

for the authors to compare their mortality rate with that in patients with burns and smoke-inhalation injuries.

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THE AUTHORS REPLY: Drs. Mutlu and Budinger inquire about diagnoses, such as diabetes mellitus, that might prevent acute lung injury. Since the King County Lung Injury Project (KCLIP) was designed to study the incidence and outcomes of patients with acute lung injury, limited information was collected from patients without this diagnosis. Therefore, this cohort cannot be used to address the question they raise.

The question asked by Dr. Maybauer and colleagues supports the importance of population-based epidemiology of critical illness syndromes. During the study period, there were 30 patients with burns treated at Harborview Medical Center who met the criteria for acute lung injury; however, 26 (87 percent) of these patients lived outside of King County and therefore did not contribute to the population incidence. Clinicians who practice in academic centers and studies restricted to these centers may overestimate the incidence of diseases on the basis of the distribution of cases referred to specialized centers. Respiratory complications of inhalation and thermal injury are associated with high morbidity and mortality; however, data from KCLIP suggest that the overall contribution of these risk factors to the population incidence of acute lung injury is small.

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Low HDL Cholesterol Levels

TO THE EDITOR: Ashen and Blumenthal (Sept. 22 issue)¹ state that caution is recommended with the use of high-dose niacin in patients with diabetes, because niacin may increase glucose levels. However, the Arterial Disease Multiple Intervention Trial (ADMIT)² showed that niacin can be used safely in patients with diabetes. Levels of glycosylated hemoglobin were unchanged from baseline in patients with diabetes who were assigned to receive niacin therapy. In fact, there were no differences in niacin discontinuation, niacin dosage, or hypoglycemic therapy in patients with diabetes who received niacin, as compared with baseline.

Previous reports of niacin-induced glucose intolerance are derived largely from uncontrolled case reports involving small numbers of subjects. Since niacin is effective in treating the dyslipidemia (low levels of high-density lipoprotein [HDL] cholesterol and elevated triglyceride levels) that is commonly seen in patients with diabetes, this medication should not be withheld because of concern about glycemic control.

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TO THE EDITOR: Ashen and Blumenthal do not mention a potentially important ocular side effect of niacin therapy. Niacin has been linked to a loss of central vision owing to the development of a form of cystoid macular edema.¹⁻³ The cystoid macular alterations in niacin maculopathy appear to be biomicroscopically identical to those seen in cystoid macular edema after cataract extraction.² Cystoid macular edema is usually seen in men between the ages of 30 and 60 years.³ The edema usually resolves when niacin therapy is stopped.² Prompt recognition of the association

of visual loss with niacin in patients taking this drug is critical.

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TO THE EDITOR: Ashen and Blumenthal do not correctly describe the effects of dietary fat on low-density lipoprotein (LDL) cholesterol and on HDL cholesterol. HDL cholesterol levels indeed decline when fat intake is reduced, but when the fat that is reduced is unsaturated, LDL cholesterol levels do not go down but, rather, go up.¹ Such unsaturated fats make up more than 60 percent of the fat in the U.S. diet. Moreover, the beneficial effects of vegetable oils on HDL cholesterol are not specifically due to their n-3 fatty acid content but to the monounsaturated fatty acids and n-6 polyunsaturated fatty acids that make up the bulk of most vegetable oils. The effects of n-3 polyunsaturated fatty acids on HDL cholesterol do not differ from those of other unsaturated fats²; therefore, the high HDL cholesterol levels in Alaskan populations must be due to other factors. Finally, the alleged beneficial effect of carbohydrates with a low glycemic index on HDL cholesterol is only tentative and still needs to be confirmed in additional randomized trials.

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2. Harris WS. n-3 Fatty acids and serum lipoproteins: human studies. *Am J Clin Nutr* 1997;65:Suppl:1645S-1654S.

