Editorials

Is Academic Medicine for Sale?

In 1984 the *Journal* became the first of the major medical journals to require authors of original research articles to disclose any financial ties with companies that make products discussed in papers submitted to us.[1] We were aware that such ties were becoming fairly common, and we thought it reasonable to disclose them to readers. Although we came to this issue early, no one could have foreseen at the time just how ubiquitous and manifold such financial associations would become. The article by Keller et al.[2] in this issue of the *Journal* provides a striking example. The authors' ties with companies that make antidepressant drugs were so extensive that it would have used too much space to disclose them fully in the *Journal*. We decided merely to summarize them and to provide the details on our Web site.

Finding an editorialist to write about the article presented another problem. Our conflict-of-interest policy for editorialists, established in 1990,[3] is stricter than that for authors of original research papers. Since editorialists do not provide data, but instead selectively review the literature and offer their judgments, we require that they have no important financial ties to companies that make products related to the issues they discuss. We do not believe disclosure is enough to deal with the problem of possible bias. This policy is analogous to the requirement that judges recuse themselves from hearing cases if they have financial ties to a litigant. Just as a judge's disclosure would not be sufficiently reassuring to the other side in a court case, so we believe that a policy of caveat emptor is not enough for readers who depend on the opinion of editorialists.

But as we spoke with research psychiatrists about writing an editorial on the treatment of depression, we found very few who did not have financial ties to drug companies that make antidepressants. (Fortunately, Dr. Jan Scott, who is eminently qualified to write the editorial,[4] met our standards with respect to conflicts of interest.) The problem is by no means unique to psychiatry. We routinely encounter similar difficulties in finding editorialists in other specialties, particularly those that involve the heavy use of expensive drugs and devices.

In this editorial, I wish to discuss the extent to which academic medicine has become intertwined with the pharmaceutical and biotechnology industries, and the benefits and risks of this state of affairs. Bodenheimer, in his Health Policy Report elsewhere in this issue of the *Journal*,[5] provides a detailed view of an overlapping issue — the relations between clinical investigators and the pharmaceutical industry.

The ties between clinical researchers and industry include not only grant support, but also a host of other financial arrangements. Researchers serve as consultants to companies whose products they are studying, join advisory boards and speakers' bureaus, enter into patent and royalty arrangements, agree to be the listed authors of articles ghostwritten by interested companies, promote drugs and devices at company-sponsored symposiums, and allow themselves to be plied with expensive gifts and trips to luxurious settings. Many also have equity interest in the companies.

Although most medical schools have guidelines to regulate financial ties between their faculty members and industry, the rules are generally quite relaxed and are likely to become even more so. For some years, Harvard Medical School prided itself on having unusually strict guidelines. For example, Harvard has prohibited researchers from having more than $20,000 worth of stock in companies whose products they are studying.[6] But now the medical school is in the process of softening its guidelines. Those reviewing the Harvard policy claim that the guidelines need to be modified to prevent the loss of star faculty members to other schools. The executive dean for academic programs was reported to say, "I'm not sure what will come of the proposal. But the impetus is to make sure our faculty has reasonable opportunities."[7]

Academic medical institutions are themselves growing increasingly beholden to industry. How can they justify rigorous conflict-of-interest policies for individual researchers when their own ties are so extensive? Some academic institutions have entered into partnerships with drug companies to set up research centers and teaching programs in which students and faculty members essentially carry out industry research. Both sides see great benefit in this arrangement. For financially struggling medical centers, it means cash. For the companies that make the drugs and devices, it means access to research talent, as well as affiliation with a prestigious "brand." The time-honored custom of drug companies' gaining entry into teaching hospitals by bestowing small gifts on house officers has reached new levels of munificence. Trainees now receive free meals and other substantial favors from drug companies virtually daily, and they are often invited to opulent dinners and other quasi-social events to hear lectures on various medical topics. All of this is done with the acquiescence of the teaching hospitals.

