

CORRESPONDENCE



THE INTERNET AND THE JOURNAL

To the Editor: The editorial "The Internet and the *Journal*" (June 22 issue)¹ addresses the pros and cons of electronic "publishing" of articles on the Internet. You mentioned abstracts in passing, but the specter of electronic publishing of abstracts raises even more serious questions.

Any flaws in the proposal for electronic publication of articles would be magnified enormously for electronic abstract publication. The selection process for abstracts already has demonstrable shortcomings. One study found that abstracts frequently were never published, and if they were it was only after a long interval. The number of citations of abstracts (a measure of interest in their content) was not a predictor of subsequent successful publication.² Subsequent analyses have expanded these observations.³ Negative abstract results were published less often as papers,⁴ and even when publication did result, long delays were common.⁵

The electronic publication of data in an abstract, even when they are published later as an article, can lead to the acceptance of flawed or preliminary information by the medical community long before the data have been subjected to critical peer review. The risk of disseminating this unvalidated information is obvious.

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1. Kassirer JP, Angell M. The Internet and the *Journal*. *N Engl J Med* 1995;332:1709-10.
2. Goldman L, Loscalzo A. Fate of cardiology research originally published in abstract form. *N Engl J Med* 1980;303:255-9.
3. Meranze J, Ellison N, Greenhow DE. Publications resulting from anesthesia meeting abstracts. *Anesth Analg* 1982;61:445-8.
4. Yentis SM, Campbell FA, Lerman J. Publication of abstracts presented at anaesthesia meetings. *Can J Anaesth* 1993;40:632-4.
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To the Editor: . . . Without hyperbole, it can be argued that mass access to electronic data transfer presents an order of change in communications that ranks with the development of the automatic printing press. Like that of the wide availability of cheaply printed books and gazettes, the impact of the Internet won't be clearly understood until our use of it has evolved further.

The limited distribution of the results of a medical investigation, whether in part or whole, can easily expand through redistribution. Although it is a point of professional etiquette that no correspondence can be recirculated on electronic mailing lists or posted on bulletin boards without the express permission of the author, it is difficult to enforce professional etiquette. Moreover, anyone with access to one of the electronic gateways to the Internet has access to most of the electronic information storage available on the Internet. Discussion groups are open-ended. No matter how esoteric the specialty orientation, nonspecialists often browse the lists or message data bases. They may include medical journalists, concerned patients, and sensationalists. The more controversial or newsworthy the information, the more likely it is to be promulgated rapidly and indiscriminately. . . .

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To the Editor: In your thought-provoking editorial on the potential dangers of medical publication on the Internet, you and Dr. Angell raise some cogent and important questions. However, your assertion that information published on the Internet is intrinsically susceptible to alteration by the recipient is untrue. World Wide Web and other Internet documents are uploaded by the author or authors and stored on a "server" computer, and are then available for viewing or downloading by the end user. There is no mechanism for altering the document's contents on the server by unauthorized parties.

Regarding the concern that nonmedical personnel will misinterpret Internet medical information, this phenomenon already occurs with information from libraries, newspapers, radio, and television and is not unique to the Internet nor sufficient reason to throw out the baby with the bath water in advocating the widespread restriction of Internet medical publication.

Although your emphasis on the principles of peer review and preserving the integrity of original papers is unarguable, your supposition that these principles are intrinsically threatened by Internet technology is unsupported. Appropriately used, these technologies offer the potential to maintain the high standards of traditional medical publication and add to it the efficiency of the electronic world. Our task is to ensure that it is employed responsibly.

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To the Editor: Just as the word "publishing" has taken on new meaning, so, perhaps, has the word "meeting." You and Dr. Angell state that "posting a manuscript, including its figures and tables, on a host computer to which anyone on the Internet can gain access will constitute prior publication." In a previous editorial,¹ however, Dr. Angell and you stated that you would exempt all presentations at scientific meetings from the policy of considering a manuscript for publication only if its substance has not been submitted or reported elsewhere (the Ingelfinger Rule). An important issue in terms of the Internet is, what constitutes a "meeting"?

Recently, we and our colleagues created an interactive poster session on the Internet entitled "PosterNet." When PosterNet is operational, computer users will be able to register from any location in the world at no charge to add a poster to the session, gain access to a poster, make comments about a poster to which the authors can respond, and read the previous comments of other viewers and responses from the authors. Although the current demonstration contains posters that were presented previously at a scientific meeting, we anticipate that investigators may place on PosterNet posters that have not been presented previously.

We believe that the editors should consider presentations at a virtual meeting on the Internet that requires registration by participants to be like presentations at any other meeting. We also believe that the editors should not consider posters such as those currently demonstrated on PosterNet to be "manuscripts" or to be "prior publications." Such a policy will preserve the advantages of peer-reviewed publication without placing unwieldy and potentially chilling restrictions on communications among investigators.

