

Correspondence



Small Abdominal Aortic Aneurysms

To the Editor: Two randomized trials reported by Lederle et al.¹ and the United Kingdom Small Aneurysm Trial Participants² (May 9 issue) revealed that early surgery in patients with small abdominal aortic aneurysms can only be expected to have a benefit if the risk of surgery is consid-

erably smaller than the risk of spontaneous rupture. Operative mortality rates in these studies ranged from 2.7 to 5.5 percent, and the annual risk of a spontaneous rupture was 0.6 percent in one study and ranged from 1.6 to 3.2 percent in the other.

The decision about whether to perform early surgery or to institute surveillance should be made on an individual basis, after an evaluation of the perioperative risk. In a group of 661 patients (mean age, 67 years; 532 of them men) who underwent elective abdominal aortic surgery in our institution between 1991 and 2000, the perioperative mortality was 9.1 percent (mortality from cardiac causes, 4.1 percent). Patients without chronic pulmonary disease or cardiac risk factors — including angina, myocardial infarction, diabetes mellitus, heart failure, stroke, and renal failure — represent a population at low risk for operative death. Patients with

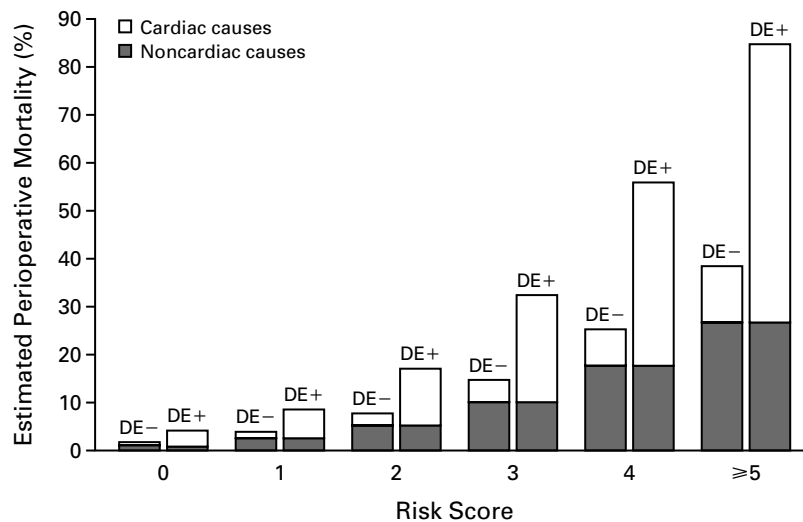


Figure 1. Estimate of the Perioperative Risk of Death from Noncardiac and Cardiac Causes.

The risk score was determined by the number of risk factors present; risk factors included chronic pulmonary disease, angina, myocardial infarction, diabetes mellitus, heart failure, stroke, and renal failure. Patients with a negative result on dobutamine echocardiography (DE-) were considered not to have stress-induced ischemia, and those with a positive result (DE+) were considered to have stress-induced ischemia.

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one or more cardiac risk factors were further stratified according to the absence or presence and extent of myocardial ischemia, as determined by dobutamine echocardiography (Fig. 1). Patients without stress-induced ischemia had a low-to-intermediate perioperative risk, despite the presence of clinical risk factors.

In view of these data, we suggest that risk assessment and modification be undertaken for each patient. This process includes the identification of risk factors, an objective evaluation of myocardial ischemia, and the administration of proper perioperative medical therapy (beta-blockers) or coronary revascularization.

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1. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1437-44.

2. The United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1445-52.

To the Editor: The articles by Lederle et al. and the United Kingdom Small Aneurysm Trial Participants both suggest that aneurysms can be followed carefully until their diameter reaches 5.5 cm. If perioperative mortality is high, and if patients are more likely to die from other causes than from the aneurysm in the several subsequent years, then the conservative strategy will look even better. The older a patient is, the more likely it is that these two conditions will be met. The mean age in both trials was less than 70 years. Can the authors make any more specific recommendations about how older age should affect the decision to repair electively abdominal aortic aneurysms that are discovered incidentally?

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To the Editor: In their controlled, randomized study, Lederle et al. found that long-term mortality did not differ between the surveillance group and the immediate-surgery group. The authors conclude that these data "support a policy of reserving elective repair for abdominal aortic aneurysms at least 5.5 cm in diameter." Given the fact that an accumulated 70 percent of the surveillance group underwent repair by the end of the study — and more strikingly, that half of this population required surgery by three and a half years — we find this conclusion remarkable.

