Correspondence

Prevalence of Hepatitis C Virus Infection in the United States

To the Editor: Alter et al. (Aug. 19 issue)[1] present valuable data on the prevalence of hepatitis C virus (HCV) infection in the United States. However, their analyses of risk factors for HCV infection are flawed because the third National Health and Nutrition Examination Survey (NHANES III) data did not contain information necessary to control for confounding by the single most important risk factor for HCV infection — namely, injection-drug use. Their conclusions regarding the transmission of HCV by illegal drug use and sexual promiscuity should not be used to counsel patients or to set public health policy.

Although the omission of a question of injection-drug use from NHANES III is unfortunate in itself, the inability to control for injection-drug use should have led the authors either to omit this analysis or to be much more circumspect in their conclusions. They acknowledge in the discussion that injection-drug use is the single most important risk factor for HCV infection; other authors have estimated that the odds ratio for HCV seropositivity associated with injection-drug use is more than 100.[2] Since injection-drug use is also associated with smoking marijuana, inhaling cocaine, and sexual promiscuity, it is likely that the associations with these variables were confounded by its omission from the logistic-regression model.

The authors correctly discount marijuana use as a means of HCV transmission and recognize that the previously reported associations of cocaine inhalation with HCV infection may have been confounded by injection-drug use.[3] In contrast to the findings in the few references cited by Alter et al., a broader review of the literature suggests that sexual transmission of HCV is inefficient at best.[4] In the light of these facts and the probable confounding mentioned above, the conclusion of Alter et al. that "the strongest factors independently associated with HCV infection were illegal drug use and high-risk sexual behavior" is unfortunate.

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To the Editor: Alter et al. acknowledge the biologic implausibility of the transmission of HCV through marijuana use and suggest that the associations between transmission and the use of illegal drugs may be due largely to an association with a history of injection-drug use. In contrast, the authors appear to dismiss the considerable biologic and epidemiologic evidence that sexual transmission of HCV occurs rarely. First, HCV is uncommonly found in either seminal fluid or vaginal secretions, even among persons who are coinfected with human immunodeficiency virus type 1 or transplant recipients, in whom the serum viral load is generally higher.[1] Second, prospective and cross-sectional partner studies among HCV-infected groups without injection-drug use, such as women infected through the receipt of contaminated anti-D immune globulin and men with hemophilia, suggest that transmission to sexual partners is

rare.[2] Third, although a relatively high prevalence of HCV infection has been found among people treated in sexual-health clinics and homosexual men, after adjustment for a history of injection-drug use, there is often no association with the number of sexual partners or sexual practices.[3]

Associations between HCV infection and the number of sexual partners or reported sexual contact with an HCV-positive person are most likely the result of confounding by injection-drug use in studies in which no history of injection-drug use is sought or the result of residual confounding in studies in which such a history is sought. Recent evidence suggests that survey methods can considerably influence the reporting of illegal and stigmatized behavior. In a national survey of adolescent boys in the United States, participants who were randomly assigned to computer-assisted self-interviewing were almost four times as likely to report a history of injection-drug use as those who were randomly assigned to the more traditional self-administered questionnaire.[4]

Other independent associations with HCV infection in the study by Alter et al., such as those of marital status, level of education, and the poverty index, are also almost certainly explained on the basis of confounding by injection-drug use.

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To the Editor: Italy has a different epidemiologic pattern of HCV infection from the United States. Community-based surveys[1,2] (and unpublished data) of samples of the general population selected from the census by a systematic random sampling procedure have shown much higher prevalence rates, particularly among the elderly (Table 1). The risk of HCV infection seems to be lower in the recent past than in the distant past. The now-abandoned practices involving risk of percutaneous exposure, such as repeated use of a nondisposable glass syringe for medical purposes, were a strong predictor of HCV infection in the communities studied. The decreased use of glass syringes over time may explain the change in prevalence rates in the youngest age groups in Italy. Thus, HCV infection was widespread in the distant past in Italy, whereas in most cases in the United States transmission was recent. Moreover, the modes of transmission have differed. A similar increase in the prevalence of HCV infection with age has been observed in a community-based survey in Spain[3]: subjects who were 50 to 65 years old were more than eight times as likely to be positive for HCV infection as those who were 18 to 29 years old.

