Letters

Sterile Injection Equipment To Prevent HIV Infection

TO THE EDITOR: From outside the United States, the article by Burris and colleagues (1) on prescribing needles and syringes seems to be a benchmark in the management of injection drug users. The United States has responded more cautiously to a problem considerably greater than ours. Key developments in U.S. policy have been of annual (and now biannual) interest at the international AIDS meetings since 1986, when great interest was shown in the British policy of syringe and needle exchange programs. These programs were developed after the 1985 discovery, through the newly available HIV antibody test, of an HIV epidemic among injection drug users in Edinburgh in 1982 and 1983 (2). Massive media coverage stimulated a national committee to consider a response, and within 12 months the first needle exchange programs and legal sanctions were in place (3). Although this seemed like the first national response to this type of crisis, the committee discovered that in Amsterdam in 1985, 100,000 sets of injection equipment had been distributed in a one-for-one needle exchange scheme. The committee also discovered that injection equipment was already sold at community pharmacies in many Italian cities. Since 1986, provision of injection equipment has become standard practice throughout the United Kingdom and many parts of Europe, and the United Kingdom has seen no instances of transmission from discarded needles and syringes. Most of the equipment is sold by community pharmacies with a wide network of distribution or by nonstatutory community groups. General medical practitioners in poorer areas are heavily involved in individual and local programs.

The initial legal anxieties and requirements for legal change emerged from the early committee work in Scotland and the subsequent statutory U.K. committee (4). Concern has arisen regarding the prescription of water for injection and the provision of other injection paraphernalia, but for most of us the system has worked extremely well, with few visible side effects. Now, however, renewed anxiety has developed about the level of needle- and paraphernalia-sharing required to transmit hepatitis C virus, which continues to be identified in new and young injection drug users. Our data indicate that the sharing of spoons, filters, and water requires more attention. Physicians in the United States should be encouraged by these successes but should be aware of the detail required to adequately prevent hepatitis C virus transmission.

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References

IN RESPONSE: Dr. Robertson’s eloquent letter makes an important point not made in our article, namely that in many parts of the world, whether by physicians, pharmacists, or public health workers, provision of sterile syringes to injection drug users is viewed as good medical practice. His letter highlights the gulf between the policies of the United States and the rest of the industrialized world on this issue. Moreover, he also points out that in the United Kingdom, there have been no reports of needlestick disease transmission as a result of improperly discarded syringes outside of the workplace. We are also unaware of any such cases of HIV transmission in the United States or elsewhere. The important experiences of our colleagues abroad should further reassure U.S. physicians of the appropriateness of prescribing syringes to injection drug users to prevent the spread of HIV and hepatitis B and C viruses.

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Using Cost-Effectiveness To Target Cholesterol Reduction

TO THE EDITOR: Dr. Garber argues that physicians and patients should use cost-effectiveness analysis to help make decisions about statin therapy (1). This a bad idea. Economists since the time of Adam Smith have known that the value of anything has two components: what it is worth to the person who has use of it and what can be gotten for it in exchange for something else (2). The first component is “value in use.” The second is “value in exchange.” Cost-effectiveness analysis is an economic tool that uses exchange value to measure what society can get for its health care dollars.

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References

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Cost-effectiveness analysis can tell us how much it will cost society to prevent a myocardial infarction in a population (3, 4). It cannot tell us how much it is worth to individual patients to try to prevent their own infarctions. This is because the “value in use” of health is very different from the “value in exchange” of health. As individuals, we almost never think in terms of exchange value for our health. We do not think about “time-discounted quality-adjusted life-years.” If you think you do measure your health by its exchange value, ask how much someone would have to pay you to induce you to willingly have a myocardial infarction.

There are good arguments against treating low-risk patients with statins. We should ask whether the patient’s risk for disease is greater than the risks associated with treatment. We should ask how our patient views taking drugs and having laboratory tests. These questions raise important issues that will often lead us away from treatment, but they are issues of value in use, not exchange.

Cost-effectiveness analysis belongs in the hands of system planners studying issues of exchange value. It does not belong in our treatment, but they are issues of value in use, not exchange.