If the majority of patients will need surgery anyway, why follow them until they do? Why subject patients to the anx-

ety, expense, and inconvenience of being scanned for a period of years instead of just fixing the problem and being done with it? As long as operative mortality is under 2 percent, surveillance provides no advantage beyond repeated confirmation of the natural history.

Caution must be exercised in applying the results of clinical trials to clinical practice. Women, who are known to have a higher rate of rupture for aneurysms of a given size,¹ made up less than 1 percent of the study population. In cases in which computed tomographic scanning is indicated, the expense of watchful waiting in terms both of dollars and exposure to radiation is high. Mortality among patients who do not comply with surveillance was not studied, and such noncompliance could be disastrous.

This study shows that surveillance is equivalent to immediate surgery with respect to long-term mortality under highly controlled conditions. Whether it is effective clinical practice is another matter entirely.

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To the Editor: The results of the study by Lederle et al. confirming the conclusions of the United Kingdom Small Aneurysm Trial will undoubtedly have a striking influence on the management of small abdominal aortic aneurysms. However, we wonder about the advisability of generalizing the final recommendation — that small abdominal aortic aneurysms should be observed until they reach at least 5.5 cm in diameter and that repair should be avoided unless they expand rapidly or symptoms develop.

The safety of ultrasonographic surveillance is dependent on meticulous follow-up that is unlikely to be achievable in routine practice outside a controlled trial. It is no surprise that Valentine et al.¹ report, in a program based on watchful waiting involving 101 veterans with small abdominal aortic aneurysms, that 32 percent did not comply with the follow-up, missing at least three consecutive appointments and accounting for a rate of aneurysm rupture of 13 percent in 34 months. The selected patients enrolled in the study by Lederle et al. were not high-risk patients and were therefore presumably most likely to benefit from elective repair. In practice, many good candidates for repair become poor candidates during the period of watchful waiting, as congestive heart failure develops, chronic obstructive pulmonary disease worsens, or other problems occur.¹⁻³

Moreover, the fact that 61.6 percent of patients in the surveillance group underwent repair within 4.9 years confirms that the issue of aneurysm repair for such patients with a good life expectancy is a matter of when rather than if. Given the relatively low risk of rupture for small abdominal aortic aneurysms, for early repair to be recommended, the

perioperative outcome has to be outstanding and consistent with the situation reported in the trial.

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1. Valentine RJ, Decaprio JD, Castillo JM, Modrall JG, Jackson MR, Clagett GP. Watchful waiting in cases of small abdominal aortic aneurysms — appropriate for all patients? *J Vasc Surg* 2000;32:441-50.
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3. Nicholls SC, Gardner JB, Meissner MH, Johansen HK. Rupture in small abdominal aortic aneurysms. *J Vasc Surg* 1998;28:884-8.

The authors reply:

To the Editor: Because more than half of our surveillance group underwent aneurysm repair, Miller et al. and Ballotta and Toniato question our conclusion that elective repair should be reserved for abdominal aortic aneurysms of 5.5 cm or larger. Any operative threshold based on the diameter of the aneurysm (such as 5.5 cm) will eventually be crossed in many patients whose aneurysms are smaller at the outset. Lowering the threshold would result in the same scenario, in which abdominal aortic aneurysms in many patients eventually reach the new threshold; this logic would lead to repeated lowering of the threshold and ultimately to the repair of all abdominal aortic aneurysms. If all small abdominal aortic aneurysms (which are common and have a low risk of rupture) were repaired, the number of operative deaths as a result would probably greatly exceed the number of rupture-related deaths prevented. The 5.5-cm threshold has been shown in two randomized trials to result in a safe reduction of the number of operations performed (by an estimated 20 percent in our study), and we see no advantage to changing it. Surveillance with ultrasonography is adequate and inexpensive and does not require exposure to radiation. The assertion by Ballotta and Toniato that operative mortality will increase when surgery is deferred is not supported by our findings.

The most important consideration in applying our results to clinical practice is that higher operative mortality in other settings or groups of patients may be an indication for raising the threshold for elective repair beyond 5.5 cm, as implied by the letters from Finucane and Kertai et al. Our trial data do not support precise recommendations for patients who differ from the trial patients, although we have reported rupture rates among patients with large abdominal aortic aneurysms and high operative risk elsewhere.¹ Women are not well represented in our study, but there is more evidence for increased operative mortality among women²⁻⁴ than there is for a higher rate of rupture,⁵ making it difficult to justify a lower threshold in women.