TABLE 1. AGE-SPECIFIC PREVALENCE OF ANTIBODIES TO HCV IN THE GENERAL POPULATION IN ITALY.

AGE GROUP	681 SUBJECTS*	1352 SUBJECTS†	488 SUBJECTS‡
	antibodies to HCV (%)		
<30 yr	0	1.3	1.2
30–39 yr	3.7	2.3	5.2
40–49 yr	4.4	5.0	6.5
50–59 yr	11.4	18.4	24.6
≥60 yr	18.4	33.1	42.1
Overall	8.4	12.6	16.2

*Data were obtained from Stroffolini et al.[1]
†Data were obtained from Guadagnino et al.[2]
‡Unpublished data were used.

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The authors reply:

To the Editor: We agree that HCV is spread inefficiently through sexual activity, and the Centers for Disease Control and Prevention does not routinely recommend changes in sexual practices for HCV-infected persons with one long-term steady partner. However, the low risk of transmitting HCV infection through sexual intercourse is not inconsistent with the results of both incidence and prevalence studies showing that high-risk sexual behavior accounts for 15 to 20 percent of HCV infections in the United States.[1,2] A substantial proportion of adults in the United States have had multiple sexual partners, and there are a large number of people with chronic HCV infection. Although other types of exposure are more likely to transmit HCV (such as transfusion from an HCV-infected do-

nor), they account for a much smaller proportion of infections because of the relatively small proportion of people with such exposure.

Neither the inability to identify users of injection drugs nor the potential underreporting of illegal behaviors is likely to account for the significant associations we found between HCV infection and both sexual behavior and sociodemographic variables. We used a history of cocaine or marijuana use as a surrogate for injection-drug use. Most users of injection drugs have also used cocaine and marijuana, and the prevalence of cocaine and marijuana use in the United States is much higher than that for injection-drug use alone. Thus, it is likely that our analysis, which included adjustment for sociodemographic characteristics, resulted in more conservative estimates of the adjusted odds ratios for the sexual-behavior variables.

The epidemiology of HCV infection in other countries may differ from that in the United States, as indicated by Stroffolini et al. In some countries, geographic clustering of high rates of HCV infection among older persons appears to be associated not only with blood transfusion from unscreened donors, but also with unsafe injection practices and the use of unsterilized equipment during medical, surgical, and folk-medicine procedures.[3,4] Such practices continue to have a role in the transmission of HCV and other blood-borne pathogens in some areas.

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Revascularization for Cardiogenic Shock

To the Editor: Hochman et al. (Aug. 26 issue)[1] reported the results of a randomized clinical trial in which they compared early revascularization with medical management in patients who had cardiogenic shock after an acute myocardial infarction. They did not find a statistically significant difference in mortality between the groups at 30 days. Mortality at six months, however, was significantly lower in the revascularization group.

A survival advantage at 30 days would have implied salvage of ischemic myocardium by revascularization that led to early improvement in left ventricular pump function. In this study, the authors' failure to show improvement in survival at 30 days probably resulted from the relatively long time to revascularization (>12 hours on average), too long a time for salvage of ischemic myocytes.[2] The improvement in survival at six months in the revascularization group may have been due to the salutatory effects of a patent infarct-related artery at the time of left ventricular remodeling. Clinical and laboratory studies have demonstrated that having a patent infarct-related artery has a beneficial effect on postinfarction left ventricular remodeling and the subsequent development of congestive heart failure.[3,4]

We wonder whether patients treated with delayed revascularization would have a result similar to those treated with revascularization on an emergency basis. The authors could shed light on this question by comparing the outcome in the patients in the medically treated group who underwent late revascularization (>54 hours after randomization) with that in patients who did not undergo revascularization. If our hypothesis is correct, the patients who underwent revascularization late should have had a survival benefit at six months that was similar to the benefit in patients treated on an emergency basis. This long-term benefit would be due to amelioration of the negative effects of postinfarction left ventricular remodeling on long-term ventricular function.

