

## AIDS-Related Opportunistic Illness and Potent Antiretroviral Therapy

**To the Editor:** Dr Ledergerber and colleagues<sup>1</sup> presented data on the incidence of opportunistic infections and cancers in human immunodeficiency virus (HIV)-infected persons. They compared the incidence of specific illnesses in the 6-month period before potent antiretroviral therapy with the incidence in periods after initiation of therapy, and concluded that a decreased incidence of some (but not all) illnesses indicated an effect of therapy. However, analytic difficulties complicate interpretation of these trends for individual opportunistic illnesses.

Pretherapy incidence rates are not strictly comparable with posttherapy rates. Unlike posttherapy rates, pretherapy rates are calculated retrospectively for a group known to be alive at the end of the pretherapy period. These conditional incidence rates are too low for illnesses with a high mortality rate because some affected persons do not survive to start therapy. The effect of therapy is then underestimated if these low rates are included in trend tests. For example, diseases caused by cytomegalovirus and nontuberculous mycobacteria occur late in HIV infection. In the analysis by Ledergerber et al, mortality-induced underestimation of pretherapy incidence of these diseases may have diminished the estimated effect of therapy.

Furthermore, pretherapy rates (and, thus, trends in incidence) could have been affected by clinicians' decisions regarding when to begin antiretroviral therapy. For instance, the study found a slight effect of antiretroviral therapy on tuberculosis risk. This effect may be underestimated because rifampin is a mainstay of tuberculosis treatment, but use of rifampin prohibits concomitant use of protease inhibitors.<sup>2</sup> Delayed initiation of antiretroviral therapy would lead to artifactually low pretherapy tuberculosis incidence rates and underestimation of the effect of therapy. Similarly, no effect of therapy on non-Hodgkin lymphoma risk was seen, but lymphoma risk in untreated patients may have been underestimated if chemotherapy precluded antiretroviral therapy. Conversely, clinicians' decisions may have caused apparent increases in pretherapy incidence if, in general, clinicians were likely to provide antiretroviral therapy to patients who had shown disease progression (ie, who had had recent opportunistic illnesses). This bias would lead to overestimation of the effect of therapy.

Given that antiretroviral therapy has dramatically reduced overall HIV-related morbidity and mortality,<sup>3</sup> it is important to clarify effects of therapy for specific opportunistic illnesses. To this end, the authors might repeat their trend analyses, limiting their observations to the period following antiretroviral therapy. Alternatively, they could compare individuals who started therapy with appropriately matched control subjects who

never received therapy. One would expect pretherapy incidence to be similar to that in control subjects and to be lower after starting therapy for diseases for which antiretroviral therapy is preventive.

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1. Ledergerber B, Egger M, Erard V, et al. AIDS-related opportunistic illnesses occurring after initiation of potent antiretroviral therapy: the Swiss HIV Cohort Study. *JAMA*. 1999;282:2220-2226.
2. Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR Morb Mortal Wkly Rep*. 1998;47(RR-20):1-58.
3. Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med*. 1998;338:853-860.

**In Reply:** Dr Engels and colleagues argue that in our study of the incidence and risk factors of acquired immunodeficiency syndrome (AIDS)-related opportunistic illnesses after the initiation of potent antiretroviral therapy, we may have underestimated or overestimated the effectiveness of antiretroviral therapy. Our aim was not to estimate the effectiveness of antiretroviral combination therapy, which has been conclusively demonstrated in randomized controlled trials<sup>1</sup> and prospective cohort studies.<sup>2-4</sup> Rather, we set out to examine incidence trends and risk factors for individual opportunistic illnesses in a stable cohort of HIV-infected adults, covering defined periods before and immediately after starting potent therapy.