As noted by Miller et al. and Ballotta and Toniato, compliance with follow-up imaging is extremely important, but the optimal management of aneurysms in noncompliant patients remains unclear. The conclusions of the study by Valentine et al. (cited by Ballotta and Toniato) are based on only three episodes of rupture, and the operative mortality for elective repair in that study was 8 percent — which again

makes it difficult to justify a lower threshold for repair. Physicians who wish to individualize patient care should be aware that there is no group of patients for whom elective repair of abdominal aortic aneurysms that are less than 5.5 cm has been shown to be beneficial.

Recently obtained medical records have allowed our outcomes committee to reclassify one death of a patient in the surveillance group in our study as a rupture-related death (so that the risk of such death is now 0.7 percent per year), and five deaths (two in the immediate-repair group and three in the surveillance group) have been classified as indirectly due to aneurysm repair (including the one following the repair of a ventral hernia that was mentioned in the article). There have thus been 19 deaths related to abdominal aortic aneurysm in each group (relative risk in the surveillance group, 1.03; 95 percent confidence interval, 0.54 to 1.94).

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1. Lederle FA, Johnson GR, Wilson SE, et al. Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair. *JAMA* 2002;287:2968-72.
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To the Editor: The increasing importance of patients' involvement in decision making makes high-quality evidence and honesty essential. First, as Kertai and colleagues note, in the "real world," operative mortality rates for elective aneurysm repair are likely to be as high as 8 to 9 percent — 1 in 12 patients will die as the result of prophylactic elective surgery.¹ Second, the safety of surveillance for small aneurysms has been demonstrated in the two trials recently reported in the *Journal* and in the care of patients with aneurysms detected through screening studies.² The study mentioned by Ballotta and Toniato was very small. Third, there is currently no prospectively validated method of risk assessment for patients undergoing open aneurysm repair, although the revised Goldman Cardiac Risk Index holds promise.³ In the United Kingdom Small Aneurysm Trial, with its pragmatic approach to preoperative assessment, physiological age appeared to be more important than chronological age: poor renal and lung function were the most important predictors of postoperative mortality.⁴ Fourth, neither the study by Lederle et al. nor ours identified a subgroup of patients, defined according to age or aneurysm diameter, who benefited from early surgery.

Given the rapid advances in endovascular repair and pharmacology, why not wait safely, with the potential for a less

invasive method of management later, rather than take a 1-in-12 chance of death now? Cost-conscious health economies are also likely to support this approach.⁵ The focus should now be on advancing endovascular technology, so that a higher proportion of patients with aneurysms of 5.5 cm or more in diameter can undergo endovascular correction with low operative mortality and assured durability.

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Therapy to Prevent Type 1 Diabetes Mellitus

To the Editor: The results of the Diabetes Prevention Trial—Type 1 Diabetes Study (DPT-1) (May 30 issue)¹ show that parenteral insulin therapy does not prevent type 1 diabetes in the relatives of patients with the disease. We made a similar observation in a smaller population of young, nondiabetic first-degree relatives of patients with diabetes. A total of 29 children and adolescents (median age, 10.3 years; interquartile range, 7.5 to 13.8; range, 3.4 to 18.0) were identified through screening of a population of 4000 relatives of patients with type 1 diabetes for diabetes-related autoantibodies. These children and adolescents participated in a double-blind trial (the European Prediabetes Prevention—Subcutaneous Insulin Trial), in which they received either an injectable placebo preparation² or ultralente insulin (0.2 U per kilogram of body weight before breakfast [Ultratard, Novo Nordisk]). Subjects were followed for a median of 3.3 years (interquartile range, 1.6 to 4.5). Diabetes developed in 6 of the 14 subjects in the insulin group and 8 of the 15 subjects in the placebo group. The cumulative incidence of diabetes was similar in the two groups and similar to that observed in the DPT-1 (Fig. 1). These results strengthen the conclusions of the DPT-1, because our trial was double-blind and placebo-controlled and used a different insulin regimen. The use of parenteral insulin to prevent type 1 diabetes through the modulation of the anti-islet immune response (“beta-cell rest”) did not prove efficacious in two independent controlled trials. Moreover, the concept of beta-cell rest appears to have little basis

