



LETTERS

Comments in Response to “Low-Dose Aspirin Increases Aspirin Resistance in Patients with Coronary Artery Disease”

To the Editor:

We read with great interest the recent article by Lee et al, “Low-Dose Aspirin Increases Aspirin Resistance in Patients with Coronary Artery Disease.”¹ Using a novel point-of-care device, the authors report a significant association between aspirin dose and a failure to respond according to a predetermined aspirin resistance threshold. The use of this and other means and methods have been used to determine whether an appropriate response to aspirin has been achieved. Despite the number of studies, none has prospectively correlated aspirin resistance to an increased risk for cardiovascular events.²

The current study exclusively enrolled Chinese patients who averaged a particularly low body mass index (BMI). We believe this provides difficulty in extrapolating the findings to patients in the US and Europe, as well as those with higher BMIs. Recent data have suggested that increased weight is associated with a variable response to low-dose aspirin therapy.^{3,4} Also with respect to BMI, the Women’s Health Study reported results from patients with baseline BMIs <25.0, 25.0 to 29.0, and ≥30.0. There appeared to be a trend which suggested that women with a higher BMI responded less to very low dose aspirin (100 mg every other day).

Furthermore, the authors cite several limitations, including the failure to confirm adequate compliance to aspirin therapy. The issue of aspirin compliance and subsequent platelet response was recently investigated.⁵ Schwartz et al reported that in 129 patients with a history of myocardial infarction, 9% failed to respond to aspirin therapy, but upon observed aspirin ingestion, all but one patient responded appropriately. It also is known that concomitant use of ibuprofen and possibly other NSAIDs may attenuate the intended antiplatelet effects provided by aspirin therapy.^{6,7} Finally, a previous study utilizing the same technology appears to be inconsistent with the current findings, including no relationship to aspirin dose (beta-coefficient: -0.0015, *P* value = not significant, 95% confidence interval: 0.997-1.000).⁸

We hope future efforts in this important area take into account compliance and drug-drug interactions, as well as

emerging areas such as the impact of obesity. The focus of future work should relay clinically meaningful and practically applicable information given the broad role of aspirin in the primary and secondary prevention of cardiovascular events.

Matt Fisher, PharmD
 Volker Knappertz, MD
 Bayer HealthCare
 Morristown, NJ

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The Reply:

We would like to thank Drs Fisher and Knappertz for their interest in our study.¹ The relationship of aspirin resistance and adverse cardiovascular events has been reported in several studies.²⁻⁵ One of those is our observation on the increased risk of myonecrosis following elective percutaneous coronary intervention among aspirin-resistant patients measured by the same device used in the current study.

We agree that there may be potential ethnic differences in the response to aspirin, and extrapolating our findings to a different population should be made with caution. We are

aware of the study by Maree et al on the increased likelihood of heavier patients to have an inadequate response to the platelet inhibitory effect of aspirin.⁶ Differences in the methodology of measuring aspirin resistance may explain the disparity concerning the relationship of body weight and the prevalence of aspirin resistance.

We fully agree that treatment compliance and coadministration of drugs having platelet inhibitory effect are important considerations in studies on aspirin resistance, and efforts should be made to eliminate these confounding factors.

The inconsistency between our study and that from Wang et al,⁷ as mentioned in our discussion, is possibly due to the differences in the type of atherothrombotic disease affecting the studied populations and the pattern of prescribed aspirin dosage.

Wai-Hong Chen, MBBS, FACC
Pui-Yin Lee, MBBS
Division of Cardiology
Department of Medicine
The University of Hong Kong
Queen Mary Hospital
Hong Kong, China

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What Is the Answer You Got?

To the Editor:

I appreciated your editorial, "The Answer You Get Depends on the Question You Ask," in the July 2005 issue of the *Journal*.¹ I was pleased that as editor-in-chief of *The American Journal of Medicine*, you ask yourself whether the question being asked by an article is important and

whether the outcome is predictable. Careful consideration of these issues, as well as of how questions and answers are reported, is critical to a great journal.

I was, therefore, surprised to read the article in the same issue by Lee et al entitled, "Low-Dose Aspirin Increases Aspirin Resistance in Patients with Coronary Artery Disease."² I thought about "the question" of whether using low-dose aspirin (something now commonplace) might have negative effects in patients with coronary disease. With excitement I read the article, expecting to learn "the answer" that the use of low-dose aspirin somehow desensitizes platelets to cyclooxygenase inhibition by aspirin and produces measurable aspirin resistance. Instead, I read that in a group of patients with stable coronary disease, aspirin dose was directly associated with the prevalence of aspirin resistance. Although intriguing, the study by Lee et al certainly did not prove the cause-and-effect relationship between low-dose aspirin and aspirin resistance suggested by the title.

Although I may be in the minority of readers of the *Journal* who were misled by the title, I believe that "the question you ask" should be reflected in the title, as should the answer to that question. We must recognize that, particularly given the time constraints many practitioners face, readers of medical journals often peruse titles and abstracts and do not read full articles. Although this is disappointing, an article's title (which appears in references, abstracts and Internet citations) is therefore very important and may be all that a reader recalls. Although a physician who prescribes high-dose aspirin out of concern about causing aspirin resistance based simply on this article's title is clearly not practicing good medicine or demonstrating the highest standards of professionalism, reviewers and editors of medical journals also bear responsibility for ensuring that the message communicated to the public is clear and precise. We also should recall that summaries of medical articles are frequently made available to the lay public and that patients with coronary disease can draw their own conclusions about what aspirin dose to take to prevent ischemic complications.

I am sure that the commitment to high quality reflected in the July 2005 issue's editorial¹ was impressive to readers of the *Journal*; I know it was to me. I hope that reviewers of articles submitted to the *Journal* not only ensure that the question asked is important, but also that the question or the answer is readily apparent. . . even in the title.

Roy Charles Ziegelstein, MD
Johns Hopkins University School of Medicine
Baltimore, Md

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