Given these considerations, a more appropriate interpretation of the data might be that all patients in shock after myocardial infarction should undergo revascularization of their infarct-related artery before discharge to prevent the negative effects of postinfarction left ventricular remodeling on long-term left ventricular function. Early emergency revascularization would be reserved for patients in whom patency of the infarct-related artery could be achieved very early (less than six hours) after the beginning of the infarction. Such a strategy would limit the number of interventions in moribund patients and provide the best long-term benefit to patients who could be treated.

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The authors reply:

To the Editor: We agree that there may be benefits of early revascularization associated with myocardial salvage that are different from the potential for late revascularization to improve long-term ventricular remodeling and electrical stability. The distinction between early and late reperfusion is often blurred, particularly in the setting of cardiogenic shock. Salvage of myocardium can be achieved more than 12 hours after myocardial infarction because of ischemic preconditioning and intermittent opening and closing of the infarct-related artery. Furthermore, relief of the severe ischemia and progressive necrosis that result from the sustained coronary hypoperfusion that occurs in shock may allow myocardial salvage up to 24 to 48 hours after myocardial infarction. In addition, late revascularization for patients who have triple-vessel and left main dis-

ease with impaired left ventricular function should improve long-term survival. We agree that it is also possible that patency of the infarct-related artery after an apparently complete infarction may improve long-term outcome by multiple mechanisms.[1,2] A randomized clinical trial testing this hypothesis is beginning.

The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) study was not designed to distinguish between the benefits of early and late opening of infarct-related arteries. Our data can directly assess only the effect of a strategy of early revascularization, a median of 14 hours after myocardial infarction (interquartile range, 8 to 26 hours), as compared with no revascularization or late revascularization, at a median time of 119 hours (interquartile range, 95 to 181 hours). We did not demonstrate that there was no benefit associated with early revascularization at 30 days; rather, we failed to prove that there was a benefit. The distinction is important. Although the difference in survival rate was statistically significant only beginning at 6 months, the curves were separating by 30 days. We agree with the statement in Ryan's editorial (Aug. 26 issue)[3] that the difference between the groups in survival at 30 days (although only a trend) was large, at 9.3 lives saved per 100 patients treated, in contrast to 2 lives saved per 100 patients treated with thrombolytic agents.[4] For patients less than 75 years old the difference at 30 days was large (15.4 lives saved per 100 patients) and statistically significant.

The six-month mortality rate for patients assigned to medical therapy who survived long enough and were clinically selected to undergo late revascularization was relatively low, at 38 percent (14 of 37 patients), as expected. The superiority of early revascularization, however, is suggested by the similar 1-year survival rate among 30-day survivors in the medical-therapy group, whether or not they underwent delayed revascularization. Analyses are being performed to try to assess the effect of early as compared with late revascularization on longer-term survival, but any conclusions will be limited because patients in the initial medical-therapy group were not randomly assigned to late or no revascularization.

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Surgery to Cure the Zollinger–Ellison Syndrome

To the Editor: Norton et al. (Aug. 26 issue)[1] report 10-year surgical-cure rates of 34 percent in 123 patients with sporadic gastrinomas and 0 percent in 28 patients with multiple endocrine neoplasia type 1. The authors' objective was limited to the elimination of discoverable gastrinoma, as determined by measurements of serum gastrin, secretin tests, and imaging studies. A preferable objective would have been to eliminate reliably the aggressive peptic ulcer disease and diarrhea that characterize the Zollinger–Ellison syndrome by suppressing acid secretion with the use of proton-pump–inhibitor therapy.[2]

Norton et al. provide little information on morbidity or the functional outcome after surgery — for example, the number of patients who still required drug treatment. At 10 years, the rates of cure, or disease-free survival, were much lower than the rates of disease-specific survival (95 percent in the patients with sporadic gastrinomas and 85 percent in those with multiple endocrine neoplasia type 1). This good outcome despite the failure to achieve a cure with surgery can just as readily be achieved by treatment with a proton-pump inhibitor alone.[2]