TO THE EDITOR: Ashen and Blumenthal suggest in their illustration of reverse cholesterol transport that the large intestine is a relevant source of lipid-poor, apolipoprotein A-I-containing pre- β HDL cholesterol. Although there is certainly evidence that cell lines in the fetal human colon¹ and in some colon-cancer cell lines² synthesize and secrete apolipoprotein A-I, to our knowledge

there are no data that demonstrate this capacity in the normal adult colon. Avian species such as chickens synthesize and secrete apolipoprotein A-I from a variety of extrahepatic, extraintestinal tissues,³ including the colon, but even in chickens, intestinal expression of apolipoprotein A-I messenger RNA is predominantly restricted to the small intestine. The synthesis of intestinal apolipoprotein A-I in mammals^{4,5} and, as a corollary, the secretion of pre- β HDL cholesterol should be viewed as virtually exclusively confined to enterocytes of the small intestine.

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THE AUTHORS REPLY: With regard to niacin therapy: we agree with Dr. Itskowitz that such therapy is effective in treating dyslipidemia and may be used safely in patients with diabetes, as demonstrated in ADMIT. However, we continue to recommend caution in the use of niacin therapy in patients with diabetes, according to the recommendations of the American Diabetes Association,¹ as cited in our article. Niacin therapy can result in hyperglycemia and should be used with caution. Dr. Pollock notes a very important ocular side effect of this therapy — namely, cystoid macular edema. Prompt recognition of visual loss in men between the ages of 30 and 60 years who are receiving niacin therapy is of critical importance.

In response to Dr. Katan: we agree that the effects of n-3 polyunsaturated fatty acids do not differ from those of other unsaturated fats and that the high HDL cholesterol levels in Alaskan

populations may be due to other factors. We are also in agreement that although the dietary glycaemic load is negatively correlated with HDL cholesterol levels, as mentioned in our article, this relationship needs to be confirmed in additional randomized trials.

In response to Drs. Xie and Davidson: we agree that the diagram in our article misrepresents the actual relevant source of lipid-poor, apolipoprotein A-I-containing pre- β HDL; it should indicate the small intestine rather than the large

intestine. This was an oversight on our part. The figure legend indicates “intestinal mucosa” but should more accurately indicate “mucosa of the small intestine.”

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Medical Mystery: Extensive Ecchymosis — The Answer

TO THE EDITOR: The Medical Mystery in the December 1 issue¹ involved a 71-year-old man with lower-extremity ecchymosis (Fig. 1) and gingivitis (Fig. 2, arrows). He was a retired Army man living alone with a modest income. He had poor nutritional intake, had a history of 150 pack-years of smoking cigarettes, and consumed two glasses of red wine each day.

Scurvy was suspected and confirmed by a low level of ascorbic acid (3.6 μmol per liter; normal range, 30 to 40). Other nutritional deficiencies that were identified included those of folic acid (1.37 ng per milliliter [3.1 nmol per liter]; normal range, 3 to 17 ng per milliliter [6.8 to 38.5 nmol per liter]); calcium (1.96 mmol per liter; normal range, 2.22 to 2.61); and 25-hydroxyvitamin D (7 mmol per liter; normal range, 27 to 175). Ascorbic acid was given orally at a dose of 500 mg per day. Eight days later, the patient was able to walk alone, the ecchymosis gradually disappeared, and the congestive periodontitis was notably improved.

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Editor's note: We received 2001 responses to this Medical Mystery, including 58 percent from physicians in practice, 23 percent from physicians in training, and 11 percent from medical students. Responses were received from 81 countries. Of those, 69 percent correctly identified this case as due to a deficiency of vitamin C, or scurvy. Other proposed diagnoses were leukemia (especially

monocytic variants), suggested by 14 percent of respondents; a variety of other nutritional deficiencies, by 8 percent; and many other conditions (such as autoimmune diseases, an overdose of medication, amyloid, and sepsis), by the remaining 9 percent.



Figure 1. Ecchymosis on the Lower Extremities.



Figure 2. Severe Gingivitis.