Physicians and Joint Negotiations

TO THE EDITOR: The position paper on joint negotiations (1) and the accompanying editorial (2) consider the role of joint negotiations in maintaining physician autonomy. The Canadian experience may be of some interest.

In Canada, unlike in the United States, state governments are the sole providers of medical insurance, but like in the United States, physicians are in fee-for-service private practice. Government (socialized) medical insurance means a monopsonistic (single) payer. This is an apparently insurmountable obstacle to physician autonomy, especially when the monopsonist (the government) has the power to unilaterally determine “the terms and conditions of physician service,” as the law stated when the system was started in Saskatchewan, Canada, in 1962.

Months of previous negotiations over this clause were fruitless, which led Saskatchewan physicians to withdraw all but emergency services (strike) on the implementation date. It took 23 days to reach an agreement that required the government to amend the law to meet our concerns, an end not reachable by negotiations alone. Striking tarnished our reputation outside the province but not inside—voters soundly trounced the governing political party in the general election a few months later. The strike was also prophylactic. There has never been a need for a repeat.

Doctors struck, but patients won. In return for 23 days of inconvenience, patients have had 39 years of care managed by physicians, not insurers. Patients’ rights and physician autonomy are of the same coin.

This does not mean that all is well in Canadian Medicare. The system has warts (especially related to access time), but the strike fulgurated the threat to physician autonomy. Incidentally, Canadians have trouble understanding how the U.S. psyche can tolerate “managed care.” It is the beatification of conflict of interest.

Although the Canadian insurance system covers 100% of the population and the insurance is physician managed, compared with 85% of the population insured and an insurer-managed system in the United States, Canadian health care (measured as a portion of the gross domestic product) is 30% cheaper. Some of this cost difference may be due to high levels of the antioxidant lutein. In a recent experiment using epidemiologic data, an in vitro model, and a mouse model, Dwyer and coworkers (2) showed that lutein, a carotenoid with no pro–vitamin A activity, protected against progression of arteriosclerosis.

TO THE EDITOR: Joshipura and colleagues (1) presented epidemiologic evidence suggesting that consumption of green leafy vegetables and vitamin C–rich fruits and vegetables protects against coronary artery disease. The cardioprotective effect of green leafy vegetables may be of some interest.

References

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References

Blue Light and Milk

TO THE EDITOR: I am an enthusiastic reader of “On Being a Doctor,” which is usually the first section I turn to in Annals. These essays have consistently described experiences and insights that were interesting, original, and thought provoking. My disappointment in the essay “Blue Light and Milk” (1) was therefore acute. This memoir struck me as sentimental and self-indulgent and the language as both trite and pretentious. I have no doubt that Dr. Morowitz is a warm, loving, and totally admirable father, but his reminiscences would have been more appropriate in a parenting magazine than in Annals of Internal Medicine.

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Reference
TO THE EDITOR: We read with interest the study by Joshipura and colleagues (1), which reported that the consumption of one additional daily serving of fruit or vegetables (beyond the median level of consumption) was associated with a 4% reduction in coronary events. Relative terms often do not give a good sense of the benefit of interventions. Increasingly, there is a call for the use of absolute numbers, such as the number needed to treat for benefit (NNTB), as a way of addressing the "clinical bottom line" when interpreting the results of clinical studies (2). In applying this concept to the study by Joshipura and colleagues, we recognized that the NNTB may not adequately convey the magnitude of the behavioral change required to prevent one event. As an alternative, we propose a new term, the number needed to eat for benefit, or NNEB.

We calculate the NNEB in the following manner: In the Nurses’ Health Study (3), the annualized rate of coronary events was 0.096% (1127 events in 84,251 women over 14 years). A 4% reduction in this rate would yield an absolute risk reduction of 0.004%, which can be translated into a NNTB of 25,000 (that is, 25,000 women like the women in this study would need to eat one daily portion of fruit or vegetables to prevent one coronary event over 1 year). Multiplying the NNTB over 1 year by 365 portions per year gives us a NNEB of 9,125,000. In other words, the women in this study would need to consume 9,125,000 more portions of fruit or vegetables to prevent a single coronary event. We estimate that the NNEB for the men in the Health Professionals’ Follow-Up Study (4) would be 2,807,580 portions.

