Editorial

Is It Time To Measure Apolipoprotein B?

For some time, evidence that apoproteins may provide information about the risk of premature coronary disease beyond that evident in the plasma or lipoprotein lipids has been accumulating.1,2 However, almost all of this has been derived from cross-sectional studies, and therefore, appropriately, there has been reluctance to endorse the use of these measurements for routine clinical use. We believe the recent results of Brown et al.3 should result in a reassessment of this view. Brown and his colleagues studied patients with documented coronary disease and elevated apoprotein (apo) B treated with dietary and pharmacologic regimens that were designed to lower the apo B particle number in plasma. The trial was prospective and blinded, and hard end points were used. The "aggressively" treated groups displayed clearcut evidence of angiographic regression, whereas the control group did not. More important still, the treatment groups fared better clinically than did the control group. The differences were all highly statistically significant, and the parameters that best predicted angiographic regression and favorable clinical outcome were the percent decrease in apo B and the percent increase in high density lipoprotein (HDL) cholesterol, the same two parameters, in fact, that earlier had been shown to predict the progression of disease in native coronary vessels and in saphenous vein bypass grafts.4

But if the issue is to be joined, on what grounds should we reach judgement? We suggest that such decisions should not be based entirely on the results of multiple regression analyses. This view does not ignore or minimize the major achievements, which have come from the application of this technique. It does, however, maintain that we should not ignore the limitations inherent in this method. The extent of the first of these may be easier for the lipidologist than the epidemiologist to appreciate: namely, that multiple regression treats all examined variables as if they were physiologically independent. And clearly that is often not the case; important metabolic interactions exist between triglycerides, HDL cholesterol, and cholesterol ester transfer protein—interactions that have been studied in some detail by the lipidologist but are not usually taken into account by the epidemiologist.

More relevant in the present instance is the fact that very low density lipoprotein (VLDL) and low density lipoprotein (LDL) levels can be closely linked because the former is the precursor of the latter. Interestingly, hypertriglyceridemia has, under most circumstances, been dismissed by most epidemiologists as a risk factor for premature coronary artery disease. But hypertriglyceridemia has different causes, and measurement of apo B is one tool that has been used to separate them. Thus, hypertriglyceridemic patients who have elevated apo B—
been concerned that introduction of new diagnostic parameters such as apo B would engender confusion among practicing clinicians. Fair enough, yet few lipidologists seem to recognize just how confusing and logically inconsistent the present lipid-based system is to the non-afficionado. Consider hypertriglyceridemia again: Which patients should be treated with anti-apo B therapy, as Brown and his colleagues have done, if apo B is not to be measured? The same dilemma applies to normolipidemic individuals if apo B is left out of the diagnostic approach. Moreover, every lipidologist is well aware of just how frequently the lipid pedigree shifts in patients with familial combined hyperlipidemia; the regular clinician can only be bewildered by it. We would argue that elevated apo B provides a reliable clinical tool to recognize the many lipid guises that overproduction of hepatic apo B particles can present. Working without it conveys no advantage, and given the results of Brown et al. there is considerable disadvantage for both patient and physician. High apo B levels in patients with coronary disease should be lowered regardless of the lipid phenotype.

The only important reservation we now have as to the utility of apo B in clinical practice relates to the unresolved issue of the standardization of clinical assays. Certainly this must be settled. At the same time, though, such issues do not apply only to apo B. The measurement of HDL cholesterol in the real clinical world is often far from perfect, and yet it has gone forward.

We do not argue against further gathering of evidence. At the same time, the results of Brown et al. pose a difficult dilemma: if our theory is valid, large numbers of patients will benefit if the measurement of apo B is introduced into clinical practice. If its introduction is delayed, the corollary holds: large numbers will be injured because they did not have the opportunity to benefit. Although time may yet prove us wrong, given all the present evidence, we have concluded that the practicing physician now has the right to this diagnostic test.

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