We agree with Engels et al that the pretreatment incidence rates in the study group may not necessarily represent the experience of the whole cohort. However, as we stated in our article, it is noteworthy that the pretherapy incidence of any new opportunistic illness in our study sample (15.1 per 100 person-years) was similar to the incidence (15.7 per 100 person-years) in the whole cohort for 1992 to 1994, before potent thera-

**GUIDELINES FOR LETTERS.** Letters discussing a recent *JAMA* article should be received within 4 weeks of the article's publication and should not exceed 400 words of text and 5 references. Letters reporting original research should not exceed 500 words and 6 references. All letters should include a word count. Letters must not duplicate other material published or submitted for publication. Letters will be published at the discretion of the editors as space permits and are subject to editing and abridgment. A signed statement for authorship criteria and responsibility, financial disclosure, copyright transfer, and acknowledgment is required for publication. Letters not meeting these specifications are generally not considered. Letters will not be returned unless specifically requested. Also see Instructions for Authors (January 5, 2000). Letters may be submitted by surface mail: Letters Editor, *JAMA*, 515 N State St, Chicago, IL 60610; e-mail: [JAMA-letters@ama-assn.org](mailto:JAMA-letters@ama-assn.org); or fax (please also send a hard copy via surface mail): (312) 464-5824.

**Letters Section Editors:** Phil B. Fontanarosa, MD, Deputy Editor; Stephen J. Lurie, MD, PhD, Contributing Editor.

**Table.** Acquired Immunodeficiency Syndrome–Related Opportunistic Illnesses in Patients Not Receiving Potent Antiretroviral Therapy\*

Opportunistic Illnesses	Incidence per 100 Patient-Years (95% Confidence Interval)	
	In 1995-1997, Within 6 Months Before Start of Potent Antiretroviral Therapy (n = 2410)	In 1992-1994, Before Potent Antiretroviral Therapy Became Available (n = 4755)
Esophageal candidiasis	3.14 (2.09-4.54)	4.21 (3.80-4.66)
Nontuberculous mycobacteria	1.79 (1.03-2.91)	2.58 (2.26-2.93)
Cytomegalovirus disease	2.24 (1.37-3.46)	1.96 (1.68-2.27)
Non-Hodgkin lymphoma	0.67 (0.25-1.46)	0.58 (0.44-0.76)
<i>Mycobacterium tuberculosis</i>	0.78 (0.31-1.61)	0.86 (0.68-1.07)
<i>Pneumocystis carinii</i> pneumonia	2.35 (1.46-3.59)	2.41 (2.10-2.75)
Toxoplasmosis	1.45 (0.77-2.49)	1.76 (1.50-2.05)
Kaposi sarcoma	2.02 (1.19-3.19)	1.87 (1.60-2.17)
Progressive multifocal leukoencephalopathy	0.22 (0.03-0.81)	0.50 (0.37-0.67)

\*Data are shown for patients who were subsequently treated with potent antiretroviral therapy (1995-1997) compared with the entire cohort before potent antiretroviral therapy became available (1992-1994).

pies became available. As shown in the TABLE, incidences for specific illnesses were also similar, and no pattern emerged that would indicate overestimation or underestimation of incidence rates (including those of tuberculosis and non-Hodgkin lymphoma) in the sample of patients later treated with potent therapies.

The estimation of incidence trends in the entire cohort for calendar periods covering the introduction of potent therapies circumvents some of the problems mentioned by Engels et al. A recent analysis<sup>4</sup> of the Swiss HIV Cohort Study comparing data from 1992-1994 with the 12-month period from July 1997 to June 1998 showed an 80% reduction in the risk of progression to any opportunistic infection (hazard ratio, 0.20; 95% confidence interval [CI], 0.15-0.27), but no significant trend was evident for non-Hodgkin lymphoma (hazard ratio, 0.60; 95% CI, 0.30-1.29). These findings are quite similar to those that we reported. Survival bias and other potential selection biases (eg, due to concomitant treatments or recent clinical progression) thus do not appear to have distorted estimates of pre-therapy incidence rates.

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1. Hammer SM, Katzenstein DA, Hughes MD, et al. A trial comparing nucleoside monotherapy with combination therapy in HIV-infected adults with CD4 counts from 200 to 500 per cubic millimeter. *N Engl J Med.* 1996;335:1081-1090.