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1. Angell M, Kassirer JP. The Ingelfinger rule revisited. *N Engl J Med* 1991; 325:1371-3.

To the Editor: We laud your message and share your view that posting a manuscript on a publicly available Internet host computer qualifies as prior publication. Implicit in your message is acceptance of the Internet as a venue for publication of original manuscripts, a step we feel to be inevitable.¹ What particularly intrigued us, however, was the statement "medicine is not physics." This statement aptly summarizes our first-hand experience in establishing a cancer-information resource on the Internet. We discovered that Internet publishing tests the fine line between free speech, academic freedom, and responsible dissemination of clinically relevant information.

We were surprised to be confronted by such challenges when we introduced an Internet-based resource for cancer information (<http://www.oncolink.upenn.edu/>) last year. A dispute ensued with the medical physicist who helped us launch the service and edit its contents. The issue was whether to post any manuscript without review or to mandate a review process. The physicist vehemently refused to agree to prior review, citing academic freedom and free speech as his reasons. The dispute was taken to a higher level within our university and culminated in the reaffirmation of the review process.

Subsequently, we received strongly negative reactions. Many electronic-mail messages took the physicist's position, favoring the open posting of manuscripts. The story found its way into the lay press,² and there, too, the tone was negative. Few nonmedical Internet users acknowledged the need for our cautious approach.

We relate these events for two reasons. First, we anticipate that others in our profession may find themselves in a similar position, especially given the relative novelty of the Internet as a means of distributing medical information. Indeed, within a day of the publication of your editorial, your views were sharply criticized by Internet users on public Internet bulletin boards.

Second, the risks involved in distributing medical information over the Internet may be obvious to physicians but not to others. The Internet has traditionally provided a venue for "open" communications, where ideas, no matter how far-fetched, have been shared. Medicine is not well suited to this, and those outside the medical profession may object to our traditional peer-review mechanisms. The Internet should not be used as a means of circumventing such processes. We are advocating responsible distribution of medical information, not censorship.

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1. Goldwein JW, Benjamin I. Internet-based medical information: time to take charge. *Ann Intern Med* 1995;123:152-3.
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To the Editor: We agree with the conclusions you and Dr. Angell drew in your editorial. One year ago, we created Astmanet, an electronic forum for physicians interested in asthma. Our experience is still limited, but we would like to share an example.

Some weeks ago, a woman was hospitalized with a pneu-

monia due to dapsone, which had been prescribed for urticaria. It was the first time such a case had been encountered. We sent a description of the case to the members of Asmanet — a limited number of colleagues but many more than a dozen or two. Within 24 hours we received interesting reactions from experts, as well as references.

Asmanet is a moderated forum; that is, we have editorial responsibility for its contents. In our opinion, exchanging such case reports on the Net would increase information available to professionals. The Internet could be a fantastic tool, but Asmanet or any other forum on the Net will not replace peer-reviewed journals. Yet it will add something new.

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To the Editor: Your interesting discussion relates that “physicists” have long circulated preprints by electronic mail. There exists a wide range of fields or cultures in physics — physics is not monolithic (any more, one supposes, than is medicine). This January, at the American Physical Society Units meeting (composed of representatives of each of the units of the society), the electronic circulation of papers was discussed at some length. Before the advent of the Internet, it was not uncommon for large physics groups to send out several hundred copies of their papers before publication. Opinions expressed at the meeting ranged from those of the Los Alamos people (typically high-energy physicists) espousing free Internet circulation of papers, and hinting that referees are redundant, to those of many who think as do you and Dr. Angell and the *Journal*.

Your editorial states, “But medicine is not physics.” Surely physicians and physicists share, in addition to the original meaning of the names, an overwhelming desire to present their work as accurately as is humanly possible, including discussions of known limitations in their work. To this end, the peer-review system has evolved; it can certainly be improved upon, yet it is an essential part of the modern scientific method. For, in effect, all papers are equal, but some are more equal than others. It is these latter, which have the imprimatur and imprint of careful and rigorous reviewing, that will have the greatest weight and impact by far.

As an end user of medicine, I appreciate that medical research has a social responsibility to get it right. I would personally feel more comfortable if *all* research were done as well as possible, whatever its (often unforeseen) ultimate use. So, I suspect (and hope) that good people will still give the most attention to rigorously refereed work, be it presented to them by any of the solid-state methods in use — computer-monitor screen, optical compact disc, magnetic floppy disc — or the printed page.