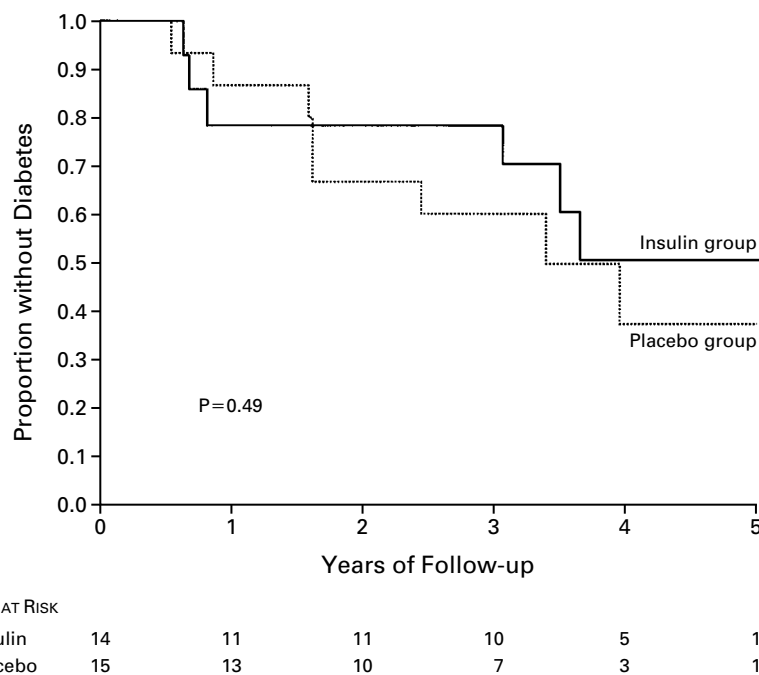


Figure 1. Kaplan–Meier Curve Showing the Proportion of Subjects without Diabetes, According to Treatment-Group Assignment.

in reality, at least for humans under the conditions used in these studies.³

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1. Diabetes Prevention Trial–Type 1 Diabetes Study Group. Effects of insulin in relatives of patients with type 1 diabetes mellitus. *N Engl J Med* 2002;346:1685–91.
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To the Editor: We conducted a pilot trial of isophane insulin suspension in a group of high-risk, nondiabetic, first-degree relatives of patients with type 1 diabetes^{1,2} and found that this approach had only minor effects on some immunological markers and did not prevent overt diabetes.² Considering the scarcity of information concerning the use of insulin in humans to prevent or delay the onset of type 1 diabetes,^{3,4} we believe that our results, which confirm the results of the DPT-1, are of interest.

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Anti-CD3 Monoclonal Antibody in New-Onset Type 1 Diabetes Mellitus

To the Editor: The report by Herold et al. (May 30 issue)¹ on the use of anti-CD3 monoclonal antibody in patients with new-onset type 1 diabetes and the accompanying editorial by Gale² leave important questions unanswered. The

authors suggest that treatment with anti-CD3 antibody mitigates the deterioration in insulin production and improves metabolic control. Moreover, they suggest that because of differences in the glycosylated hemoglobin levels between the treatment and control groups at entry, the true effect of the antibody treatment may even have been greater than that reported.

I would suggest a different possibility: regression toward the mean. It is very unlikely that the partial depletion of the lymphocyte pool (mean [\pm SD] nadir, 26.5 \pm 9.0 percent), with an increase in lymphocytes evident during treatment and a level of lymphocytes that was 123.0 \pm 52.0 percent of the pretreatment level 2 weeks after the completion of treatment, is responsible for the sustained decrease in glycosylated hemoglobin 12 months after treatment. Another monoclonal antibody, humanized anti-CD52, used in another autoimmune disease,³ depleted 95 percent of circulating lymphocytes, and lymphocyte counts were 30 to 40 percent of pretreatment values 18 months later.

The rationale behind the regimen used by Herold et al. seems unclear. The first aim of lymphocyte-depletion studies should be to establish a dose that is both safe and effective. The titration of individual doses on the basis of the levels of remaining cells may be helpful in finding dosage regimens that are more likely to induce consistent suppression of target cells.⁴

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1. Herold KC, Hagopian W, Auger JA, et al. Anti-CD3 monoclonal antibody in new-onset type 1 diabetes mellitus. *N Engl J Med* 2002;346:1692–8.
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The authors reply:

To the Editor: Our study found that treatment of patients with new-onset type 1 diabetes with a humanized monoclonal antibody against CD3 that does not bind to the Fc receptor reduced the deterioration in insulin production over the course of the first year of disease, even though the patients received only a 14-day course of the drug. We agree with Dr. Killestein that the depletion of lymphocytes does not account for the effects of the anti-CD3 antibody. In fact, we have proposed that the mechanisms accounting for those effects are complex and involve anergy of T cells, induction of regulatory cells, or both. In this regard, data from our patients showed an increase in the production of interleukin-10 and a change in the relative proportion of CD8+ and CD4+ T cells, raising the possibility that cytokines or cells that inhibit the autoimmune response may be induced by the drug. Thus, given the immunomodulatory activity of the antibody, it was not our goal to deplete the T cells; our approach was consistent with work performed by many

laboratories, where the most robust immune regulation is achieved by nondepleting antibodies.^{1,2}

The clinical benefits of the drug treatment persisted beyond one year. Even 18 months after treatment, there was a significant improvement in the glycosylated hemoglobin levels in the 12 patients in the drug-treatment group as compared with 10 of the patients in the control group (7.08 ± 0.39 percent vs. 8.57 ± 0.26 percent, P=0.01), which is inconsistent with a regression toward the mean at 12 months. Thus, the short course of treatment with hOKT3γ1(Ala-Ala) has clinical benefits for an extended period in the absence of continuous immune suppression.