2. Egger M, Hirschel B, Francioli P, et al. Impact of new antiretroviral combination therapies in HIV infected patients in Switzerland: prospective multicentre study. *BMJ.* 1997;315:1194-1199.

3. Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med.* 1998;338:853-860.

4. Ledergerber B, Telenti A, Egger M. Risk of HIV related Kaposi's sarcoma and non-Hodgkin's lymphoma with potent antiretroviral therapy: prospective cohort study. *BMJ.* 1999;319:23-24.

## A Critical Pathway for Treatment of Community-Acquired Pneumonia

**To the Editor:** Dr Marrie and colleagues<sup>1</sup> concluded that “the implementation of a critical pathway [for treating community-acquired pneumonia in Canada] reduced the institutional resources without causing adverse effects on the well-being of the patients.” However, several issues should be evaluated before this recommendation is widely adopted.

First, the average length of stay (LOS) for the institutions using a pathway was 8.2 days, almost 3 days longer than the national average in the United States.<sup>2</sup> The large difference between the mean and median implies a skewed distribution in the LOS. This calls into question whether some patients were being treated for complications of pneumonia or an unrelated event. On average, patients stayed more than 3 additional days in the hospital after being converted from intravenous antibiotics to oral therapy regardless of type of institution. This is inconsistent with data from the United States, where patients are discharged approximately 1 day after conversion to oral therapy.<sup>3</sup>

Second, instead of a statistical analysis on the means of the means or medians, a more appropriate method would have been to perform a multifactorial analysis taking into account the severity of illness (eg, risk class) and type of institution. Our data from Texas suggest that teaching and community hospitals differ in their treatment of community-acquired pneumonia.<sup>4</sup> In addition, comparing the LOS before and after implementation of the pathway at the individual institutions would have been valuable.

It would also be helpful to know which antibiotic therapy was used at conventionally managed institutions and whether that therapy was appropriate based on the American Thoracic Society or Infectious Diseases Society of America guidelines. The use of inappropriate antibiotic therapy can negatively affect outcomes in community-acquired pneumonia.<sup>5</sup> Also, if there was only 1 antibiotic regimen involved in the critical

pathway, why did the sum of patients receiving monotherapy not equal 100%? If patients at the intervention institutions received other antibiotics, their outcomes could have been compared with those receiving the study drug. Finally, if individuals at critical pathway institutions were not receiving therapy consistent with the pathway, it would be difficult to conclude that the decrease in LOS was due to the pathway.

We applaud the efforts of the authors to examine this issue, which has long needed clarification. However, we feel that more careful examination of the data is required to justify the conclusion.

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1. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK, Feagan BG, for the CAPITAL Study Investigators. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. *JAMA*. 2000;283:749-755.
2. *Length of Stay by Diagnosis and Operation, United States*. Baltimore, Md: HCIA Inc; 1999.
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4. Burgess DR, Burgess DS, Patel NN. Are there differences in the treatment of community-acquired pneumonia between a community and university hospital [abstract]? *Pharmacotherapy*. 1999;19:491.
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**In Reply:** We acknowledge that the average LOS is shorter in the United States than in Canada. Differences also may exist in quality of care, patient satisfaction, and outcomes. However, the optimum LOS for community-acquired pneumonia has not been established. The statement of Drs Burgess and Lewis that “patients are discharged approximately 1 day after conversion to oral therapy” in the United States is based on a single-center, uncontrolled, descriptive study.<sup>1</sup> Importantly, quality of life was not evaluated. Therefore, whether this policy is consistent with good patient care or is common throughout the United States is unknown.