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To the Editor: You and Dr. Angell present a limited and somewhat pessimistic view of the relation between medical journals and the emerging electronic resources of the Internet and World Wide Web. To be sure, the current hodgepodge of unedited hypotheses, comments, and conjecture found at most medical Web sites cannot serve as a basis for informed

clinical decision making. To reject the medium because of its content, however, is unwarranted.

If we agree that the method of peer review best ensures the quality and importance of published material, then the key issue becomes how to translate that process to the Internet. Ideally, if the most respected journals were to convert to primary electronic publishing, several benefits would accrue. First, the enormous savings from eliminating the costs of printing, shipping, and delivering the physical mass of the journal would allow lower costs per issue, decreased environmental impact, and decreased storage-space requirements. Subscribers would pay for the service of peer review in a more direct fashion. As more journals come on-line, the ability to access directly an article’s references (or the author himself or herself) would allow a more critical reading of the literature, complete with the opportunity for direct response.

Because of the exponential accumulation of information, we are ever more dependent on the prudent editing and manuscript review that the *Journal* offers. Nevertheless, we would be imprudent to ignore the numerous advantages of converting to a primary electronic medium.

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The editors reply:

We believe that peer review is essential to maintaining the quality of the information that journals provide, and our policy is designed to preserve the integrity of this process. Because they appreciate that posters and abstracts presented at medical meetings are preliminary, most physicians wait until a report has been subjected to peer review and published before deciding about its applicability to their practices. If abstracts, posters, or preprints were made available on the Internet, they could be seen by anyone, as Dr. Watson points out. Although people misinterpret medical information now, as Dr. Wiviott states, the amount of such information available could be multiplied infinitely if the Internet were used for preliminary reports. We think it likely that the public would end up more confused than ever.

We have always been willing to review manuscripts that had been presented first at medical meetings, but we have asked authors not to submit their figures and tables to reporters, so that peer review could take its course.¹ Like preprints, any poster incorporated into a host computer with free access by anyone on the Internet (such as those on PosterNet) will be considered previously published, and we will not review for publication any manuscripts based on such posters. Because figures and tables are a necessary ingredient of posters in published CD-ROM collections, manuscripts based on the data in these collections will also be excluded from review.

Although experience with World Wide Web sites and Usenet groups is fragmentary, the Oncolink and Asmanet experiences illustrate some of the issues that have been anticipated for the time when medical care is adapted to an electronic medium.² As Drs. Goldwein and Benjamin learned and as our June 22 editorial pointed out, attitudes toward information differ considerably among scientists in different domains and — as Mr. Finegold reports — even within those domains. The Asmanet experience shows that rapid communication among cadres of practitioners can have considerable promise; never-

theless, the particular case related by Godard and Godard only suggests the hypothesis that the drug and pneumonia are causally related, nothing more.

We have no quarrel with the point made by Dr. Wiviott and Dr. Pignone that peer review can be implemented entirely electronically and that manuscripts that have undergone peer review and been accepted for publication could be released rapidly by electronic means. Although the number of papers for which the immediate health of the public requires such rapid dissemination is small, it is only a matter of time before many journals will be able to publish such papers electronically immediately after acceptance and final editing.

Finally, we did not claim that a recipient could change the content of information downloaded from the Internet (though a clever hacker undoubtedly could), only that the person who submitted the document to a file server could replace it with a different draft.

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MARCIA ANGELL, M.D.

1. Angell M, Kassirer JP. The Ingelfinger rule revisited. *N Engl J Med* 1991; 325:1371-3.
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CLINICAL PROBLEM-SOLVING: COSTLY ERRORS

To the Editor: In the Clinical Problem-Solving case presented by Dr. Duffy (June 1 issue),¹ concerning a patient with hemolytic anemia due to cold agglutinins who later received a diagnosis of large-cell lymphoma, there was a failure to probe for an important pathogenetic link that might have led to more rational and effective therapy. Serum electrophoretic and immunofixation studies in patients with cold-agglutinin anemia and lymphoma usually reveal a monoclonal immunoglobulin of the IgM type, and in rare cases of the IgG or IgA type.²

Coupled with phenotypic studies of lymphoma tissue (i.e., heavy and light chains and CD5 expression), such studies might have indicated the likelihood of monoclonal IgM production by the lymphoma, as in Waldenström's macroglobulinemia. Sometimes, the serum must be collected under warm conditions to prevent the false negative results produced by a type I cryoglobulin that may coexist with the cold agglutinin. Thus, the presumed "large-cell lymphoma" may have reflected the presence of plasmacytoid B lymphocytes, a finding consistent with the low-grade lymphoma of Waldenström's disease. Although there is no consensus on the definition of Waldenström's macroglobulinemia, the presence of monoclonal IgM and plasmacytoid B-cell lymphoma suggests this diagnosis and identifies patients who may benefit from treatments similar to those for macroglobulinemia.³