New South Wales, an estimated 500 Aborigines were killed between 1836 and 1838, with a single military officer responsible for the deaths of 200 to 300 (3). The massacres of the Aborigines continued until 1928, when the last punitive expedition took the lives of more than 100 Aborigines in central Australia in the span of 1 month (3).

The heightened sensitivity of Australians to the 1996 massacre may seem surprising, given the history of the country. A cynical view would be that the massacre of white persons is more shocking that that of black persons. Or perhaps it is because of her tragic past, rather than despite it, that Australia is dismayed and outraged when a massacre occurs. The attempted extermination of a race did not take place without protest or without a sense of guilt. Perhaps in addition to the horror of the recent event itself, its power to evoke countless past and more brutal massacres is what truly “touches a nerve” for today’s Australians.

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References

Update in General Internal Medicine

TO THE EDITOR: In their otherwise excellent review of recently published studies on osteoporosis treatment and prevention, Roach and colleagues (1) state that “Raloxifene and tamoxifen reduce the risk for breast cancer.” This statement is misleading because it implies that the two drugs are equally effective for this purpose. Although the Multiple Outcomes of Raloxifene Evaluation noted a significant reduction in breast cancer risk (2), this trial was not designed with breast cancer incidence as a primary end point. Tamoxifen is approved by the U.S. Food and Drug Administration for reduction of incidence of breast cancer in high-risk women, but any recommendation regarding the use of raloxifene for this purpose should await the results of further studies. The Study of Tamoxifen and Raloxifene, a national, multicenter trial designed to assess the relative efficacies of tamoxifen and raloxifene for breast cancer prevention, will ultimately provide this information.

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References
TO THE EDITOR: On the basis of an article by Destache and colleagues (1), Anzueto and Angel (2) report that third-line antibiotics may be more cost-effective for the management of acute exacerbations of chronic bronchitis. After reviewing the referenced article, we are disappointed that Anzueto and Angel make this statement, given its substantial clinical and cost implications. Destache and colleagues’ article, an unblinded, retrospective study published as a supplement funded by Bayer (makers of ciprofloxacin), has several flaws that render it questionable.

Destache and colleagues reported that third-line antibiotics (amoxicillin–clavulanate, azithromycin, and ciprofloxacin) improved clinical outcomes of acute exacerbations of chronic bronchitis when compared with first-line agents (amoxicillin, cotrimoxazole, tetracycline, and erythromycin) and second-line agents (cephradine, cefuroxime, cefaclor, and cefprozil). For nonviral acute exacerbations of chronic bronchitis, the most commonly cultured bacteria include Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae. Amoxicillin was used in 44% of the episodes treated with first-line antibiotics. Because amoxicillin does not reliably cover these organisms, it is no surprise that it was associated with a higher failure rate. In a similar study, of which Anzueto was a coauthor, patients treated with amoxicillin had the highest relapse rate (3). Equally problematic, Destache and colleagues did not stratify patients by severity of illness. While they report that results of pulmonary function tests did not differ significantly among groups, a clinically significant difference in lung function was seen in the first-line and third-line groups (FEV1, 1.27 ± 0.73 L vs. 1.71 ± 1.06 L). This difference in severity of illness clearly confounds the results of the study.

The study by Destache and colleagues should not be used to support third-line antibiotics for acute exacerbations of chronic bronchitis. Promoting such use has enormous implications not only for cost but also for development of resistance. Decreased susceptibility of S. pneumoniae to fluoroquinolones, recently observed, is probably related to increased use (4). Until peer-reviewed journals report appropriately performed trials supporting use of broad-spectrum antibiotics for acute exacerbations of chronic bronchitis, we believe that antibiotics should be chosen according to local sensitivity patterns and that narrow-spectrum antibiotics should be used.

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References

TO THE EDITOR: In the report by Gilbert and colleagues (1) comparing cardiac risk indices, the principal point seems to be that the receiver-operating characteristic (ROC) curve areas are rather poor and that the indices are therefore of little utility. The observed predictive values seem to contradict this point. If the clinical significance of the indices is based on their ability to generate a change in risk estimate that will assist decision making, the ROC curve areas do not seem to capture it. In general, a preoperative cardiac risk index will be used in a population with an overall “low” risk for complications (1% to 6%) to discern groups with “high” risk (10% to 50%). The discriminating power that accomplishes this may not look impressive when viewed through the metric of an ROC curve area or likelihood ratios. To illustrate, in Gilbert and colleagues’ study, the class 3 score of the Goldman index moved clinical probability from 6% to 18%. Although most would find this information clinically significant, the likelihood ratio is only 3.