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Editor's note: Dr. Bluestone has a financial interest in the monoclonal antibody hOKT3γ1(Ala-Ala), consisting of a patent application and a commercial agreement with Centocor and Johnson & Johnson Pharmaceuticals.

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Case 16-2002: Neurocysticercosis

To the Editor: Case 16-2002 (May 23 issue)¹ describes a 41-year-old woman with generalized headache and a hemorrhagic lesion on neuroimaging; on brain biopsy, her condition was diagnosed as cerebral venous thrombosis. Several factors, however, suggest that the cerebral venous thrombosis may have been secondary to a separate, underlying process.

Given the patient's country of origin (El Salvador) and her "frequent trips back" there, along with the presence of separate intracerebral calcifications, the possibility of neurocysticercosis should have been considered in the differential diagnosis and appropriate serologic tests performed. Supporting this possibility are the absence of risk factors for cerebral venous thrombosis, the known association of intracerebral hemorrhage with neurocysticercosis,² and the presence on neuroimaging of considerable vasogenic edema with an enhancing satellite lesion, a finding that is more compatible with the presence of neurocysticercosis than of cerebral venous thrombosis. The discussant notes the clinical features of a previous transient headache that were suggestive of increased intracranial pressure and mentions as possible causes hydrocephalus or cerebral venous or sinus thrombosis, which may have remitted spontaneously. He does not mention transient hydrocephalus, a condition associated with neurocysticercosis,³ as a possible cause. Furthermore, brain biopsy does not always reveal cysticercus,⁴ and the cerebral venous thrombosis may have resulted from an underlying inflammation associated with a cysticercosis lesion. It would be helpful to know whether the patient underwent or can un-

dergo serologic testing to rule out the possibility of neurocysticercosis.

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1. Case Records of the Massachusetts General Hospital (Case 16-2002). *N Engl J Med* 2002;346:1651-8.
2. Alarcon F, Vanormelingen K, Moncayo J, Vinan I. Cerebral cysticercosis as a risk factor for stroke in young and middle-aged people. *Stroke* 1992; 23:1563-5.
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The neurologist and the pathologist reply:

To the Editor: We appreciate Dr. Finelli's thoughtful reading of Case 16-2002. We concur that this patient probably had long-standing neurocysticercosis, on the basis of her birthplace and the calcifications seen on imaging; however, we do not see a role for serologic testing in the evaluation of her acutely evolving problem. In fact, in patients with proven single cysticercosis lesions in the brain, the sensitivity of the immunoblot assay is less than 50 percent, according to the Centers for Disease Control and Prevention (<http://www.dpd.cdc.gov/dpdx/html/cysticercosis.htm>).

Several features suggest that this patient's brain lesion at presentation was unrelated to the parasitic infection. The lesion seen on magnetic resonance imaging was hemorrhagic. Although intracystic hemorrhage has been reported by Alarcon et al.¹ (in 1 of 31 patients), parenchymal hemorrhages are exceedingly unusual.² In addition, the surgical specimen did not show any of the histologic features associated with cysticercosis: the organism itself, a well-defined capsule, or an acute inflammatory reaction (which often includes numerous eosinophils). We are concerned by the designation of neurocysticercosis as a cause of otherwise unexplained stroke in the absence of modern investigations of hypercoagulability and in a population in which the disease has a high prevalence.¹

Finally, because of space limitations, descriptions of subsequent clinical events, including a documented pulmonary embolism and deep venous thrombosis in one leg, were edited from the case discussion. These events provide support for the supposition that this patient has a tendency toward thrombotic events. She has continued to receive anticoagulation therapy, without any further complications.

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Authorship Limits

To the Editor: The change in the *Journal's* policy on authorship (July 4 issue),¹ which previously restricted the number of authors for an article, is appropriate and is to be welcomed. However, this change does not protect persons who have contributed substantially to a scientific work but who are deliberately excluded from the list of authors. To avoid this problem, we suggest that the *Journal* go a step beyond the guidelines of the International Committee of Medical Journal Editors² and require authors to declare that no person who would meet the criteria for authorship has been excluded.