If monoclonal macroglobulinemia due to lymphoma were confirmed, the optimal treatment would differ from that usually given for large-cell lymphoma. Primary treatment of macroglobulinemia with a combination of an alkylating agent and a glucocorticoid has induced remissions in approximately 50 percent of patients, but we have reported a response rate of 80 percent among patients treated with two courses of the nucleoside analogue 2-chlorodeoxyadenosine.⁴ The median duration of remission after the completion of treatment has been 18 months, with an 80 percent frequency of recontrol with the same treatment among patients with relapses. The treatment has usually been well tolerated, and although a central venous catheter is currently required for a

short period, recent studies suggest that subcutaneous administration is likely to be equally effective.⁵

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1. Duffy TP. Costly errors. *N Engl J Med* 1995;332:1503-5.
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3. Dimopoulos MA, Alexanian R. Waldenström's macroglobulinemia. *Blood* 1994; 83:1452-9.
4. Dimopoulos MA, Kantarjian H, Weber D, et al. Primary therapy of Waldenström's macroglobulinemia with 2-chlorodeoxyadenosine. *J Clin Oncol* 1994; 12:2694-8.
5. Juliusson G, Haldal D, Hippe E, et al. Subcutaneous injections of 2-chlorodeoxyadenosine for symptomatic hairy cell leukemia. *J Clin Oncol* 1995;13:989-95.

To the Editor: We found the article by Dr. Duffy thought-provoking. It stimulated us to voice our concern about quality assurance in laboratory medicine and the interactions between laboratory professionals and clinicians in practice. We believe that the attribution of the "first mistake" to the blood bank was perhaps misplaced. Given what we know about staff training and standards of good laboratory practice in the United States, the failure of laboratory personnel to understand the implications of a positive Coombs' test seems unlikely. Most laboratorians would agree that a peripheral-blood smear should routinely accompany a bone marrow aspirate. Alarm bells may have rung in the ears of the laboratory technologists involved, but communication beyond that point clearly failed. It may not be so easy for concern at the laboratory to be passed on to a patient's physician. In 1978 Benson noted that it is often difficult for pathologists to communicate with clinicians.¹ Shulman et al. have noted that when communication is successful, improvement occurs.²

When discussing diagnostic mishaps, clinicians and pathologists should focus more on communication and less on the errors of the individual persons involved. They must adopt a paradigm for quality that examines the interaction among all professionals who may be involved in a case (i.e., nurses, physicians, laboratory directors, medical technologists, and clerical staff). At the same time, all branches of the medical profession must collaborate with laboratorians to develop studies that examine the determinants of the quality of laboratory work as they affect clinical outcomes.³

Duffy has done us a great service by calling this case to our attention. We would be interested to know what steps were taken by the various professionals involved to improve communication after this experience.

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1. Benson ES. Strategies for improved use of the clinical chemistry laboratory in patient care. In: Benson ES, Rubin M, eds. *Logic and economics of clinical laboratory use*. New York: Elsevier, 1978:245-58.
2. Shulman IA, Lohr K, Derdiarian AK, Picukaric JM. Monitoring transfusionist practices: a strategy for improving transfusion safety. *Transfusion* 1994; 34:11-5.
3. Boone DJ, Steindel SJ. Conducting outcomes research: past experience and future directions. *Clin Chem* 1995;41:795-8.

To the Editor: I take strong exception to the statement that "In retracing the events of this complex case, it seems that the

first mistake was made by the blood bank." What did the blood bank report? Was the test performed as a pretransfusion test, or was it performed at the specific order of a physician?

Some blood banks still routinely perform a Coombs' test as part of a pretransfusion serologic evaluation, although this test is not required according to current standards.^{1,2} The Coombs' test is known to have a high false positive rate (i.e., relatively few patients with positive results have identifiable factors suggesting hemolysis). Easily 10 to 15 percent of hospitalized patients and a larger number of patients infected with the human immunodeficiency virus have positive Coombs' tests.^{2,3} Furthermore, as many as 1 in 1000 healthy blood donors has a positive test.²

Most blood banks routinely use a "nonspecific" reagent to perform an initial Coombs' test in order to detect molecules of either IgG or C3 on circulating red cells. Further testing to determine whether IgG or C3 (or both) is present is not recommended unless the patient has recently undergone transfusion or there is evidence of hemolysis.²

It is not the clinical laboratory's responsibility to do further testing unless the clinician responds to the initial test results by requesting further testing for the purposes of clarification and diagnosis. To suggest that, without a request by the clinician to perform further testing, the blood bank should have tested for cold agglutinins (a test optimally performed with blood collected and kept warm during the process of separating serum and cells) because hemolysis was suspected is unreasonable and not cost effective. It is also unreasonable to expect the blood bank to have collected the other data, such as the discrepancy between the hemoglobin and hematocrit values and the high sedimentation rate, in order to decide to do additional testing. That was the clinician's job, and the clinician failed. Perhaps the costly error here was the attempt to treat a severe (transfusion-requiring) hemolytic anemia by a clinician without enough experience in hemolytic syndromes and without the benefit of an initial evaluation by a more experienced hematologist. With the current emphasis on primary care and efforts to reduce costly, unnecessary laboratory testing, primary care physicians are going to need to learn when to call for help in time.

