Is Lipoprotein(a) an Independent Risk Factor for Myocardial Infarction at a Young Age?

To the Editor:

I read the recent paper by Sandkamp et al. (Clin Chem 1990;36:20–3) with interest. Its conclusion, that lipoprotein(a) (Lp(a)) is an independent risk factor for myocardial infarction at a young age, agrees well with other work indicating that high concentrations of Lp(a) predispose to coronary and carotid atherosomatous disease (1). However, recent work must raise a question regarding this conclusion, on both theoretical and methodological grounds.

Although Lp(a) is, in general, an independent risk factor for atherosclerosis, with a plasma concentration unrelated to that of low-density lipoprotein (LDL), high concentrations of Lp(a) have been described in association with familial hypercholesterolemia (2, 3). Because this condition presents with myocardial infarction at a young age, one would expect it to be overrepresented in the patient group of Sandkamp et al. The significantly higher mean LDL cholesterol and apo-lipoprotein B concentrations in this group are in keeping with this expectation. Therefore, one might look for some association between concentrations of LDL cholesterol and Lp(a) in their results.

The failure to show such an association may be due to the time at which Sandkamp et al. measured Lp(a) in serum, i.e., as much as four weeks after the infarction. While concentrations of LDL cholesterol in serum are decreasing after myocardial infarction (4), the concentrations of Lp(a) increase and may not return to normal for more than a month (5). This latter finding, published after completion of the study by Sandkamp et al., must throw doubt on their results. Clearly, this area needs further investigation.

References

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One of the authors of the paper in question responds:

To the Editor:

We agree that in the myocardial infarction group familial hypercholesterolemia may be overrepresented. However, the suggested look for the association between LDL cholesterol and Lp(a) is exactly done, and the independency of Lp(a) is shown in Figure 2 of our paper. Dr. Hutchesson’s second objection is due to imprecise reading of our paper. Our measurements were carried out “two to four weeks after their release from acute care” and not “as much as four weeks after infarction.” The influence of acute-phase increases of Lp(a) on our results can be excluded because the blood samples were taken at least five weeks after the infarction, the mean interval being eight weeks.

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Effects of Diphenhydramine on Immunoassays of Phencyclidine in Urine

To the Editor:

One aspect of the drug-testing protocol in this laboratory is to screen all urine specimens for drugs of abuse by fluorescence polarization immunoassay (FPIA) on the TDx analyzer (Abbott Instruments, N. Chicago, IL). Recently, two specimens that screened positive for phencyclidine (PCP) at the National Institute on Drug Abuse cutoff value of 25 μg/L had apparent PCP concentrations of 37 and 32 μg/L, respectively. However, subsequent analysis of these specimens by gas chromatography/mass spectrometry failed to detect PCP at a limit of detection of 5 μg/L. These samples were then analyzed by radioimmunoassay with Abuscreen (Roche Diagnostics, Nutley, NJ) and EMT (Syva Co., Palo Alto, CA); each tested negative by both assays. Comprehensive drug testing revealed that each specimen contained a large quantity of diphenhydramine, an antihistamine commonly present in over-the-counter and prescription medication. No other therapeutic or abused drugs were detected in either specimen. The urine concentrations of diphenhydramine were 120 and 50 mg/L, respectively.

To further document this phenomenon, we added diphenhydramine to several aliquots of drug-free urine to yield concentrations between 50 and 200 mg/L and analyzed these samples by FPIA. The average percent cross-reactivity was 0.042%, in agreement with the TDx assay manual, which states that diphenhydramine has a cross-reactivity of <0.1 to 0.2%. Because drug concentrations in urine may vary by several orders of magnitude, even drugs with very low cross-reactivities, as in this case, may produce positive screening results.

Subsequent to this work, these two specimens were tested with the TDx PCP II assay, which is currently undergoing clinical evaluation. Neither specimen tested positive in this assay.

Disclaimer: The views in this report are those of the authors and not those of the Department of Defense.

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Frequent Contamination of Taq Polymerase with DNA

To the Editor:

The polymerase chain reaction (PCR) is a recently developed technique in which a defined DNA sequence can be amplified thousands of times (1). Since the introduction of this rapidly developing methodology, PCR has already been applied in clinical medicine, e.g., for the diagnosis of genetic diseases or viral infections (2, 3). The power of PCR, however, is also its weakness, because even the smallest amount of contaminating DNA can be amplified, thereby resulting in misleading or ambiguous results (4).

During our investigations with PCR to study the structure of bacterial ribosomal RNA, my coworkers and I used “universal primers” (5) to am-