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1. Drazen JM, Curfman GD. On authors and contributors. *N Engl J Med* 2002;347:55.
2. Authorship. Philadelphia: International Committee of Medical Journal Editors, October 2001. (Accessed September 13, 2002, at <http://www.icmje.org/index.html#authorship>.)

Dr. Drazen replies:

Drs. Mehta and Singhal raise the issue of exclusion of authors. We believe that the onus lies with the corresponding author to ensure that all named authors meet authorship criteria. It stands to reason that the corresponding author would also be responsible for ensuring that all authors who merited inclusion were included. Such matters need to be adjudicated locally, with the corresponding author making the final decisions about authorship.

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The Nursing Shortage and the Quality of Care

To the Editor: The findings reported by Needleman and colleagues (May 30 issue)¹ provide further evidence of what hospital nurses have feared for quite some time: there are too few registered-nurse (R.N.) staff members, and there is too little support to provide safe and beneficent care for patients. Although there is no simple fix, change may come too late and at too high a price. As hospitals balance the costs of technological means of delivering care with the costs of hiring more nurses, the cost-benefit calculation is not in nurses' favor. Nurses are compassionate, altruistic providers, yet they have not successfully met the challenge of costing out their productivity and remain financially undervalued.

Financial compensation alone, however, may not reduce the dissatisfaction and stress that nurses experience; other supportive measures are critically needed. As ethical, genetic, and technological challenges associated with the provision of care demand our attention, the need for nursing expertise will escalate. The research of Needleman et al.

should give us pause for ethical reflection. As Peter Drucker noted, "There is nothing less productive than making more efficient that which should not be done at all."² Reducing staffing ratios and having fewer R.N.s on staff may be efficient and may reduce expenses, but at what cost to patients? All health care providers must advocate urgent change within the system. Creative strategies and further research are warranted to find new solutions to these difficult problems. Hospitals need intelligent, educated, and dedicated nurses, but nurses need support. It is time nurses were rightfully recognized, respected, championed, and — yes — financially compensated.

(The opinions expressed in this letter are those of the authors and do not necessarily reflect the policies of the National Institutes of Health and the Public Health Service or the Department of Health and Human Services.)

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To the Editor: The American Nurses Association commends the *Journal* for publishing the research on the impact of nurse-staffing levels and for bringing the issues facing nursing to the forefront. In addition to the potential solutions mentioned in the article, there is Nursing's Agenda for the Future, a strategic plan representing the shared vision of more than 60 nurses' organizations that have put forth strategies to address the complex, interrelated factors behind the nation's growing shortage of nurses.

This shortage, projected to reach unprecedented levels by 2010, is the result of a confluence of demographic, economic, and cultural factors. If the problem is left unattended, health care consumers can anticipate a decline in access to care and in the quality of care — just as baby boomers reach an age at which they will demand more health care services.

For this reason, the nursing community has united around a shared vision for the future of the profession and has developed a comprehensive strategic plan to address the nursing shortage and the factors driving it. Nursing's Agenda for the Future focuses on strategies that will move the profession forward while ensuring that consumers have access to high-quality nursing care. Through Nursing's Agenda for the Future, we hope to join with other stakeholders in strengthening the profession, thus ensuring that consumers will continue to have access to high-quality nursing care and a safe health care environment.

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To the Editor: I certainly agree with the findings reported by Needleman et al. and with Steinbrook's discussion (May 30 issue) of the issues underlying the nursing shortage,¹ but I would like to interject another important perspective. Although we all agree that the nursing shortage has significant consequences for health care outcomes, there are two different approaches one can pursue in addressing the nursing crisis. The first approach is to increase the recruitment of nurses. Factors affecting recruitment include the number of nurses entering the profession and their willingness to work in the hospital setting. The second approach is to improve the retention of nurses. The factors affecting retention are related to the workplace environment and to feelings of value and respect. This is a multidimensional problem, encompassing issues related to scheduling, workload, and responsibilities for patient care. In this regard, one often-overlooked factor is the day-to-day relationships nurses have with physicians. A disturbingly high number of nurses decide to leave their hospital jobs because of less than satisfactory relationships with physicians.² Before we recruit more nurses, we need to make it at least an equal priority to keep the nurses we have. In order to accomplish this task, all of us (physicians included) must take responsibility for addressing the underlying issues affecting nurses' job satisfaction and morale and do our part to improve the conditions and ambience of their work environment.