We need a clearer understanding of the true therapeutic benefit of surgery in patients with the Zollinger–Ellison syndrome and of when to avoid surgery. Many patients cannot be cured surgically, and among those who are, only 40 percent no longer require drug treatment postoperatively.[2]

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The authors reply:

To the Editor: We thank Dr. Hirschowitz for his comments. There are two distinct clinical problems with the Zollinger–Ellison syndrome. First, the hypersecretion of gastric acid causes severe peptic ulcer disease and diarrhea, as Dr. Hirschowitz points out. These symptoms can be effectively controlled with antisecretory drugs in all patients except those few who cannot or will not take oral medications.[1] However, these drugs have no effect on the second problem, which is tumor growth.

In our study of 212 patients with the Zollinger–Ellison syndrome,[2] 31 percent of the patients died over a mean follow-up period of 14 years (range, 0.1 to 31 years); half the deaths were related to tumor growth, and none to hypersecretion of gastric acid. At present, there is no established antitumor treatment except effective surgery. In our study, the morbidity and mortality associated with surgery remained less than 12 and 1 percent, respectively, as we reported previously.[3] In our study comparing the outcome of medical treatment alone with that of surgical resection, surgery did not prolong survival ($P=0.085$)[4]; however, surgery decreased the probability of subsequent metastasis ($P<0.003$), which is the main prognostic factor for tumor-related death.[2]

Surgery also has important effects on the requirement for antisecretory drugs. We are still determining the exact proportion of patients cured who will be able to stop drug therapy; in our preliminary analysis, it is 40 to 50 percent.[5] With curative resection, there is a 75 percent decrease in basal acid output and a 44 percent decrease in maximal acid output in response to pentagastrin, and among patients continuing to require antisecretory-drug treatment, the majority require a low dose of an antisecretory agent, usually a histamine H_2-receptor antagonist. For the reasons reviewed above and because surgery can cure a substantial proportion of these patients, as demonstrated by our study, we recommend surgery in patients with the sporadic form of the Zollinger–Ellison syndrome.

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Guidelines for Healthy Weight

To the Editor: Willett et al. (Aug. 5 issue)[1] have highlighted the importance of taking early action to prevent increases in measures of obesity and the associated risks, including type 2 diabetes, hypertension, and dyslipidemia. The data to which they refer, however, concern predominantly white populations and are not necessarily representative of other racial or ethnic groups.

Unlike the situation in many Western countries, the prevalence of obesity in Chinese populations remains relatively low. In Hong Kong, approximately 6 percent of the population have a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or higher, although a third have a body-mass index of 25 or higher.[2] Despite these relatively lower levels of obesity, the disorders associated with the metabolic syndrome are reaching epidemic proportions in Hong Kong.[3] Ten percent of the adult population 25 to 74 years of age have type 2 diabetes (as determined on the basis of a 75-g oral glucose-tolerance test), 17 percent have hypertension (defined as a systolic blood pressure of 140 mm Hg or more and a diastolic blood pressure of 90 mm Hg or more), and more than 50 percent have dyslipidemia (defined as a total cholesterol level of 5.2 mmol per liter [200 mg per deciliter] or more and a triglyceride level of 2.0 mmol per liter [180 mg per deciliter] or more).[2] However, we found that the mean body-mass index and measurements of waist circumference of patients with components of the metabolic syndrome fall near or under the cutoff used to define overweight in whites. Furthermore, when we investigated risk factors among Chinese persons in Hong Kong, the anthropometric levels associated with the lowest prevalence were in subjects with a body-mass index below 22 or a waist circumference below 70 cm.

It is apparent from our data that, for Chinese persons, the criteria for obesity should be lowered. Our patients should be encouraged to reduce their body-mass index below 22 and their waist circumference below 70 cm. It is important for clinicians to recognize that cutoff values in guidelines are inherently arbitrary and that those currently used for whites are inappropriately high for Asian patients, including Chinese. Such patients may be within the "normal" range for weight, but their risks of type 2 diabetes, hypertension, and dyslipidemia and the illnesses associated with these disorders are more than double those of persons at optimal weight levels.