The potential effects of disease severity and type of institution were considered in the design of the study. Randomization was stratified by the type of institution and matched by the historical LOS. Burgess and Lewis suggest that differences exist in LOS between teaching and community hospitals based on data from a pair of institutions in Texas.<sup>2</sup> Patients at the community hospital in that study were considerably older but had a substantially shorter LOS than those at the teaching hospital. This counterintuitive finding suggests that other confounding factors such as the nature of the patient population accounted for the differences. In our study, randomization was stratified by type of institution to ensure that the treatment allocation was balanced. We also matched by the historical LOS to control for other confounders such as disease severity. This appears to have been successful, since the baseline Pneumonia Severity Index scores for the 2 arms were similar (84.1 in the critical pathway vs 86.8 in conventional management,

$P=.18$ ). Although it might be interesting to compare results before and after implementation of the pathway, we believe the prospective randomized design of our study allows us to draw more credible conclusions.

Regarding antibiotic use, at the conventional institutions the adherence rate to American Thoracic Society guidelines was 77.3%. Since the sample of institutions was relatively large, this figure likely reflects usual practice in Canada. Levofloxacin use was not 100% at the intervention sites; however, we know of no critical pathway in which complete adherence has been observed. The analysis suggested by Burgess and Lewis, excluding patients who did not adhere to the pathway, would be inappropriate because critical pathways are introduced and perceived at the institution level. Hence an “effectiveness” analysis using data from all eligible patients was performed.

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1. Ramirez JA. Switch therapy in community-acquired pneumonia. *Diagn Microbiol Infect Dis*. 1995;22:219-223.
2. Burgess DR, Burgess DS, Patel NN. Are there differences in the treatment of community-acquired pneumonia between a community and university hospital [abstract]? *Pharmacotherapy*. 1999;19:491.

## Gifts to Physicians From the Pharmaceutical Industry

**To the Editor:** While reading Dr Wazana's<sup>1</sup> article about pharmaceutical gifts, my first thought was that I was reading this in a journal I had received courtesy of the pharmaceutical companies who advertise in it. However, I was most disturbed by the implication that I could be bought and that I did not have the intelligence to decide for myself what was fact and what was a commercial.

Having been practicing for the past 20 years, I have seen a significant improvement in the quality and content of pharmaceutical-supported conferences. Rarely do I attend one that is strictly a commercial. It is also rare today to attend any conference that does not have some pharmaceutical support.

I agree with Wazana's conclusion that prescribing habits are affected by these conferences, but I disagree that it is because of the perks. It is the perks that help draw physicians, but the quality of the presentation determines whether they alter their prescribing habits. I suspect that if physicians do alter their pre-

scribing habits it is because they are more knowledgeable about the product and more comfortable with its use, and not because of the influence of perks. It is also quite cost-effective to provide perks, such as a dinner or a golf game, rather than paying physicians for the cost of their time.

Physicians are being inundated by outside influences on their practice. Physicians should be given some credit for being intelligent and principled. They should decide which conferences to attend, which perks to accept or reject, and ultimately which medicines to prescribe.

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1. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA*. 2000;283:373-380.

**To the Editor:** Dr Tenery's Commentary<sup>1</sup> about physicians and the pharmaceutical industry and the article by Dr Wazana<sup>2</sup> seem to take a limited view of financial reality. The issue in which these articles appeared contained 135 pages of advertisements. Of the \$11 billion the industry spends each year to promote itself, only \$5 billion is being spent on activities involving pharmaceutical representatives.<sup>2</sup> At least some of the rest of this money appears to subsidize publication of scientific articles, including Tenery's.

Business entities exist only to make profits, and to do so successfully they depend on name or product recognition. It is naive to expect that a business would provide money or other support without some reciprocal expectation; to blame an industry for fulfilling its prime directive is simply scape-goating. It is similarly wrong to blame the profession for this change in culture. It is, in fact, the culture that is at fault for changing the profession. The reality is that the clinical practice of medicine is no longer simply a profession; with the intrusion of corporate control, it increasingly functions like the big business that it is.