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To the Editor: Steinbrook and others avoid tackling the primary dilemma within nursing. Nursing is not "an embattled profession," as Steinbrook says, but rather an embattled vocational trade group, which is why promising, young, career-oriented students should be directed away from nursing.

Approximately 75 diploma training programs, involving little or no college study, provide preparation for the nursing workforce. Similar programs train vocational workers, who receive a salary commensurate with their apprenticeship.

Approximately 900 junior colleges educate the largest number of entry-level nurses. Graduates of junior colleges are called "assistants" (e.g., dental assistant, physical-therapy assistant, engineering assistant, or computer-network assistant). Only nursing maintains the hypocrisy of allowing these graduates to have the same title as students who pursue a bachelor of science degree in nursing (B.S.N.), offered by more than 500 universities. In no other career group do graduates of vocational schools, community colleges, and universities lay claim to the same licensure.

Salaries are commensurate with education and experience, except in nursing; all nurses are lumped into one category and paid at the lowest denominator. Most nurses have only a two-year associate's degree or a diploma from a three-year vocational program. The salaries of the nursing workforce reflect this low standard of education. At the heart of the

poor image of nursing, the nursing shortage, and disharmony within this vocational trade group is the lack of a B.S.N. requirement for entry-level positions in nursing.

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To the Editor: As one solution to the shortage of registered nurses, I would suggest a return to the hospital-based nursing program. Not every young person feels the urge to go to college to receive a B.A. degree in nursing or has the money to pay for such a program. The subsidized hospital-based program of old was the mainstay of nursing training, and these programs produced excellent bedside nurses. This is what we need again.

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The Wendland Case

To the Editor: The commentary by Lo et al. (May 9 issue)¹ demonstrates concern about the impact of the California Supreme Court's decision in the *Wendland* case² and provides some welcome advice for physicians with regard to their responses to that decision.

The decision itself acknowledged its very limited application, including the application only to court-appointed conservators. It is ironic that if Robert Wendland's wife had not allowed herself to be made a legal conservator, she would have remained the common-law surrogate, and Mr. Wendland's physician could have removed the tube feedings at her request on the basis of the patient's best interest or the legal standard of a preponderance of evidence as proof of the patient's wishes, or both.

Would not justice be better served if, through the court or legislative action, a wife appointed as a conservator were given as much authority as a wife not appointed as a conservator?

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Delayed Neuropathy and Myelopathy after Organophosphate Intoxication

To the Editor: Massive organophosphorus-compound intoxication is relatively common. Although uncommon, delayed neurotoxicity may also occur in humans.¹ Persons with organophosphorus-compound poisoning have acute toxic ef-

fects, with a cholinergic crisis due to inhibition of acetylcholinesterase. Some persons subsequently have organophosphate-induced delayed neuropathy, which may be related to the inhibition of neurotoxic esterase.² Organophosphate-induced delayed neuropathy results in damage to both the peripheral and the central nervous systems.³ The exact sequence of lesions in these systems remains controversial, and few reports have discussed central nervous system neuropathological changes in humans. We describe a patient who had a classic acute cholinergic crisis after exposure to organophosphates, with the subsequent development of organophosphate-induced delayed neuropathy. Magnetic resonance imaging (MRI) showed diffuse spinal cord atrophy that persisted long after the cholinergic effects had subsided.

A 28-year-old Taiwanese woman attempted suicide by drinking organophosphate insecticides — 100 ml of 50 percent phosphamidon (2-chloro-3-(diethylamino)-1-methyl-3-oxo-1-propenyl dimethyl phosphate; $C_{10}H_{19}ClNO_5P$) and 20 percent mevinphos (methyl 3-[(dimethoxyphosphinyl)oxy]-2-butenate; $C_7H_{13}O_6P$). When she arrived at our emergency department, she was unconscious, with nonreactive, pinpoint-sized pupils; massive oral foaming; and bilateral crackles over the lung fields. We performed gastric lavage and administered a large dose of atropine (up to 80 mg per hour, with a total dose of 11,665 mg in 17 days) and pralidoxime (3 ampules) intravenously. The patient's red-cell acetylcholinesterase level decreased to 2 μmol per second per liter of whole blood (normal range, 20 to 46), and her serum pseudocholinesterase level decreased to 1 μmol per second per liter of whole blood (normal range, 20 to 61). On day 4, she regained consciousness. On day 17, she reported calf pain with paresthesia.