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To the Editor: Willett et al. endorse the use of the body-mass index because published studies demonstrate a fairly strong correlation between body-mass index and the results of hydrodensitometry or dual-energy x-ray absorptiometry. At our primary care clinic, we perform direct measurement of body fat using infrared interactance and bioelectrical impedance. We find that the measured percentage of body fat consistently correlates with body-mass index only in persons with a body-mass index of more than 35. As the body-mass index drops, the correlation becomes much weaker. Many people with a "normal" body-mass index have body-fat readings well into the range for obesity. More important, when interventions are introduced, measured body fat and body-mass index can travel in opposite directions. For example, one of our patients recently lost 20 lb (9 kg) by following a calorie-restricted diet only, but her body fat rose from 35 percent to over 40 percent. Virtually every pound she lost came from lean body mass. We believe that clinicians should use the available technology to measure the component that actually creates the risk — elevated body fat.

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To the Editor: The body-mass index is helpful, since it translates the values on the height and weight charts into a single number. But the body-mass index does not dis-

criminate between adipose tissue and muscle, and it may contain other systematic flaws.

Consider professional basketball players, hardly an overweight group. At 1.98 m and 95 kg, Michael Jordan has a body-mass index of 24, which falls in the upper end of the healthy-weight group, as stratified by the International Obesity Task Force, although his body fat is under 10 percent. Shaquille O'Neal's body fat is reported to be near 5 percent, but his dimensions (2.18 m and 141 kg) indicate that he is grossly overweight — nearly obese — on the scale of the International Obesity Task Force, with a body-mass index of 29.7. The Chicago Bulls drafted four rookies this year. Their body-mass indexes ranged from 27.3 to 29.8, perhaps another bad sign for season-ticket holders, but hardly a sign that these players are overweight.

The body-mass index needs a simple correction factor. Perhaps if one multiplied the body-mass index by the waist circumference fat stores could be discriminated from muscle mass and a simple, useful number could be generated. The index could be called the WHW index, for weight–height–waist. Alternatively, it could be called the BM-W index, a reminder of the connection between affluence and body fat. In the example above, Michael Jordan's body-mass index of 24 could be corrected by his waist circumference (0.88 m) to an index of 21. A fan 68 in. (1.73 m) tall weighing 72 kg would also have an uncorrected body-mass index of 24. But his 39-in. (0.99-m) waist means his corrected BM-W is 24, so this corrected index helps to discriminate the fit from the fat. Sadly, Shaq still comes in as overweight.

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The authors reply:

To the Editor: We appreciate the data provided by Thomas et al. that reinforce our point that the upper limit of 25 for body-mass index typically used to define the cutoff of healthy weights is far from optimal for many persons. Determining whether the range of healthy weights is truly different for populations in Hong Kong and the United States requires more thorough population-based studies.

We also agree with Drs. Wilson and Davis that the body-mass index is an imperfect measure of body fat, mainly because it does not discriminate between muscle and fat mass. However, the body-mass index actually works quite well as a simple surrogate measure in most young and middle-aged adults, if one excludes persons who are trained athletes or who are involved in muscle-building programs. As we have noted elsewhere, the correlation between body-mass index and fat mass adjusted for height is approximately 0.9.[1] Moreover, as we documented in our review,[2] the body-mass index strongly predicts the risk of major health events, even within the range of 20 to 30. However, because of the limitations of the body-mass index, we suggested the use of the amount of weight gained since young adulthood (from about the age of 21 years in men and from several years younger in women). This simple measure will identify those at higher risk due to fat accumulation in midlife, even though many still have a body-mass index of less than 25. Bioelectric impedance may be helpful, but it, too, is not perfect and has not been shown to be clearly superior to simple measures of weight and height in a well population.

As Dr. Davis points out, waist circumference can be a useful ancillary measure. The index he proposes is one way to incorporate this information, but it needs further evaluation. The failure of this index to pass the "Shaq" test is a reminder that physicians should not forget to look at the patient and use clinical judgment when interpreting any measurement.