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1. Compatibility testing and selection of components. In: Standards for blood banks and transfusion services. 16th ed. Bethesda, Md.: American Association of Blood Banks, 1994:25-9.
2. Investigation of a positive DAT. In: Walker WH, ed. Technical manual. 11th ed. Bethesda, Md.: American Association of Blood Banks, 1993:355-87.
3. McGinniss MH, Macher AM, Rook AH, Alter HJ. Red cell autoantibodies in patients with acquired immune deficiency syndrome. *Transfusion* 1986;26:405-9.

Dr. Duffy replies:

To the Editor: Telen's exemption of the blood bank from any role in the routine investigation of a positive Coombs' test is countered by Keenlyside and Steindel's suggestion that communication between pathologists and clinicians would improve the overall quality of patient care. It would not be cost effective for a blood bank to perform a full workup of every positive Coombs' test, but with the increasing reliance on primary care, there must be greater interaction among all professionals involved. Physicians trained in blood banking and laboratory medicine are ideally situated to communicate with and educate those who are the recipients of their laboratory data. Such communication would have been appropriate in the cur-

rent case, when one considers that the long duration of the problem must have been evident to all the parties involved.

Weber et al. highlight the important role of 2-chlorodeoxyadenosine in the treatment of plasmacytoid lymphomas associated with monoclonal IgM production. The pathological features in the case under discussion, however, were not those of a plasmacytoid lymphoma but rather those of a diffuse, large-cell lymphoma. The "important pathogenetic link" in this case of cold-agglutinin hemolytic anemia and lymphoma is that successful treatment of the hemolytic problem resided in the recognition and treatment of the lymphoma.

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ALCOHOL CONSUMPTION AND MORTALITY AMONG WOMEN

To the Editor: The article by Fuchs et al. (May 11 issue)¹ on the relation between alcohol consumption and mortality among women should set women's minds at ease, especially women at risk for coronary heart disease who drink. It appears that such women profit most from a beneficial effect of alcohol, which is already known for men. Consumption of alcohol by men is cardioprotective in large part because of an increase in serum high-density lipoprotein (HDL) levels,² whereas cigarette smoking has a deleterious effect on serum HDL levels.³

The standard dietary interview used in the lipid research clinic at our hospital has enabled us to extend these observations in men to women at risk for coronary heart disease. Experienced dietitians estimated daily alcohol consumption among a total of 631 patients with hypercholesterolemia (272 women and 359 men), 44 percent of whom had coronary heart disease. Serum lipoprotein levels were reported as the mean of two serum samples, measured under standardized conditions.³ Thirty-one percent of the women were nondrinkers, 64 percent were light-to-moderate drinkers (up to 30 g daily), and 5 percent were heavier drinkers (more than 30 g daily). Fifteen, 64, and 21 percent of the men were nondrinkers, light-to-moderate drinkers, and heavier drinkers, respectively. The highest HDL levels were observed in the heavier drinkers, the women as well as the men. Using a regression model that simultaneously estimated the effects of alcohol consumption and cigarette smoking, we estimated an increase of 3.5 mg of HDL per deciliter (95 percent confidence interval, 1.3 to 5.6) for every 10 g of alcohol consumption per day in the women. The corresponding estimate in men was 1.1 mg per deciliter (95 percent confidence interval, 0.5 to 1.6), which is similar to earlier observations.² In contrast, smoking was associated with lower HDL levels in both women (7.8 mg per deciliter lower in smokers; 95 percent confidence interval, 4.2 to 11.3) and men (3.8 mg per deciliter lower in smokers; 95 percent confidence interval, 2.7 to 4.8). An additional adjustment for serum triglyceride levels did not alter the effects of alcohol consumption and smoking on HDL levels. Apparently, urging women at risk for coronary heart disease to refrain from smoking is more advantageous than dissuading them from consuming alcohol.

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1. Fuchs CS, Stampfer MJ, Colditz GA, et al. Alcohol consumption and mortality among women. *N Engl J Med* 1995;332:1245-50.
2. Gaziano JM, Buring JE, Breslow JL, et al. Moderate alcohol intake, increased levels of high-density lipoprotein and its subfractions, and decreased risk of myocardial infarction. *N Engl J Med* 1993;329:1829-34.
3. Sijbrands EJ, Westendorp RG, Hoffer MJ, et al. Effect of insulin resistance, apoE2 allele, and smoking on combined hyperlipidemia. *Arterioscler Thromb* 1994;14:1576-80.