Nerve-conduction studies on day 34 showed that there was no pickup of compound muscle action potential or sensory action potential. Electromyography showed active denervation changes in sampled muscles. Pathological examination of a right sural-nerve biopsy specimen on day 53 showed axonal degeneration and severe demyelination neuropathy, with large-caliber nerve fibers most severely affected (Fig. 1A). At the 18-month follow-up visit, a disorder of the upper motor neurons was suspected because of spasticity and an increase in the deep-tendon reflexes of the lower extremities. A somatosensory evoked-potential study of the patient's bilateral tibial nerves showed that there was still no pickup of a cortical response. A subsequent MRI study showed marked atrophy of the spinal column (Fig. 1B).

We concluded that this patient's spasticity and increased deep-tendon reflexes were caused by central distal axonopathy, leading to diffuse atrophy of the spinal column. One report⁴ describes pyramidal signs and central nervous system involvement, with partial functional recovery, after severe organophosphate-induced delayed neuropathy. Studies in chicks with organophosphate-induced delayed neurop-

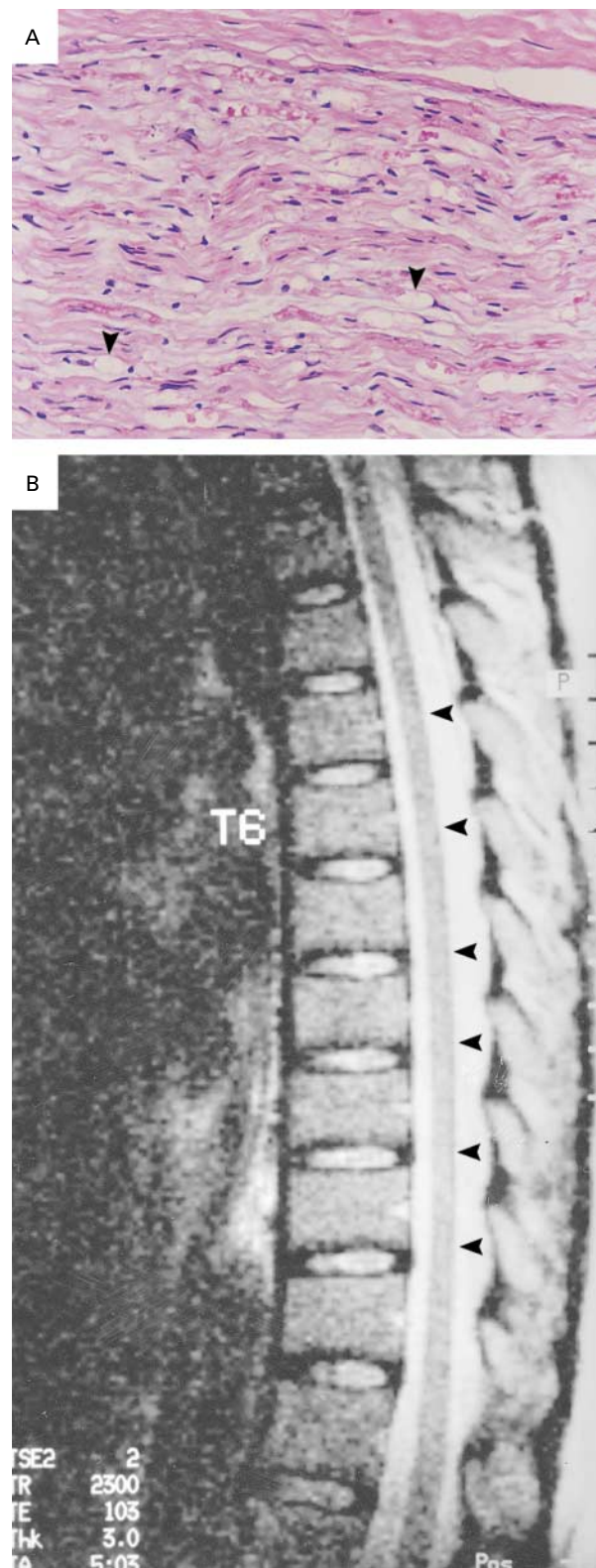


Figure 1. Specimen from a Sural-Nerve Biopsy Showing Axonal Degeneration with Vacuolization (Arrowheads) of the Nerve Fibers (Panel A, Hematoxylin and Eosin, $\times 200$) and a Sagittal, T_2 -Weighted MRI Scan Showing Diffuse Atrophy of the Spinal Column, Especially at the Level of the Thoracic Spinal Cord (Panel B, Arrowheads).

athy⁵ have shown severe damage in the ventral and lateral tracts of the thoracic and lumbar spinal cord. The same neuropathological changes may have been associated with the prominent diffuse spinal cord atrophy, especially in the thoracic column, that we observed in our patient.

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