What is the justification for this large-scale breaching of the boundaries between academic medicine and for-profit industry? Two reasons are usually offered, one emphasized more than the other. The first is that ties to industry are necessary to facilitate technology transfer — that is, the movement of new drugs and devices from the laboratory to the marketplace. The term "technology transfer" entered the lexicon in 1980, with the passage of federal legislation, called the Bayh–Dole Act,[8] that encouraged academic in-

stitutions supported by federal grants to patent and license new products developed by their faculty members and to share royalties with the researchers. The Bayh–Dole Act is now frequently invoked to justify the ubiquitous ties between academia and industry. It is argued that the more contacts there are between academia and industry, the better it is for clinical medicine; the fact that money changes hands is considered merely the way of the world.

A second rationale, less often invoked explicitly, is simply that academic medical centers need the money. Many of the most prestigious institutions in the country are bleeding red ink as a result of the reductions in Medicare reimbursements contained in the 1997 Balanced Budget Act and the hard bargaining of other third-party payers to keep hospital costs down. Deals with drug companies can help make up for the shortfall, so that academic medical centers can continue to carry out their crucial missions of education, research, and the provision of clinical care for the sickest and neediest. Under the circumstances, it is not surprising that institutions feel justified in accepting help from any source.

I believe the claim that extensive ties between academic researchers and industry are necessary for technology transfer is greatly exaggerated, particularly with regard to clinical research. There may be some merit to the claim for basic research, but in most clinical research, including clinical trials, the "technology" is essentially already developed. Researchers are simply testing it. Furthermore, whether financial arrangements facilitate technology transfer depends crucially on what those arrangements are. Certainly grant support is constructive, if administered properly. But it is highly doubtful whether many of the other financial arrangements facilitate technology transfer or confer any other social benefit. For example, there is no conceivable social benefit in researchers' having equity interest in companies whose products they are studying. Traveling around the world to appear at industry-sponsored symposiums has much more to do with marketing than with technology transfer. Consulting arrangements may be more likely to further the development of useful products, but even this is arguable. Industry may ask clinical researchers to become consultants more to obtain their goodwill than to benefit from their expertise. The goodwill of academic researchers is a very valuable commodity for drug and device manufacturers. Finally, it is by no means necessary for technology transfer that researchers be personally rewarded. One could imagine a different system for accomplishing the same purpose. For example, income from consulting might go to a pool earmarked to support research or any other mission of the medical center.

What is wrong with the current situation? Why shouldn't clinical researchers have close ties to industry? One obvious concern is that these ties will bias research, both the kind of work that is done and the way it is reported. Researchers might undertake studies on the basis of whether they can get industry funding, not whether the studies are scientifically important. That would mean more research on drugs and devices and less designed to gain insights into the causes and mechanisms of disease. It would also skew research toward finding trivial differences between drugs, because those differences can be exploited for marketing. Of even greater concern is the possibility that financial ties may influence the outcome of research studies.

As summarized by Bodenheimer,[5] there is now considerable evidence that researchers with ties to drug companies are indeed more likely to report results that are favorable to the products of those companies than researchers without such ties. That does not conclusively prove that researchers are influenced by their financial ties to industry. Conceivably, drug companies seek out researchers who happen to be getting positive results. But I believe bias is the most likely explanation, and in either case, it is clear that the more enthusiastic researchers are, the more assured they can be of industry funding.

Many researchers profess that they are outraged by the very notion that their financial ties to industry could affect their work. They insist that, as scientists, they can remain objective, no matter what the blandishments. In short, they cannot be bought. What is at issue is not whether researchers can be "bought," in the sense of a quid pro quo. It is that close and remunerative collaboration with a company naturally creates goodwill on the part of researchers and the hope that the largesse will continue. This attitude can subtly influence scientific judgment in ways that may be difficult to discern. Can we really believe that clinical researchers are more immune to self-interest than other people?