With many state medical boards now mandating continuing medical education (CME) requirements, CME has, in essence, become an unfunded political mandate, and an expensive one at that. Thus, the demand for CME has spawned its own business opportunities. While the intent of this type of regulatory micromanagement may be understandable, absolutely no scientific evidence has demonstrated that these mandates actually improve care, decrease malpractice claims, or reduce patient risk. They do, however, increase costs for physicians and their employers. In addition, the implication that nonapproved education is somehow tainted is nonsense. One need look no further than the simple-minded, multiple-paged, cartoonish advertisements that festoon any major medical journal for examples of this widespread practice. Perhaps medical journal editors should consider renouncing funding from all advertisers related to health care as a fundamental and irreparable conflict of interest. They would certainly be free to solicit advertising money from other unrelated industries. With good business practices, most journals would be affected little by such a policy.

Finally, I was puzzled by the inconsistency of Tenery's comment that "[t]he practice should be judged by degree. The concern is the pursuit of these practices to excess. . . ." This struck me as another version of the old adage that "we've already established what you are; now we're just haggling over the price."

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1. Tenery RM Jr. Interactions between physicians and the health care technology industry. *JAMA*. 2000;283:391-393.

2. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA*. 2000;283:373-380.

**To the Editor:** Dr Wazana's review<sup>1</sup> strongly suggests that the present extent of physician-industry interactions affects not only prescribing behavior but the professional standing and identity of the medical profession in general. During my sabbatical visit to the United States, I encountered physicians who managed to have lunch provided by pharmaceutical companies on most of their work days. Others only attended seminars or lectures in CME that included free meals.

The practice of accepting meals provided by drug companies is problematic for at least 3 reasons: (1) the potential for conflict of interest can affect physicians' clinical judgment; (2) the pattern undermines the trust of patients that medications will be prescribed based solely on their medical needs; and (3) such physician behavior tacitly teaches medical students and residents that it is appropriate to expect or even demand meals, gifts, and other incentives as part of clinical practice and that clever and successful physicians are characterized by their success in extracting these favors.

In the long run this behavior will undermine the respect and trust of physicians and the standing of the entire medical profession. Instead of perpetuating the current pattern of physician-industry interactions, one should expect physicians to pay for their own meals and to participate in CME because it is a professional duty. At the same time, society has to provide sufficient resources for medical education if it wants to have its physicians behave as professionals rather than adopt the behavior of the marketplace.

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1. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA*. 2000;283:373-380.

**To the Editor:** We read with interest the article by Dr Wazana<sup>1</sup> that reviewed the medical literature on the relationship between physicians and the pharmaceutical industry and its impact on the knowledge, attitudes, and behavior of physicians. Despite enhanced discussion of the issues, a plethora of publications, and official guidelines produced by professional organizations,<sup>2,3</sup> these concerns are remarkably similar to those expressed a decade ago.<sup>4,5</sup> However, there is evidence of a worrisome new marketing strategy, pharmaceutical sponsorship of events involving not only physicians, but their families as well.

Recent examples of such events in Louisville, Ky, and Omaha, Neb, highlight these concerns. At 1 such event, physicians and their families were invited to a “day at Kentucky Kingdom,” a large outdoor theme park, for a 30-minute program for physicians followed by lunch for everyone and the remainder of the day to enjoy the rides. At another, dinner with families at a pizza restaurant and children’s game center was followed by a 15-minute presentation to physicians, while “spouses and children play games and ride bumper cars.” A different pharmaceutical corporation invited physicians in Omaha to the zoo for a 45-minute presentation followed by an IMAX film, lunch for physicians and their families, and the chance to “enjoy an afternoon at the zoo.”

While such events may appear to support traditional family values, they also involve the physician’s spouse and children in the gift relationship, potentially increasing their perceived indebtedness to the pharmaceutical company. Major professional guidelines would seem to discourage participation in such activities, although they do not explicitly mention family involvement in sponsored events. The guidelines<sup>2</sup> of the American Medical Association stipulate that “[s]ubsidies for hospitality should not be accepted outside of modest meals or social events that are held as part of a conference or meeting.” The events we describe would appear to violate these guidelines. Revision of major professional guidelines may be required to address these newer forms of marketing and to assure the public of the independence of physician judgment regarding selection of pharmaceuticals.