The meaning of such qualitative terms as “high” and “low” risk is crucial. In the accompanying editorial, Bach and Eagle (2) assert that “the frequency of adverse events among patients with positive risk scores is actually quite low in low-prevalence populations” (2). Most patients facing a postoperative risk of 18% to 36% would be inclined to disagree, as would their physicians. The confusion stems from appraising the prognostic index with metrics developed for diagnosis. A diagnostic test that yields post-test probabilities of 18% to 36% is frequently not useful, but a prognostic index that does this is nearly ideal. Just as it would be misleading to transpose a notion of what constitutes a “high” post-test probability from the diagnostic realm to this one, it may be equally misleading to transpose a notion of what constitutes a good or “accurate” ROC curve area. The authors state that the most striking finding of the study was “a poor degree of accuracy” of the risk indices, but they gauge “accuracy” by the area under the ROC curve, which does not correspond with clinical significance.

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TO THE EDITOR: Maurer and colleagues’ article (1) indicated that an additive effect between meal ingestion and upright posture contributed to the development of symptomatic hypotension in older adults. Patients in this study were functionally independent.

We studied a group of ambulatory, elderly nursing home residents to investigate the relation between postprandial hypotension and falls. The study was conducted at an 899-bed skilled-nursing facility in Long Island, New York. Two groups of ambulatory residents 65 years of age or older were randomly selected. One group (n = 12) had a history of one or more falls since admission to the nursing home. The other group (n = 32) had no history of falls. The incidence of falls in this facility, estimated from a previous study, was 18% (2). Blood pressure was measured manually in all patients 30 minutes before and 30 minutes after each meal. The same investigator took all preprandial and postprandial blood pressure measurements while the patients were sitting. A 10-mm Hg decrease in systolic blood pressure, assessed 30 minutes after meals, was noted (Table).

These findings indicate that although postprandial hypotension seems frequent in institutionalized elderly persons, it is unlikely to be an important risk factor for falls in elderly persons in general. Our findings and those of Maurer and coworkers emphasize that many factors contribute to falls in older adults, especially nursing home residents.

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Table. Frequency of Postprandial Hypotension after Different Meals in Relation to Fall History

<table>
<thead>
<tr>
<th>Meal</th>
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<th>Frequency of Postprandial Hypotension in Patients with No History of Falls</th>
<th>P Value</th>
</tr>
</thead>
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<tr>
<td>Breakfast</td>
<td>8</td>
<td>17</td>
<td>&gt;0.05</td>
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<tr>
<td>Lunch</td>
<td>0</td>
<td>37</td>
<td>0.01</td>
</tr>
<tr>
<td>Dinner</td>
<td>25</td>
<td>17</td>
<td>&gt;0.05</td>
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</table>

References

TO THE EDITOR: Dr. Williams touches on a vital ethical issue that deserves more attention (1). He tells of a physician who labeled a loving son a murderer for wanting to stop his dying mother’s dialysis treatments. Our research interviews with family members who participated in the decision to withdraw life-sustaining treatments revealed the anguish that can occur after such miscommunication (2). Of the 49 families we interviewed, 7 spontaneously volunteered concerns about killing or murdering and used such emotionally charged language as “I killed him, I know I did.” One family member spoke of his request to withdraw the ventilator, which resulted in charges of murder by a physician. At 6-month follow-up, many of these families continued to be distraught because of these implications.

Physicians often experience similar distress (3). Solomon and colleagues (4) have shown that both physicians and nurses have reservations about the withdrawal of life-sustaining treatments. In a study of five hospitals, only 43% of medical attendings agreed with the statement “There is no ethical difference between forgoing a life support measure and stopping it once it has been started” (4). Given that the American College of Physicians Ethics Manual supports this statement (5), this finding is alarming. If the emotional impact of withdrawing unsuccessful treatments is too high, one consequence will be greater reluctance to initiate trials of treatments that might substantially benefit the patient. To avoid this, we must reduce our use of language that adds to the anguish of families. Let us undertake a more honest professional dialogue about our own discomfort and confusion over the legal, moral, and ethical parameters of withholding and withdrawing life-sustaining treatments.