To the Editor: Fuchs and coworkers report that light-to-moderate drinkers have some survival advantage over nondrinkers. Their data suggest that the consumption of what might be considered homeopathic amounts of alcohol (i.e., a few grams per day) is beneficial. Are these results real, or do they reflect the arbitrary stratification of a group of "light" drinkers into several subgroups? Would it be wiser and safer to combine the lowest three categories of alcohol consumption, creating a more realistic base-line group of women who consume less than 5 g of alcohol per day?

In Table 2 of the article, in which nondrinkers are the reference group, J-shaped curves are noted for several diseases, including two known to be associated with increased alcohol consumption: death from external injuries and death from hepatic cirrhosis. It would be worthwhile to reanalyze the data after combining the lowest three consumption categories into a single base-line group of women consuming less than 5 g of alcohol per day. The J-shaped curves might disappear, along with the temptation for the large group of nonconsumers to become drinkers.

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The authors reply:

To the Editor: Sijbrands and colleagues provide further evidence of the protective effect of alcohol consumption and the deleterious effect of smoking on serum lipoprotein levels. Their findings are consistent with our results, which demonstrate that, among women, the mortality benefit associated with light-to-moderate drinking is largely confined to women with risk factors for coronary heart disease (defined as a history of hypertension or diabetes, smoking, a high cholesterol level, a myocardial infarction in a parent ≤ 60 years of age, and a body-mass index [the weight in kilograms divided by the square of the height in meters] > 29.0). For women without cardiac risk factors, we observed no significant mortality benefit associated with light-to-moderate drinking.

Dr. Lowenfels questions the association of relatively light drinking (1.5 to 4.9 g of alcohol per day) with a significant reduction in mortality among women. As compared with men, women have higher blood alcohol concentrations for a given amount of alcohol consumed,¹ are more susceptible to alcoholic liver disease,^{2,3} and as Sijbrands and colleagues note, have similar increases in HDL levels with considerably lower levels of alcohol consumption.

Dr. Lowenfels also expresses concern about the categorization of alcohol intake. As we state in our article, all categories of alcohol consumption were established before any data were analyzed. Furthermore, to address the issue of a bias resulting from such categorization, we performed analyses in which alcohol consumption was measured continuously, without any potentially "arbitrary" categorization. This continuous variable was entered into the multivariate model as both linear and quadratic terms (alcohol and alcohol²). As previously

demonstrated,³ there was a negative regression coefficient for the linear term ($\beta = -1.3 \times 10^{-2}$, $P = 0.02$) and a positive coefficient for the quadratic term ($\beta = 4.9 \times 10^{-4}$, $P = 0.001$) — findings consistent with a U- or J-shaped relation. Independently of any categories one might choose, we observed a U-shaped relation between the level of alcohol consumed and overall mortality among women.

Finally, we do not agree with Dr. Lowenfels that our results will encourage a "large group of nonconsumers to become drinkers." We observed that light-to-moderate drinking was associated with a mortality benefit only among women with risk factors for coronary heart disease. Many of these risk factors are modifiable (e.g., hypertension, hypercholesterolemia, obesity, and smoking),⁴ and our study demonstrates the deleterious as well as the protective effects of drinking.

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DISCONTINUATION OF ANTIHYPERLIPIDEMIC DRUGS

To the Editor: In their article on the discontinuation of anti-hyperlipidemic drugs, Andrade et al. (April 27 issue)¹ discuss the generalizability of the results of randomized trials. Specifically, they state that discontinuation rates in randomized trials may not accurately reflect the tolerability or effectiveness of therapy in the general population. In reaching their conclusions, however, they appear to overlook an additional factor. There were 2369 study patients and 3223 courses of therapy. During the study period 854 participants therefore changed therapy.

The period of the study corresponds to the clinical introduction of lovastatin and simvastatin. The early results of trials showing the superiority of lovastatin over cholestyramine and probucol were available in 1988.^{2,3} These drugs were recognized as having fewer side effects and thus being less likely to require the cessation of therapy.⁴ With the introduction and marketing of these new drugs, a proportion of patients probably changed therapy because the new drugs were perceived as better. This may explain the large differences in discontinuation rates for the bile acid sequestrants, niacin, and gemfibrozil and the minor and statistically nonsignificant differences in the rates for lovastatin.

