “condemned” as a stroke risk factor, because the “guidelines for causation” are not strictly fulfilled. Piechowski-Żoźwiak and Bogousslavsky want cholesterol “found guilty,” although they acknowledge that there appears to be some missing epidemiological evidence and rely on the circumstantial evidence provided by therapeutic weapon of statins.

So what do we think? There seems to be an unacceptable dichotomy between the weakness of cholesterol as a stroke risk factor and the potent effects of statin therapy. For example, the benefits of statins in many trials appear to be as great in those with “normal” cholesterol levels compared with those with higher cholesterol levels, similar to the effect seen with blood pressure lowering.1,3 As with blood pressure, the trials suggest that clinicians change their concepts of normal versus abnormal levels to a more continuous benefit. Interestingly, although statins have been shown to attenuate the progression of carotid atherosclerosis,4 even this biological effect may not be related to cholesterol reduction.5 Hence, it seems hard to escape the idea that the protective effect of statins may be largely due to their non–cholesterol-lowering effects.

While this is where we stand at the moment, the issue is still perplexing enough to keep this debate alive for some years to come.

References

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