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References
IN RESPONSE: Dr. Rousseau’s concerns, published in a previous issue of Annals (1), regarding my negative portrayal of hospice care are valid. I agree that new physicians should view the performance of hospice in the episode I describe as a terrible aberration. In my own experiences, I have witnessed only the most laudable performances. Surely most practitioners who have used this invaluable service have also had overwhelmingly positive experiences. I very much doubt that their overall positive perceptions of hospice will be altered in any significant way by this particular sad episode. Nonetheless, it is my belief that we can always do better. As Dr. Rousseau points out, nonmedical offerings are important in a patient’s final days. However, they will be better received and have more meaning to the dying if accompanied by appropriate doses of analgesia.

Drs. Tolle and Tilden also raise important end-of-life issues. Instructing young physicians in dealing with such delicate and difficult family decisions should have a higher priority. To debate whether this is a teachable skill is fruitless. Practitioners in a position to influence those new to our profession teach something by their own actions every day. We may as well teach properly by showing the more tactful and humane sides of our own natures when we encounter these particularly sensitive situations.

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Novel Presentation of Acute Myelogenous Leukemia as Symptomatic Galactorrhea

TO THE EDITOR: Acute myelogenous leukemia (AML) is the most common acute leukemia in adults (1). The French–American–British classification AML-M5, monocytic leukemia, is commonly associated with extramedullary disease (2). Acute myelogenous leukemia is often associated with elevated levels of cytokines or hormones, such as prolactin (3). These rarely manifest with clinical symptoms. Indeed, despite the high frequency of elevated prolactin levels in leukemic myeloblasts in one series, no patients with AML and symptomatic galactorrhea have been described (4).

We evaluated a 21-year-old woman who had had fatigue and galactorrhea for 1 month. Physical examination was notable for gingival hyperplasia, oral petechiae, extremity ecchymosis, and expressible galactorrhea. The leukocyte count was $27 \times 10^9$ cells/L, the hemoglobin level was 73 g/L (7.3 g/dL), and the platelet count was $13 \times 10^9$ cells/L. The serum prolactin level was elevated at 375.6 ng/mL. Results of tests for $\beta$-human chorionic growth factor were negative. Levels of follicle-stimulating and luteinizing hormones were decreased; levels of thyroid-stimulating hormone were normal. The diagnosis of AML-M5 was confirmed by flow cytometry and bone marrow biopsy.

Induction chemotherapy was initiated with idarubicin and cytarabine. The patient had a complete response and received consolidation chemotherapy with autologous stem-cell transplantation. She has had no recurrence of galactorrhea and has normal prolactin levels (Figure).

This case represents one of the first instances in which symptomatic galactorrhea was the presenting symptom of AML. The clinical manifestation of galactorrhea and the absence of pituitary mass or infiltration on magnetic resonance imaging indicate that the leukemic cells were the source of prolactin. Furthermore, induction chemotherapy resulted in prompt resolution of hyperprolactinemia. The role of prolactin in the pathogenesis of AML warrants further study. The differential diagnosis of galactorrhea is broad but generally has not included hematologic malignancies. This case and the previous recognition of elevated prolactin levels in patients with AML provide support for considering this uncommon diagnosis in the appropriate clinical setting of symptomatic galactorrhea.

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References

Figure. Prolactin level during chemotherapy in a patient with acute myelogenous leukemia that presented as galactorrhea.
Critical Aortic Stenosis with Severe Congestive Heart Failure

TO THE EDITOR: We describe a 62-year-old man with critical aortic stenosis and severe congestive heart failure whose left ventricular dysfunction normalized after aortic valve replacement. He had three-vessel coronary artery disease and an aortic valve area of 0.78 cm². Ejection fraction was 0.10 to 0.15, and functional status was New York Heart Association (NYHA) class IV. On rest–redistribution 201-Tl scintigraphy, the patient had a mild defect in the inferior wall, but all other segments of his myocardium were normal. Six months after aortic valve replacement and coronary revascularization, ejection fraction improved to 0.53 and functional status improved to NYHA class I.