The NNEB may be a useful measure for giving practitioners and patients a better sense of the impact of dietary changes. We suggest that authors consider using it in reports on the association between diet and clinical outcomes.

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References

IN RESPONSE: The suggestion by Drs. Alves-Rodrigues and Thomas that the cardioprotective effect of green leafy vegetables may be related to high lutein levels is based on an animal study of lutein and arteriosclerosis (1) and a study among humans examining the relation between lutein and other antioxidants and coronary disease (2). In our study, we mentioned that antioxidant vitamins, folate, fiber, and such minerals as potassium may contribute to the apparent beneficial effects of fruits and vegetables, and we agree that lutein may also partly explain this benefit.

Dr. Lindenauer and colleagues propose a new term, NNEB, as a better alternative to relative risk or to NNTB. We estimated that for one person in our study sample to avoid a coronary event, 1443 persons would have to increase consumption of fruits and vegetables by one serving per day for 12 years. Lindenauer and colleagues suggest that the NNTB may not adequately convey the magnitude of the behavioral change required to prevent one event. However, the NNEB is more difficult to interpret because it does not include information on number of participants and time. Also, as we mentioned in our study, any estimates like these are largely dependent on characteristics of the study sample and can be very misleading (for example, they could easily vary 50-fold depending on age distribution). Furthermore, it is important to differentiate between implications for drug trials and implications for fruits and vegetables, which are unlikely to have side effects and are beneficial for many diseases.

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References

Questioning the Treatment of Venous Thromboembolism

TO THE EDITOR: In their review of clinical trials that have influenced the treatment of venous thromboembolism (1), Drs. Hirsh and Bates omitted a crucial study by Nielsen and colleagues (2). The Nielsen study compared anticoagulation with heparin plus phenprocoumon and therapy with phenylbutazone in patients with deep venous thrombosis (DVT). The results of the study were negative: One of 48 patients who received anticoagulants and 0 of 42 patients who received phenylbutazone died of pulmonary embolism. The only other previously published randomized, controlled trials of anticoagulants versus placebo in DVT also showed no benefit with anticoagulation (3, 4).

Heparin and vitamin K antagonists became standard treatment for DVT and pulmonary embolism in the 1940s, before randomized, controlled trials were routinely used to prove efficacy. The U.S. Food and Drug Administration (FDA) allowed these therapies to be "grandfathered in" in the early 1960s, when proof of efficacy became required for FDA approval. Low-molecular-weight heparins have been granted indications for treatment of DVT because randomized,
controlled trials have shown their effects to be equivalent to those of heparin in trials that did not use “unanticoagulated” controls.

Drs. Hirsh and Bates referenced a randomized trial by Barritt and Jordan (5) comparing anticoagulants with placebo in patients with pulmonary embolism. That trial should not be used as a basis for medical treatment policy. Its flaws include a small number of patients (n = 35), clinical diagnosis without lung scans or angiograms, 10 days of prescribed complete bed rest, and questionable determinations of deaths from pulmonary embolism.

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References

IN RESPONSE: Our article discussed clinical trials that have influenced the treatment of venous thromboembolism: a historical perspective. Ann Intern Med. 2001;134:409-17. [PMID: 11242501]

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References
Hepatotoxicity after Prophylaxis with a Nevirapine-Containing Antiretroviral Regimen

TO THE EDITOR: Postexposure prophylaxis is recommended after high-risk occupational HIV exposure in health care workers (1). Some regimens include non-nucleoside reverse transcriptase inhibitors because these agents have favorable pharmacokinetics and dosing schedules and have successfully prevented mother-to-child HIV transmission (2). The use of nevirapine, a non-nucleoside reverse transcriptase inhibitor, is complicated by 1% rates of hepatotoxicity and the Stephens–Johnson syndrome in HIV-infected persons (3). Nevirapine-associated hepatotoxicity has been noted in 8 of 41 healthy volunteers in phase I trials and in 5 of 41 sexual partners of HIV-infected persons who received postexposure prophylaxis that contained nevirapine (4). Fortunately, in all cases, toxicity resolved after nevirapine was withdrawn.