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The Control of Labor

To the Editor: In their review of the mechanisms that control labor (Aug. 26 issue),[1] Norwitz et al. assert that magnesium sulfate is both safe and efficacious for the management of preterm labor. They also state that it has become the first-line treatment for preterm labor in North America. We were surprised by this unqualified endorsement of the usefulness of magnesium sulfate. A review of the scientific evidence has led us[2,3] and others[4-6] to different conclusions.

Although many obstetricians have had the anecdotal impression that delivery is delayed among patients undergoing tocolysis with magnesium sulfate, such an effect has never been proved in a rigorous way. In the only well-designed randomized clinical trial of the tocolytic efficacy of single-agent therapy with intravenous magnesium sulfate, as compared with saline control, Cox and associates found no difference in any measure of therapeutic effect.[6] Similarly, in a recent systematic review of the literature, Kierse and coauthors concluded that "although magnesium sulphate may be efficacious for arresting uterine contractions in women who are not actually in preterm labor, its place in established preterm labor has not been demonstrated and it can have serious side-effects."[4]

The statements by Norwitz and associates regarding the safety of tocolytic magnesium sulfate are equally controversial, with supportive data lacking.[2-4] Stating that magnesium sulfate is safe and effective as a means of tocolysis (without citing supportive references) may mislead clinicians into thinking that such conclusions are firmly established.

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The authors reply:

To the Editor: Drs. Pryde and Mittendorf express concern about the efficacy and safety of tocolytic magnesium sulfate and question the statement that magnesium sulfate has become the first-line treatment for preterm labor in North America. Nowhere in the review did we conclude that magnesium sulfate was effective in arresting preterm labor. Indeed, we specifically stated, "Although a number of [tocolytic] agents are now available . . . there are no reliable data to suggest that any of them delay delivery for more than 48 hours."[1]

Since no single tocolytic agent has a clear therapeutic advantage, the decision about which of the available agents to use is often determined by the side effects of the drugs. Although no drug is without risk, there is considerable evidence to suggest that magnesium sulfate has fewer serious maternal and fetal side effects than the other available first-line tocolytic agents.[2,3] Furthermore, there is mounting evidence to suggest that prenatal exposure to magnesium sulfate may reduce the risk of cerebral palsy and mental retardation in premature neonates. This potential reduction in risk is not due to selective mortality among infants exposed to magnesium sulfate and is independent of the putative tocolytic benefit of the drug.[4]

It is generally accepted, and Mittendorf and Pryde themselves have stated, with colleagues, that "magnesium [sulfate] ranks among the most popular tocolytics in the United States."[5] To address this issue, a questionnaire was recently sent to the directors of all 72 fellowship programs in maternal–fetal medicine in the United States that were identified by the Society for Maternal–Fetal Medicine. The response rate was 86 percent (62 of 72 questionnaires were returned). Magnesium sulfate was the reported first-line tocolytic agent in 85 percent of the responding institutions (53 of 62) (Ecker J, Greenberg J: personal communication).

In summary, although no perfect tocolytic drug exists, magnesium sulfate probably offers the most favorable benefit-to-risk ratio of all the available first-line tocolytic agents. The first rule of tocolysis is to use it only when indicated (i.e., in a patient with confirmed preterm labor before 34 weeks' gestation) and, as in all of medical practice, to tailor management to the individual patient.

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Back to the Basics

To the Editor: In a Clinical Problem-Solving article by Fisk et al. (Sept. 2 issue),[1] a 34-year-old man with paraplegia was admitted because of fever and abdominal pain. The clinician-discussant noted, "It is of interest that palpation of the left lower quadrant elicits pain in the right upper quadrant, and I wonder whether this is a manifestation of impaired innervation of the abdominal wall resulting from the accident."[1] However, there is another explanation. It was first put forward by Hamilton Bailey, who called it Rovsing's sign, after Niels Thorkild Rovsing (1862–1927), a professor of surgery in Copenhagen. To test for this sign, even pressure is exerted over the descending colon. If, when the left iliac fossa is pressed, pain is felt in the right iliac fossa, the patient probably has acute appendicitis. The sign appears to be due to the shift of coils of ileum to the right, which then impinge on an inflamed focus in the right iliac fossa.[2] I suggest that the physical findings in this case demonstrated a modified example of Rovsing's sign.