Connolly and colleagues (1) reviewed 154 patients with aortic stenosis and severe left ventricular dysfunction to identify predictors of outcome after aortic valve replacement. Improvement in left ventricular dysfunction was statistically significantly associated with absence of coronary artery disease, higher preoperative mean gradient, and a smaller aortic valve area. Morris and coworkers (2) reviewed 1012 patients with aortic stenosis undergoing aortic valve replacement and identified five independent predictors of death: advanced age, impairment of preoperative left ventricular dysfunction, extent of coronary artery disease, prosthetic valve size, and NYHA functional class. Ragosta and associates (3) and Pagley and colleagues (4) found an association between improvement in left ventricular function and myocardial viability, as measured by rest–redistribution 201-Tl scintigraphy. Di Carli and coworkers (5) studied 36 patients with ischemic cardiomyopathy undergoing coronary revascularization and found that patients with larger mismatches on positron emission tomography had the greatest improvement in symptoms of heart failure after coronary revascularization.

Our case demonstrates that no matter how severe the left ventricular dysfunction, correctable causes should be investigated. Patients with predominantly viable but hibernating myocardium, as determined by thallium scintigraphy or positron emission tomography, would be expected to benefit most from revascularization. Patients whose ventricular dysfunction is predominantly due to nonviable myocardium are less likely to benefit.

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References

Factitious Pheochromocytoma-Like Hypertensive Bouts Caused by the Valsalva Maneuver

TO THE EDITOR: A 48-year-old woman was transferred to our hospital for evaluation of severe therapy-resistant hypertension. Three months before admission to our hospital, she was admitted to another hospital because of nausea, headache, palpitations, and near-syncope, with a blood pressure of 250/160 mm Hg while taking metoprolol. Her history revealed a borderline personality disorder; she had been admitted to psychiatric hospitals several times in the past 20 years because of suicide attempts and depressive episodes. She was transferred to our hospital because extensive work-up could not demonstrate hormonal or renovascular hypertension, and several antihypertensive agents did not bring about a meaningful decrease in pressure.

Physical examination was unremarkable except for nervousness and a cuff blood pressure that varied between 95/60 mm Hg and 240/170 mm Hg. Results of tests for a pheochromocytoma were negative. To investigate short-term blood pressure variability, we performed beat-to-beat finger blood pressure monitoring using Finapres (TNO-BMI, Amsterdam, the Netherlands). We observed repeated swings in blood pressure that typically accompanied the various phases of the Valsalva maneuver. These episodes lasted well over 30 seconds. We performed simultaneous airflow measurement, CO₂ measurement in the exhaled air, and blood pressure measurement on the contralateral arm using a Dinamap recorder (GE Medical Systems, Milwaukee, Wisconsin). The tracings showed that the patient performed the Valsalva maneuver during each Dinamap measurement (Figure, left) but also repeatedly while alone and unobserved. Typical Dinamap readings during the Valsalva maneuver were 220/120 mm Hg. These blood pressure responses were identical to those evoked when the patient was instructed to do a classic Valsalva maneuver with a pressure of 20 mm Hg (Figure, right).

Severe paroxysmal hypertension always suggests a pheochromocytoma. Occasionally, factitious pheochromocytoma can be diagnosed. Patients have been found to surreptitiously inject cat-
echolamines (1–3). Substantially increased blood pressure caused by performance of the Valsalva maneuver has been described only once before (4). This phenomenon seemed to be the cause of therapy-resistant hypertension in our patient.

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References

Severe Hypersensitivity Associated with Clopidogrel

TO THE EDITOR: Clopidogrel, an antiplatelet agent, is used to prevent thrombotic complications of atherosclerosis (1, 2). Various trials found that its tolerability is similar to that of aspirin (3). Since 1998, more than 4.7 million patients throughout the world have been treated with this drug. Although rare, some reactions to clopidogrel have been described (4, 5). We report a case of hypersensitivity associated with clopidogrel.