Because of concern that similar toxicity may have occurred elsewhere and uncertainty that other hepatotoxins may complicate findings from sexual contacts of HIV-infected persons, we evaluated use of nevirapine-containing postexposure prophylaxis after occupational HIV exposures. Three hospitals and one outpatient clinic in the Chicago area used nevirapine-containing regimens as second-line postexposure prophylaxis from October 1999 to September 2000. Among 174 health care workers who received postexposure prophylaxis, 8 received nevirapine-containing regimens and 5 developed severe hepatotoxicity (Table). A liver biopsy from health care worker 1 showed centrilobular fibrosis and minimal mixed portal infiltrates containing eosinophils. Hepatotoxicity resolved after corticosteroid administration. Health care worker 4, who had fulminant hepatic necrosis, received a liver transplant. At follow-up, none of the health care workers had evidence of HIV infection or hepatitis B or C virus infection.

Nevirapine-associated hepatotoxicity may represent a hypersensitivity reaction also characterized by skin rashes, fevers, and peripheral eosinophilia; rapid onset; and absence of mitochondrial toxicity characteristic of nucleoside analogue toxicity in pathologic specimens. Although nevirapine is potentially useful for postexposure prophylaxis, our findings suggest that immunocompetent persons may be at risk for nevirapine-associated hepatotoxicity that may not be rapidly reversible or may progress to fulminant hepatic necrosis. The use of postexposure prophylaxis regimens containing nevirapine should be discouraged.

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References
Table. Cases of Hepatitis in Five Health Care Workers in One Midwestern City Who Received a Postexposure Prophylaxis Regimen Consisting of Zidovudine and Lamivudine, 150 mg Twice Daily, and Nevirapine*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Health Care Worker 1</th>
<th>Health Care Worker 2</th>
<th>Health Care Worker 3</th>
<th>Health Care Worker 4</th>
<th>Health Care Worker 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profession</td>
<td>Physician</td>
<td>Nurse</td>
<td>Nurse</td>
<td>Phlebotomist</td>
<td>Nurse</td>
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<td>HIV exposure</td>
<td>Fluid splash</td>
<td>Saliva splash</td>
<td>Needlesick</td>
<td>Needlestick</td>
<td>Needlestick</td>
</tr>
<tr>
<td>Age, y</td>
<td>38</td>
<td>39</td>
<td>33</td>
<td>43</td>
<td>47</td>
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<tr>
<td>Sex</td>
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<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
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<tr>
<td>Day of onset</td>
<td>21</td>
<td>16</td>
<td>8</td>
<td>14</td>
<td>12</td>
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<tr>
<td>Length of PEP, d</td>
<td>21</td>
<td>20</td>
<td>25</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Time receiving nevirapine, 200 mg/d, d</td>
<td>14</td>
<td>14</td>
<td>8</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Time receiving nevirapine, 200 mg twice daily dose, d</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Duration of symptoms, d</td>
<td>60</td>
<td>18</td>
<td>21</td>
<td>20</td>
<td>42</td>
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<td>Skin rash &gt; 50% of body?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Temperature &gt; 101°F?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Peak ALT level, U/L</td>
<td>–</td>
<td>248</td>
<td>215</td>
<td>1080</td>
<td>298</td>
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<tr>
<td>Peak AST level, U/L</td>
<td>97</td>
<td>356</td>
<td>117</td>
<td>2370</td>
<td>307</td>
</tr>
<tr>
<td>Peak total bilirubin level, mg/dL</td>
<td>34.0</td>
<td>6.7</td>
<td>0.7</td>
<td>1.3</td>
<td>4.8</td>
</tr>
<tr>
<td>Peripheral eosinophilia?</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Treatment (other than discontinuation of nevirapine)</td>
<td>Prednisone, 20 mg twice daily, for 60 days</td>
<td>None</td>
<td>Prednisone, 20 mg/d, for 5 days; rash and fever recurred 2 days later and prednisone therapy was re-initiated (20 mg/d for 2 wk)</td>
<td>Liver transplant</td>
<td>None</td>
</tr>
</tbody>
</table>

* ALT = alanine aminotransferase; AST = aspartate aminotransferase; PEP = postexposure prophylaxis.

References


Correction

Correction: The Reliability of Medical Record Review for Estimating Adverse Event Rates

In a recent Brief Communication (1), the name of the second author, Stuart R. Lipsitz, PhD, was omitted from the byline. The byline should read “Eric J. Thomas, MD, MPH; Stuart R. Lipsitz, PhD; David M. Studdert, LLB, ScD, MPH; and Troyen A. Brennan, MD, JD, MPH.”

Reference