When the boundaries between industry and academic medicine become as blurred as they now are, the business goals of industry influence the mission of the medical schools in multiple ways. In terms of education, medical students and house officers, under the constant tutelage of industry representatives, learn to rely on drugs and devices more than they probably should. As the critics of medicine so often charge, young physicians learn that for every problem, there is a pill (and a drug company representative to explain it). They also become accustomed to receiving gifts and favors from an industry that uses these courtesies to influence their continuing education. The academic medical centers, in allowing themselves to become research outposts for industry, contribute to the overemphasis on drugs and devices. Finally, there is the issue of conflicts of commitment. Faculty members who do extensive work for industry may be distracted from their commitment to the school's educational mission.

All of this is not to gainsay the importance of the spectacular advances in therapy and diagnosis made possible by new drugs and devices. Nor is it to deny the value of cooperation between academia and industry. But that cooperation should be at arm's length, with both sides maintaining their own standards and ethical norms. The incentives of the marketplace should not become woven into the fabric of academic medicine. We need to remember that for-profit businesses are pledged to increase the value of their investors' stock. That is a very different goal from the mission of medical schools.

What needs to be done — or undone? Softening its conflict-of-interest guidelines is exactly the wrong thing for Harvard Medical School to do. Instead, it should seek to encourage other institutions to adopt stronger ones. If there were general agreement among the major medical schools on uniform and rigorous rules, the concern about losing faculty to more lax schools — and the consequent race to the bottom — would end. Certain financial ties should be prohibited altogether, including equity interest and many of the writing and speaking arrangements. Rules regarding conflicts of commitment should also be enforced. It is difficult to believe that full-time faculty members can generate outside income greater than their salaries without shortchanging their institutions and students.

As Rothman urges, teaching hospitals should forbid drug-company representatives from coming into the hospital to promote their wares and offer gifts to students and house officers.[9] House officers should buy their own pizza, and hospitals should pay them enough to do so. To the argument that these gifts are too inconsequential to constitute bribes, the answer is that the drug companies are not engaging in charity. These gifts are intended to buy the goodwill of young physicians with long prescribing lives ahead of them. Similarly, academic medical centers should be wary of partnerships in which they make available their precious resources of talent and prestige to carry out research that serves primarily the interests of the companies. That is ultimately a Faustian bargain.

It is well to remember that the costs of the industry-sponsored trips, meals, gifts, conferences, and symposiums and the honorariums, consulting fees, and research grants are simply added to the prices of drugs and devices. The Clinton administration and Congress are now grappling with the serious problem of escalating drug prices in this country. In these difficult times, academic medicine depends more than ever on the public's trust and goodwill. If the public begins to perceive academic medical institutions and clinical researchers as gaining inappropriately from cozy relations with industry — relations that create conflicts of interest and contribute to rising drug prices — there will be little sympathy for their difficulties. Academic institutions and their clinical faculty members must take care not to be open to the charge that they are for sale.

MARCIA ANGELL, M.D.

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TREATMENT OF CHRONIC DEPRESSION

THE majority of persons who have an acute episode of a major depressive disorder will have a response to the first or second treatment tried.[1] In patients with mild or moderately severe episodes, treatment with antidepressant drugs and brief psychotherapies are equally effective; in those with severe episodes, medication is usually recommended.[2] The treatment of chronic depression is more problematic, since in 20 to 30 percent of initial episodes, there is incomplete remission after two years.[3,4] Patients with chronic depression have marked impairments in psychosocial function, poor responses to single therapies, and very high rates of use of health care resources.[3] Furthermore, even if they have a partial remission, they have a risk of relapse of 50 to 80 percent.[4]

The poor response of patients with chronic depression to treatment with antidepressant drugs alone is not fully understood, but it cannot be explained solely on the basis of inadequate dosing or the failure of patients to take their medication.[1] Psychotherapy has been advocated as an alternative. Unfortunately, a review of nine studies of psychotherapy for chronic depression that were published before 1998 revealed that in only two trials were patients appropriately randomized, and the combined sample size was only 126 subjects.[5]

Given the lack of empirical data, establishing the relative efficacy of pharmacotherapy and psychotherapy for this disorder has been difficult.[6] Nonetheless, two trends in research results are apparent. First, there is a relatively low rate of response to placebo (about