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The authors reply:

To the Editor: We agree that the introduction of new drugs creates a state of flux in patterns of drug use, which has been observed with other classes of drugs.¹ The study period, 1988 to 1990, corresponded to the clinical introduction of lovastatin (simvastatin was introduced later), and the perceived benefit of this agent, noted by Dr. Ellis, may have been one reason for the initiation of therapy with lovastatin. However, in only one case did the medical chart document a switch to lovastatin from another antihyperlipidemic agent specifically because of the perceived benefit of lovastatin. The primary reasons for the discontinuation of antihyperlipidemic therapy documented in our study were adverse effects and therapeutic ineffectiveness.

As a point of clarification, 790 patients (33 percent), not 854, as stated by Dr. Ellis, changed antihyperlipidemic therapies during the study period.

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CHILDHOOD DERMATOMYOSITIS ASSOCIATED WITH HEPATOCARCINOMA

To the Editor: Unlike dermatomyositis in adults, dermatomyositis in children is rarely associated with cancer. We describe a case of juvenile dermatomyositis associated with hepatocarcinoma.

A 14-year-old boy with a weight loss of 15 kg over a three-month period presented with clinical signs of dermatomyositis, including typical edematous rash, muscular weakness, and pharyngeal involvement. A considerable increase in muscle-enzyme concentrations was noted, and an immunodiffusion assay and Western blotting were positive for antinuclear antibodies of unknown specificity at a titer of 1:4000. The physical examination unexpectedly revealed hepatomegaly, and a computed tomographic (CT) scan showed a multinodular hepatic tumor with portal-vein thrombosis (Fig. 1). The serum alpha-fetoprotein level was normal. The patient was serologically negative for hepatitis B and C viruses. Liver biopsy showed a fibrolamellar carcinoma. Treatment with corticosteroids improved both the muscular and cutaneous signs of dermatomyositis. Chemotherapy did not reduce the tumor size, and a hepatectomy was performed in which two thirds of the liver was removed. One year after diagnosis there was a relapse of the dermatomyositis, followed two months later by CT evidence of a recurrence of the carcinoma. The patient died a few weeks thereafter.

This association of dermatomyositis with an uncommon primary carcinoma of the liver in a child is exceptional. The dermatomyositis behaved like a paraneoplastic syndrome because it heralded both the initial appearance of the carcinoma and its recurrence. Childhood dermatomyositis has very rare-

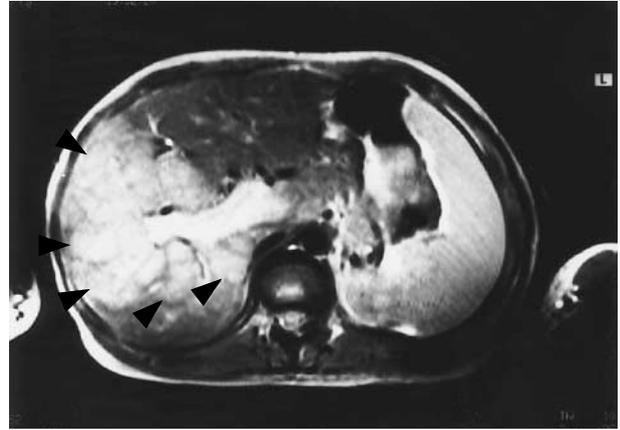


Figure 1. Initial Abdominal CT Scan in a 14-Year-Old Boy, Revealing a Multinodular Hepatic Tumor. The arrowheads show the limits of the tumor.

ly been associated with malignant tumors, usually lymphoid tumors,¹ neuroblastoma,² or unusual neoplasms such as nasopharyngeal carcinoma.³ This case report suggests the need for a careful medical evaluation for cancer in children with dermatomyositis.

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OBSERVING PATIENTS AFTER ANTIBIOTICS ARE DISCONTINUED

To the Editor: Of the more than 40 million patients hospitalized in the United States yearly, approximately 2 million acquire nosocomial infections.¹ Patients with infections frequently remain in the hospital to complete courses of antibiotic therapy lasting 7 to 14 days. The length of antibiotic therapy varies and is based on criteria that are more subjective than objective. Standard medical references allow one enormous leeway in deciding the length of therapy for many infections. For example, *Harrison's Principles of Internal Medicine* suggests that a complicated urinary tract infection should be treated with antibiotics for 7 to 21 days.² The chapter on pneumonia gives vague recommendations on the length of therapy.³ Even a perforated appendix may be treated with anywhere from 1 to 10 days of antibiotic therapy.⁴

Although there are few data on the subject, many clinicians feel that the standard of care requires them to watch a patient in the hospital for 24 hours after the antibiotics have been discontinued or treatment has been changed to oral therapy.⁵ The rationale is to monitor the patient to make certain that there is no recurrence of infection. At our 720-bed acute care university hospital, utilization programs

estimate that approximately 30 hospital days per month could be saved by eliminating this practice in the department of medicine alone. This might translate into a potential savings of 30,000 to 40,000 hospital days in the United States each year.