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1. Fisk DT, Saint S, Tierney LM Jr. Back to the basics. N Engl J Med 1999; 341:747-50.
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To the Editor: I was surprised by the explanations offered for the patient's heart rate of 95 beats per minute in the context of a body temperature of 38.8°C. In addition to the patient's relative youth and the possibility of temperature–pulse dissociation because of enteric fever or atypical pneumonia, should autonomic dysreflexia have been considered as a contributing factor?

Typically associated with lesions above T6, autonomic dysreflexia produces bradycardia in the presence of noxious stimuli, such as an inflamed appendix or, more commonly, an overdistended bladder or impacted bowels. Patients usually have substantial hypertension because an uninhibited sympathetic response below the level of injury produces severe vasoconstriction and then reflexive bradycardia. In the case of borderline sepsis or dehydration, the hypertension may have been mitigated to produce this patient's blood pressure of 126/68 mm Hg. Autonomic dysreflexia has been reported in a woman with an injury at the level of T10.[1] It may therefore be worth considering

this possibility when examining patients with injuries to the thoracic cord.

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The authors reply:

To the Editor: Dr. Sharma's suggestion is a very good one. We agree that our patient had a modified Rovsing's sign on his physical examination; in fact, we had referred to this finding as such during informal discussions about the patient.

Dr. Franklin raises the important issue of autonomic dysreflexia, a common problem in patients with spinal cord injury. Although the patient's spinal cord lesions were a bit lower than what we would expect in a patient with autonomic dysreflexia, autonomic dysreflexia is a possible contributing factor to his temperature–pulse dissociation.

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The Energy Expended in Chewing Gum

To the Editor: Indirect evidence suggests that gum chewing may have greater metabolic effects than has been appreciated. The thermic effect of food is reduced when nutrition bypasses the mouth.[1] In cows, chewing increases energy expenditure by approximately 20 percent.[2,3] We measured how energy expenditure changes with gum chewing in humans.

Energy expenditure was measured in a temperature-controlled, darkened, silent laboratory with an indirect calorimeter (model 229, SensorMedics, Yorba Linda, Calif.) that was calibrated before each measurement with two primary-standard gases (a combination of 4 percent carbon dioxide and 16 percent oxygen and a combination of 26 percent oxygen and a balance of nitrogen) and calibrated for gas flow. Expired air was collected with a specially designed face mask (0.3 by 0.2 by 0.1 m) that allowed unopposed jaw movement. Measurements were performed in seven non-obese subjects with stable weight while they were seated at rest with their arms and legs supported. Energy expenditure was first measured at rest for 30 minutes. The subjects were then provided with 8.4 g of calorie-free gum and instructed to chew at a frequency of precisely 100 Hz (a value than approximates chewing frequency at our institution) with the aid of a metronome. After 12 minutes, the gum was removed from the mouth, and energy expenditure was measured for 12 minutes after chewing.

Mean (±SD) energy expenditure increased in all subjects during chewing, from 58±11 kcal per hour at base line to 70±14 kcal per hour (two-sided $P<0.001$). After chewing, energy expenditure returned to base line (59±12 kcal per hour) in all subjects ($P<0.001$). Chewing gum led to a mean increase in energy expenditure of 11±3 kcal per hour (range, 7 to 17), a 19±4 percent increase above base-line values. For perspective, in the same subjects, standing was associated with a mean increase in energy expenditure of 11±11 percent and walking at 1.6 km (1 mile) per hour was associated with an increase of 106±26 percent above base-line values.

Non-nutritional chewing is a behavior that is shared with other primates[4] and is a component of nonexercise activity.[5] Gum chewing is sufficiently exothermic that if a person chewed gum during waking hours and changed no other components of energy balance, a yearly loss of more than 5 kg of body fat might be anticipated. Chewing of calorie-free gum can be readily carried out throughout the day, and its potential effect on energy balance should not be discounted.

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