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1. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA*. 2000;283:373-380.
2. Council on Ethical and Judicial Affairs, American Medical Association. Gifts to physicians from industry. *JAMA*. 1991;265:501.
3. American College of Physicians. Physicians and the pharmaceutical industry. *Ann Intern Med*. 1990;112:624-626.
4. McKinney WP, Schiedermaier DL, Lurie N, Simpson DE, Goodman JL, Rich EC. Attitudes of internal medicine faculty and residents toward professional interaction with pharmaceutical sales representatives. *JAMA*. 1990;264:1693-1697.
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**In Reply:** As suggested by Dr Howard and Dr Edwards, the relationship between physicians and the pharmaceutical industry extends to the advertising found in journals. Avorn et al<sup>1</sup> examined the impact of this interaction by surveying physicians on their perception of 2 drugs for which commercial messages about efficacy differed substantially from scientific sources. They found that, although most physicians report paying little attention to drug advertising and pharmaceutical representatives, their answers revealed their receptivity to commercial sources. Such findings are worrisome, but unfortunately, there are few studies looking at this interaction. Nonetheless, several journals have made it their policy not to allow advertisements related to medicine in their publications.

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Dr Vollmann highlights concerns about the incidence and attitudes of physicians regarding interactions with the industry. Howard echoes these observations, and adds that these events influence prescribing behavior but he questions whether perks themselves influence physicians. He attributes changes in physician prescription behavior to increased knowledgeability and comfort with the medications.

Two studies, however, refute Howard’s latter claim. One examined 2 CME events on the same drugs but with different sponsors and found the content to be biased each time in favor of the sponsor’s drug.<sup>2</sup> Another examined 3 CME events and found that the rate of prescribing for the sponsoring drug increased the most while that of other drugs decreased or did not increase as much. This occurred despite equal efficacy, safety, and cost of the discussed medications.<sup>3</sup> As for the influence of perks per se, the literature is limited to correlational findings. It points to the influence of gifts on attitudes toward pharmaceutical representatives, and to the impact of meals on requests for the addition of formulary drugs, which represent little or no therapeutic advantage over existing formulary drugs. In addition, it is noteworthy that many newspapers will not allow their writers to cover a topic if they have received any perks in researching their topic, however benign the topic or the perk may seem (eg, *New York Times*’ guidelines for submissions).

I share Vollmann’s concern about the example physicians set both to trainees and the public, as well as his suggestion that we should pay for our own meals. I applaud his call for nonpharmaceutical funding sources for CME. Unfortunately, our society might have trouble stepping in to take on that responsibility given the already prominent financial position in which most physicians situate themselves. One could make a cost-benefit argument about the long-term savings to the system if rational prescribing could be improved by means of less biased CME. But ultimately, we must ask ourselves on whose shoulders the responsibility of maintaining professional competency should fall. It is sobering to realize that we are facing some of the same issues a decade later and that possibly, as Drs McKinney and Rich suggest, we might even be falling behind as a result of the industry’s new marketing strategies. The Canadian Medical Association is revisiting its guidelines and perhaps other medical groups should follow this example.

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1. Avorn J, Chen M, Hartley R. Scientific versus commercial sources of influence on the prescribing behavior of physicians. *Am J Med*. 1982;73:4-8.
2. Bowman MA, Pearle DL. Changes in drug prescribing patterns related to commercial company funding of continuing medical education. *J Contin Educ Health Prof*. 1988;8:13-20.
3. Bowman MA. The impact of drug company funding on the content of continuing medical education. *Mobius*. 1986;6:66-69.

**In Reply:** Although the business interests of the pharmaceutical industry always have potentially conflicted with the best interests of patients, it is only since the 1980s that these conflicts threatened to adversely affect patient care. In addition to

promoting name recognition and access to prescribers, the pharmaceutical industry has created incentives that, in themselves, alter prescribing behaviors.