After a myocardial infarction, a 57-year-old man received clopidogrel, 75 mg/d. On day 5 of treatment, he developed fever, rash, pruritus, and abdominal pain. Three days later, he was hospitalized with shock, bilateral lung rales, and Murphy’s sign. Blood analyses showed thrombocytopenia; lymphopenia; aseptic leukocyturia; and elevated aminotransferase, amylase, and γ-glutamyltranspeptidase levels. Blood cultures were negative. Chest tomodensitometry revealed interstitial infiltrates, mediastinal lymphadenopathy, and bilateral pleural effusion. Echography showed distended and thickened gallbladder. Clopidogrel therapy was discontinued.

Cholecystectomy was performed, and histologic study revealed acute acalculous cholecystitis. Bile cultures were negative. The patient completely recovered and all blood tests returned to normal within 1 week. One month later, the patient took clopidogrel again; 4 hours later, the same symptoms appeared. Examination showed bilateral lung rales and testicular swelling. Again we found interstitial infiltrates in the lung, asptic leukocyturia, and elevated aminotransferase and γ-glutamyl transpeptidase levels. We suspected drug hypersensitivity and definitively discontinued clopidogrel therapy. No steroid treatment was given. All symptoms disappeared within a few days and did not recur in the following year.

It is highly probable that clopidogrel was responsible for these events. First, the clinical features strongly evoke drug hypersensitivity. Second, the chronology of symptoms suggests immunization against clopidogrel. Third, the patient did not receive any other drug. Despite clopidogrel’s usual good tolerability, physicians should be aware of potential severe hypersensitivity reactions with this drug.

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References
Hepatocellular Injury in a Patient Receiving Pioglitazone

TO THE EDITOR: Two new members of the thiazolidinedione family, rosiglitazone and pioglitazone, have been believed to be less harmful than their predecessor troglitazone. A few case reports have described possible hepatocellular injury associated with rosiglitazone (1–3), but no hepatotoxic adverse effects have been previously noted in patients treated with pioglitazone. I describe a patient who developed hepatocellular injury while taking pioglitazone (Actos, Takeda Pharmaceuticals, Osaka, Japan).

A 67-year-old man with type 2 diabetes mellitus visited our outpatient clinic for a regular check-up. He was asymptomatic, but laboratory tests showed liver function abnormalities. Total bilirubin level was 10 μmol/L (0.6 mg/dL), aspartate aminotransferase (AST) level was 1.95 μkat/L (117 IU/L) (normal range, 0.13 to 0.67 μkat/L [8 to 40 IU/L]), alanine aminotransferase (ALT) level was 16.69 μkat/L (normal range, 1.92 to 5.98 μkat/L), and γ-glutamyltransferase level was 8.12 μkat/L (normal range, <1.17 μkat/L). The patient had received pioglitazone, 30 mg/d, for 7 months; an α-glucosidase inhibitor, voglibose (Basen, Takeda Pharmaceuticals, Osaka, Japan), 0.6 mg/d, for 5 years; and glyburide, 2.5 mg/d, for 10 years. Results of liver function tests were normal before pioglitazone was added to his regimen and during the first 6 months afterward. Ultrasonography of the liver and viral serologic studies showed no other cause of liver injury.

Pioglitazone therapy was discontinued. On the seventh day after discontinuation, results of liver function tests showed remarkable improvement: total bilirubin level, 9 μmol/L (0.5 mg/dL); AST level, 0.32 μkat/L (19 IU/L); ALT level, 867 nkat/L (52 IU/L); alkaline phosphatase level, 16.69 μkat/L (normal range, 1.92 to 5.98 μkat/L), and γ-glutamyltransferase level was 8.12 μkat/L (normal range, <1.17 μkat/L). The patient had received pioglitazone, 30 mg/d, for 7 months; an α-glucosidase inhibitor, voglibose (Basen, Takeda Pharmaceuticals, Osaka, Japan), 0.6 mg/d, for 5 years; and glyburide, 2.5 mg/d, for 10 years. Results of liver function tests were normal before pioglitazone was added to his regimen and during the first 6 months afterward. Ultrasonography of the liver and viral serologic studies showed no other cause of liver injury.