Is the practice of observing a patient in otherwise stable condition reasonable? Most intravenous antibiotics have elimination half-lives of at least 2 hours, and some are as long as 12 hours. Hence, therapeutic levels of antibiotics will persist for hours after treatment is discontinued. In addition, relapses of infection are not likely to occur immediately after the discontinuation of antibiotic therapy or after treatment is switched to oral therapy. Patients who are given antibiotics intravenously at home are never readmitted to the hospital for observation when the therapy is stopped. If there is no agreement on how long a given infection should be treated, does it make sense to observe the patient in the hospital when the antibiotics are stopped?

It makes more sense to continue the intravenous antibiotics until the patient no longer needs them. The patient's overall clinical condition, underlying disease, and other factors must be considered in the decision to discontinue antibiotics or in determining the need for continued hospitalization. When the condition of patients is otherwise stable, it does not seem nec-

essary to observe them after antibiotics are discontinued. Given the increasing demands to decrease lengths of stay, such a practice does not seem to be worthwhile.

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FORMER TIMES

To the Editor: While cleaning out my desk, I found the enclosed bill for my one-day stay at the Children's Hospital for

Buffalo, N. Y. July 25, 1943

Mr. Solomon Messinger

252 East ferry St.

To THE CHILDREN'S HOSPITAL OF BUFFALO, Dr.

For Care of Sol

	DR.	CR.
From 7/24/43 to 7/25 Total of 1 days at \$ 5.00 per day	5 00	
Board Special Nurse days at \$ per day		
Board Special Nurse nights at \$ per night		
Operating Room Service	10 00	
X-Ray Professional Service		
Physiotherapy Service		
Electrocardiograph		
Ambulance Service		
Laboratory	2 00	
Drugs		
Telephone Calls		
Miscellaneous Charges		
Received Payment.		
Total	17 00	
By Deposit or Cash		
Balance Due		

PAID
JUL 25 1943
CHILDREN'S HOSPITAL
PER *[Signature]*

ACCOUNTS PAYABLE WEEKLY IN ADVANCE AND PAID IN FULL BEFORE PATIENT IS DISCHARGED. Form 100 20M 7-41

Figure 1. Bill for Tonsillectomy.

a tonsillectomy when I was 11 years old (Fig. 1). Several things struck me about it, especially in comparison with a hospital bill one might receive today. The most obvious is the low cost of service, although \$17 was worth much more in 1943. The second is that the bill was paid (in cash) by my father at the time of discharge. There was no health insurance, Medicare, Medicaid, or health maintenance organization then. Most striking, though, is the simplicity of the bill. One glance, and you understand it perfectly. How radically different from today's hospital bills!

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To the Editor: The man in Figure 1 is my grandfather, Harvey Winters McNeel, who received his medical degree from the University of Virginia in 1897 and afterward established a general practice in his birthplace, Hillsboro, West Virginia. He was one of the few doctors in the county then, and his practice covered more than 100 square miles



Figure 1. Dr. Harvey Winters McNeel.

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1902 Frank Scott

		And Found (D.B.) (#144)	24 50	8 50
Feb 29		To med	50	
June 12	1903	" visit & med	2 00	
Feb 20		" "	2 00	
		Pay 10 Bu Corn (Nov. 1902)		6 50
Sept 13		To visit & med	2 80 00	15 00
16		" "	2 00	
17		" "	2 00	
21		med	1 00	
22		visit & med	2 00	
Oct 1		Call "	1 00	
21		Two visits & med	4 00	
1902 J.V. Slaven				
May 2		To dressing wound	2 00	
11		" "	2 00	
14		" "	1 00	
10		" "	1 00	
Nov 15		To days work Flues	5 00	1 50
				1 50
1904		Bad	3 50	
June 29		Settled in full	3 50	3 50
			3 50	3 50

Figure 2. Ledger Page.

of the surrounding countryside, most of it mountainous wilderness. Bad weather and worse roads often made patients accessible only by horseback. The saddlebags in which he carried his medical gear on such visits can be seen slung over his shoulder in Figure 1.

Figure 2 shows a page from Dr. McNeel's ledger for the years 1902, 1903, and 1904 with the accounts of two of his patients. It shows that his fee for a house call, including medication, was typically \$2. But not all his patients paid in cash. Frank Scott settled a portion of his account with 10 bushels of corn, which my grandfather, who had a farm on the side, probably used to feed his hogs. J.V. Slaven paid some of his account, according to the ledger, with a "Days work," after which appears the word "Flues," presumably meaning that he cleaned the chimneys in my grandfather's house.

Dr. McNeel died in 1948.

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