Dr Wazana<sup>1</sup> pointed out that not only do these practices work, but they are so effective that many physicians are not even aware of the influence of these techniques on their own behavior.

Since the medical profession is built on trust by patients that their physicians will always act in their best interests, it is imperative that there be full disclosure of any conflicts of interest or potential conflicts of interest. Unfortunately, these conflicting interests often go unrecognized. Thus, those involved in an attempt to bring reason to these practices must return to the precepts of name recognition and access.

To fault a "change in culture" without attempting to find a solution betrays the very principle on which the profession was established, and is a travesty to our patients.

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## William Osler at 150

**To the Editor:** I certainly enjoyed reading Dr Golden's article on the life of William Osler,<sup>1</sup> and I commend him for accurately depicting the spirit and charm of this great physician. Granted, Osler made no momentous discoveries, was not a distinguished researcher, and never had his own clinical practice. However, he was quick to identify which purported breakthroughs were actually important, was a staunch supporter of medical research and academic centers, and revered clinical practice as the true backbone of the medical profession. He realized that the medical profession required both clinicians and scientists to ensure medical advancement and optimal patient care, and he was able to unite these factions into one harmonious group. In addition, he emphasized that every physician must teach, and he established the model for medical school curriculum that we still use today.<sup>2</sup> It has been said that there are many who have done more for the advancement of medicine than Osler but none who have done more for the advancement of the medical profession.

Osler had some faults, but they were few and minor. Bliss states in his new biography of Osler, "Try as I might, I could not justify the death of Osler's reputation. He lived a magnificent, epic, important, and more than slightly saintly life."<sup>3</sup> Osler's appreciation of the history of medicine, his uncanny ability to weed out useless medical theories and treatments, and his clear vision of the future of medicine as an art, science, and profession might never be surpassed. In essence, he was a prophet of good medicine. These qualities, combined with an engaging personality, a profound love of his profession, and a tireless spirit, made him the most influential and honored phy-

sician of his day. In the 1930s through the 1950s, many students received his book of essays, *Aequanimitas With Other Addresses*,<sup>4</sup> upon graduation from medical school. There is great wisdom in this book, and every professional can still benefit from reading it. It has now been 80 years since Osler's death, but his vision of the medical profession and what it (we) should strive to do is as meaningful as ever. It would behoove us all to be a little more like William Osler.

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1. Golden R. William Osler at 150. *JAMA*. 1999;282:2252-2258.
2. Osler W. The natural method of teaching the subject of medicine. *JAMA*. 1901;36:1673-1679.
3. Bliss M. *William Osler: A Life in Medicine*. New York, NY: Oxford University Press; 1999:xiii.
4. Osler W. *Aequanimitas With Other Addresses to Medical Students, Nurses, and Practitioners of Medicine*. 3rd ed. Philadelphia, Pa: P Blakiston's Son & Co; 1932.

**In Reply:** I thank Dr Carter for his insightful comments on my article about the life and teachings of Sir William Osler. On a minor note, it is not quite accurate to depict Osler as one who "never had his own clinical practice." He engaged in private practice throughout his career, beginning in 1874 with service as a locum tenens in Dundas, Ontario, earning his first fee of 50¢ for the removal of a speck from the cornea. Osler maintained his own office, but his main role in private practice was as a consultant. He commented, "It is not necessary for every man to be a practitioner in the ordinary sense, but long years of hospital and laboratory work constitute a better equipment for the teacher and consultant."<sup>1</sup> Indeed, for most of his career Osler was opposed to the concept of the full-time clinical teacher, although he later endorsed the idea. His private consulting practice reached its peak in Baltimore, Md, where in 1901 he traveled more than 19 000 miles and saw 780 new patients (exclusive of the hospital), including cabinet ministers and consultations at the White House.<sup>2</sup> This increasing burden was a major factor in Osler's decision to accept the Regius Professorship at Oxford University in 1904, with its far less onerous demands.

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1. Harrell GT. Osler's practice. *Bull Hist Med*. 1973;47:545-568.
2. Bensley EH, Bates DG. Sir William Osler's autobiographical notes. *Bull Hist Med*. 1976;50:596-618.