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The most likely cause of this patient’s elevated liver enzyme levels was pioglitazone-associated hepatotoxicity. Physicians who prescribe this drug should observe patients closely, even if results of liver function tests are normal during the first 6 months.

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References

Do Resistin and Resistin-Like Molecules Also Link Obesity to Inflammatory Diseases?

TO THE EDITOR: Recently, Steppan and colleagues (1) described the discovery of a novel hormone, which they called resistin (for resistance to insulin). Resistin is specifically expressed and secreted by adipocytes, apparently in proportion to fat-pad size, and it impairs glucose tolerance and insulin action; thus, it links obesity to diabetes. Resistin seems to be part of an emerging new family of secreted proteins that have a tissue-specific pattern of expression and probably have common signaling characteristics. To date, two other members of the family (resistin-like molecule [RELM-α and RELM-β] have been cloned (2). The former is expressed in white adipose tissue, mammary gland, heart, lung, and tongue and has unknown biological functions. The expression of RELM-β is observed in the gastrointestinal tract, is higher in proliferative epithelial cells, and is markedly upregulated in tumors, suggesting that this protein is involved in proliferation.

Surprisingly, the amino acid sequence of these proteins is identical to the sequence of another recently described family of proteins that seems to be involved in inflammatory processes (3). In particular, resistin is identical to FIZZ3 (found in inflammatory zone 3), RELM-α is identical to FIZZ1, and RELM-β is identical to FIZZ2. Patterns of expression of FIZZ proteins described by Holcomb and colleagues (3) are superposable to those reported by Stepan and colleagues for resistin and RELMs; this finding corroborates the idea that both families are the same. Little is known about the biological activity of FIZZ proteins. FIZZ1, the RELM-α homologue, is overexpressed in allergic inflammation. The pattern of expression and physiologic functions described for these proteins resembles that of other well-known proinflammatory cytokines, such as interleukin-6 and tumor necrosis factor-α, both of which are involved in respiratory and cardiovascular obesity-related problems (4).

Taken together, these data suggest that resistin/FIZZ3 and RELMs/FIZZ1 and FIZZ2 may be involved in the inflammatory processes associated with obesity.

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Additional text and references are available in the PDF version of the article.
Death by Diagnosis

TO THE EDITOR: I recently reviewed a malpractice claim involving a woman who died of mesenteric ischemia. She presented with pain, vomiting, and diarrhea. She had low-grade fever, but her abdomen was fairly unremarkable on examination. She was admitted, observed, and discharged several days later with a diagnosis of “chronic abdominal pain.” She returned after 2 days with similar but worsening symptoms. The emergency department physician noted her recent admission for chronic abdominal pain and, observing no deterioration since discharge, advised follow-up with her physician. She went to another hospital, where surgical exploration revealed intestinal necrosis. She died soon thereafter.

Mesenteric ischemia is often a difficult diagnosis. I was more bothered by the effect of the diagnosis of chronic abdominal pain. That label colored the judgment of the emergency department physician and negatively influenced the patient’s care. Physicians are taught to evaluate and diagnose. But a diagnosis is a double-edged sword. In general, a diagnosis is helpful if it allows institution of a therapy that improves outcomes, permits better understanding or acceptance of symptoms, improves delivery of care, or creates an economically advantageous health care situation for the patient. A diagnosis is harmful if it engenders perceptions that negatively affect care, perpetuates negative behaviors or beliefs by the patient, or negatively affects quality of life or the financial aspects of a patient’s care.

The implications of a diagnosis must always be considered. Lives can be irrevocably changed by our interpretation of symptoms, and a diagnosis is difficult to retract once rendered. The urge to make a diagnosis should never overcome the need to make the correct diagnosis. Not knowing is part of medicine, and knowing but not saying may sometimes be in the patient’s best interests. As my grandmother used to say, “There’s a reason you have two ears and one mouth.”

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Correction: Nonhypoglycemic Effects of Thiazolidinediones

In an article on nonhypoglycemic effects of thiazolidinediones (1), the second sentence under the heading “Albuminuria” on page 66 should read “Although the exact mechanism of increased cardiovascular risk in microalbuminuria is unknown, it appears that several other cardiovascular risk factors increase in the presence of microalbuminuria and correlate with the degree of microalbuminuria.”

Reference