◆*Acceptance Address: The Thin Red Line*

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In 1979, when I first went to the *New England Journal of Medicine* as assistant deputy editor, I was advised by the editor-in-chief, Bud Relman, to attend just two national meetings a year—those of the Council of Biology Editors and the Association of American Medical Colleges. These were the meetings, he said, that would help me most in my new job. I dutifully did as I was told, and before long I was deeply engaged in the activities of CBE. I remained so until the middle 1990s, when I had to pull back because of the growing demands of my own journal, of which I was then executive editor.

During the time I was active, I was privileged to be part of a number of important CBE activities. Perhaps most rewarding for me, and certainly the most fun, was the time I spent on the Editorial Policy Committee. This was the committee that, under the energetic and far-sighted leadership of John Bailar, gave birth to the 1990 book *Ethics and Policy in Scientific Publication*. I was also involved in developing the Short Course for Journal Editors and taught in it for 2 years before being replaced by my estimable colleague Bob Utiger, then deputy editor of the *New England Journal of Medicine*. And finally, I served on CBE's Board of Directors from 1992 to 1995. I very much enjoyed all of these activities, particularly the easy interactions with talented colleagues from all over the world who were deeply involved in some of the same issues I was.

In going through my papers from those days in preparation for this talk, I came upon an article I wrote for *CBE Views*, the predecessor of *Science Editor*. The article was titled "Editors and Fraud", and it was published exactly 20 years ago, in the summer 1983 issue. In rereading it, I was struck by how very dated it now seems. I'd like to say a few words about that article because it underscores one of the most important challenges facing science editors today—a challenge we're only beginning to recognize fully.

The article dealt with the causes and types of misconduct in biomedical publication. In it, I identified a spectrum of misconduct, ranging from (at the benign end) the very common practices of fragmentation and loose authorship, through selection and trimming of data, to (at the malignant end) the less frequent practices of plagiarism and fabrication. I suggested that the most important underlying cause was not psychopathology, as was widely believed at the time, but the relentless pressure to publish inherent in the system. Since academic promotion and tenure, research funding, and, indeed, reputation depended largely on the number of publications, researchers who wanted to get ahead needed to keep turning out papers as quickly as possible. To keep up the pace, they were greatly tempted to cut corners—often in little ways, sometimes in big ones. Misconduct was a byproduct of excessive ambition and weak character. All that was true enough, and remains so today, although somewhat tempered.

But what made the article seem so quaint was what was missing. Totally absent was any mention of financial conflicts of interest as a cause of misconduct. I talked only about ego and not at all about greed. The omission was not just an oversight on my part. At the time, conflicts of interest were hardly a blip on anyone's radar screen. To be sure, pharmaceutical companies supported some biomedical research, but they did so at arm's length. They had no say in how the studies they funded were carried out. The academic institutions, which actually received the grants on behalf of their faculty researchers, generally saw to that.

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How things have changed! Nowadays companies not only support biomedical research, they control nearly all aspects of it. They design studies, they claim ownership of the data, they analyze the data, and they approve papers before publication. And what about researchers? What do they do? Too often, they simply do what they're told. And they're well rewarded for doing that. In addition to receiving continued research funding, favored researchers are singled out for lucrative consulting and royalty arrangements, serve on paid advisory and speakers' boards, and even hold equity interest in the companies that sponsor their research. I'm speaking here mainly about clinical research, because that's what I know best, but my understanding is that similar changes are occurring in other fields of science. No longer is there anything like an arm's-length relationship with sponsors. That's a thing of the past, and so are the objectivity and impartiality that are supposed to characterize scientific research.

My two decades at the *New England*

Thin Red Line *continued*

Journal of Medicine coincided with these changes, and I witnessed firsthand the baleful consequences. To begin with, reports of company-sponsored drug trials became an ever-larger fraction of the papers submitted to us, as though this were the only type of research worth doing. And increasingly, papers were slanted to make sponsors' drugs look good. This can be done in many ways, some obvious, others virtually impossible to detect. For example, companies sometimes design trials to compare their new drugs not with other kinds of treatments, but with placebos or with inadequate doses of an older drug of the same type. Trials are often too short or enroll the wrong kinds of patients or omit consideration of side effects. Sometimes only positive results are reported. If there are no positive results, sponsors may suppress reports altogether. I saw these forms of misconduct—there is no other word for it—many times at the *NEJM*, more with each passing year. We rejected such papers if we spotted them. But I'm sure we missed some of them, and those we did reject were often published elsewhere.

Needless to say, these are not innocent games. They have direct effects on the practice of medicine. Doctors are increasingly practicing a drug-intensive type of medicine, and the drugs they prescribe tend to be new, expensive brand-name drugs pushed by the companies that make them, ostensibly on the basis of published research. But if the research is biased, as it so often is, what does that mean for patients? Here's an example of what it can mean.

Last December, the *Journal of the American Medical Association* published the results of the ALLHAT study—a huge National Institutes of Health–supported clinical trial comparing four classes of drugs to treat high blood pressure. The results showed that the best of the four was a simple diuretic (water pill), a generic drug that has been on the market for about 50 years and costs pennies a day. The other drugs were newer and much more expensive. Two were still on patent, one of which is the fourth-biggest-selling drug in the United States. Yet, patients receiving the newer drugs had not only higher blood pressure but also higher rates of heart failure and stroke. Recall that this trial was sponsored by NIH. The companies that made the brand-name drugs had never compared them with diuretics. Why? I assume they didn't want to know the answer.

So here's the bad part. Could it be that, little by little, new drugs reaching the market are actually worse than those they replace? Could it be that, imperceptibly, prescription drugs are getting less effective, not more? In the absence of properly designed trials, there's simply no way to know. The usual practice of comparing a new drug with a placebo is of no help.

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That's where you come in. Academic institutions used to act as watchdogs, making sure sponsors did not influence faculty research. But now many of them are deeply involved with the same companies their faculties are. They're in a poor position to take the ethical high ground, because they themselves are compromised. So it's up to editors.

One step in that direction was taken 2 years ago, when the editors of 13 medical journals published a joint editorial in all their journals. In it, they took note of the situation I've just described and said, "Many of us [note that it wasn't all] will ask the responsible author to sign a statement indicating that he or she accepts full responsibility for the conduct of the trial, had access to the data, and controlled the decisions to publish." A small step. Still, the very fact that such an editorial had to be written shows how far the research establishment has gone in accepting the notion that maybe authors wouldn't have responsibility for their own work. The editorial was even more timid about editors' own conflicts of interest. The most they were willing to advocate was that editors "disqualify themselves from any decisions where they have a conflict of interest". That isn't enough. Editors should have no financial ties with companies related to their work. During my years at the *NEJM*, we had a rule that in-house editors could have no financial interests in the health-care industry. It was no hardship, and we never had to beg off from our job or wonder whether our decisions would help or harm the fortunes of a close colleague.

The work you as editors do has always been important. But now it's more important than ever. The influence of interested companies has permeated the research establishment, and it shows in what is published. Editors must redouble their efforts to watch for bias in the papers they review. They should refuse to publish papers obviously written primarily for commercial purposes, and they should insist that authors design their own studies, have full access to the data, write their own papers, and have control over publication. I wish that the problems were prevented by strong conflict-of-interest policies in research institutions. But until that happens, you will continue to have to deal with commercially biased papers. That means editors will have to be free of their own financial conflicts and be very, very tough. Like it or not, editors are now the thin red line protecting the integrity of the scientific literature.