## RESEARCH LETTER

### Arsenic Contamination of Museum Artifacts Repatriated to a Native American Tribe

**To the Editor:** The 1990 Native American Graves Protection and Repatriation Act (NAGPRA)<sup>1</sup> provides for the inventory and return of human remains, funerary objects, sacred objects, and objects of cultural patrimony to Native Americans,

Alaskan Natives, and Native Hawaiians. Many objects, such as full head masks, have already been returned. However, concerns have arisen about risk of exposure to museum-applied pesticides (eg, arsenic, mercury, organophosphates, carbamates, organochlorines, and volatiles).

We evaluated 3 ceremonial objects repatriated under NAGPRA. The tribe's cultural preservation office requested that we neither describe the objects nor provide details of their cultural use. To our knowledge, this is the first report of a chemical analysis of repatriated artifacts.

**Methods.** Three objects were analyzed. Each was made of leather, with attached grasses, corn husks, feathers, horsehair, yarn, and paint. Associated museum catalog records were reviewed for evidence of pesticide use.

Samples were taken of adherent debris and representative surface material. Metal content, including arsenic, was measured by energy-dispersive x-ray analysis. Total object arsenic levels were estimated by weighted sample averaging applied to the total surface area. Organic pesticide residue was determined by in-line pyrolysis gas chromatography-mass spectroscopy (GC-MS). Volatiles were analyzed by GC-MS of 4-hour ambient-temperature air samples from a Mylar bag enclosing the object.

**Results.** There was no visible evidence of contamination on any object. Object 1 had arsenic on all surfaces, with the highest concentrations around eye holes, surface paint, and feathers. Total object arsenic level was 1.3 g. Catalog records confirmed that the object had been treated with sodium arsenite. Object 2 had trace amounts of naphthalene on interior surfaces, but none was detected in head-space air. There were no records of pesticide treatment. Object 3 had moderate amounts of arsenic on exterior surface paint. Total object arsenic level was 60 mg. There were no records of pesticide treatment.

**Comment.** Museums apply pesticides to preserve perishable objects, and arsenic was widely used as a museum pesticide from the 1800s through the 1970s. Objects 2 and 3, containing naphthalene and arsenic, respectively, had no documentation of pesticide treatment. Thus, museum documentation cannot be relied on to identify contaminated specimens.

Arsenic on these objects poses a potential health threat. Daily ingestion of as little as 3 to 4 mg can result in long-term toxicity, and an acute ingestion of 1 to 3 mg/kg may

be lethal.<sup>2</sup> The greatest acute danger would be to a young child who chewed on a significantly contaminated object. Long-term exposure may occur via dust in storage and usage areas, from food stored with ceremonial objects, or during ceremonial use in which objects are handled or worn.

Nationwide, hundreds of thousands of artifacts are subject to repatriation, including more than 400 similar objects to this tribe. Wipe sampling of similar objects in museums has demonstrated the presence of arsenic and mercury (Leigh Kuwanwisiwma, written communication, 1999), and other museum items carry residues of arsenic, mercury, DDT, and strychnine.<sup>3,4</sup> Our preliminary results suggest that all museum objects subject to repatriation should be tested for pesticide residues.

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## CORRECTIONS

**Incorrect Statement:** In the *JAMA Patient Page* entitled "Drug Abuse" published in the March 8, 2000, issue of *THE JOURNAL* (2000;283:1378), an incorrect statement appeared under "Withdrawal Symptoms From Opiate Abuse." Seizures are not a common symptom of withdrawal from opiate use.

**Error in Table Footnote:** In the Original Contribution entitled "Risk of Meningococcal Infection in College Students" published in the May 26, 1999, issue of *THE JOURNAL* (1999;281:1906-1910), there was incorrect wording in the table footnote. On page 1908, the second footnote to the Table should read "Aged 18 to 22 years, excluding the 4-year college population (see "Methods" section)."