

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- $\beta$  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.”

Dominique Ashen, Ph.D., C.R.N.P.

Roger S. Blumenthal, M.D.

Johns Hopkins Ciccarone Center for the Prevention  
of Heart Disease  
Baltimore, MD 21287  
rblument@jhmi.edu

1. Haffner SM. Management of dyslipidemia in adults with diabetes. *Diabetes Care* 2003;26:Suppl 1:S83-S86.

## Medical Mystery: Extensive Ecchymosis — The Answer

**TO THE EDITOR:** The Medical Mystery in the December 1 issue<sup>1</sup> 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  $\mu$ mol 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.

Denis Mulleman, M.D.

Philippe Goupille, M.D.

François Rabelais University  
37032 Tours CEDEX 1, France

1. Mulleman D, Goupille P. A medical mystery — extensive ecchymosis. *N Engl J Med* 2005;353:2384.

*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.

Scurvy is a disease of great historical interest, especially in mariners participating in long voyages. Ascorbic acid (vitamin C) has many biologic functions; the best understood is its role in

collagen synthesis — the failure of which leads to many of the clinical manifestations of scurvy. A moderate consumption of fruits and vegetables is adequate to prevent this disease.

## Cabergoline and Mitral Regurgitation

**TO THE EDITOR:** Pinero et al. (Nov. 3 issue)<sup>1</sup> describe a 74-year-old man with Parkinson's disease in whom severe mitral regurgitation developed after a relatively short course of treatment with cabergoline, an ergot dopamine agonist. Cabergoline is used in different settings at different doses. In patients with Parkinson's disease, the usual daily dose ranges from 2 to 6 mg,<sup>2</sup> whereas in hyperprolactinemia, the weekly dose ranges from 0.25 to 3.5 mg.<sup>3</sup> So far, fibrotic reactions and valvular heart disease due to the use of ergot dopamine agonists have been reported almost exclusively in patients with Parkinson's disease and thus could be related to age, dosage, or both. I would be very interested to know the dose of cabergoline used for the patient described by Pinero et al., and I wonder whether young patients receiving low-dose cabergoline therapy for hyperprolactinemia should be aware of the potential risk of fibrotic side effects.

Etienne Delgrange, M.D.

Université Catholique de Louvain  
5530 Mont-sur-Meuse, Belgium  
etienne.delgrange@mint.ucl.ac.be

1. Pinero A, Marcos-Alberca P, Fortes J. Cabergoline-related severe restrictive mitral regurgitation. *N Engl J Med* 2005;353:1976-7.
2. Lang AE, Lozano AM. Parkinson's disease. *N Engl J Med* 1998;339:1130-43.
3. Colao A, Di Sarno A, Cappabianca P, Di Somma C, Pivonello R, Lombardi G. Withdrawal of long-term cabergoline therapy for tumoral and nontumoral hyperprolactinemia. *N Engl J Med* 2003;349:2023-33.

**THE AUTHORS REPLY:** We are grateful to Dr. Delgrange for the interest in our letter. Our patient was treated initially with 2 mg of cabergoline daily; he subsequently received an additional 2 mg daily, starting at the beginning of the second

month. The serious adverse effect was observed at the end of the fourth month of treatment.

The incidence of valvular damage due to cabergoline is not established. Horvath et al.<sup>1</sup> reported polyvalvular regurgitation in a patient taking cabergoline for 20 months, with stepwise increases in the dosage from 2 mg to 4 mg per day. The cumulative dose was greater than in our patient, but the lesions were mild and reversible.<sup>1</sup> In clinical trials of cabergoline, the absence of valvular lesions could be due to short follow-up.<sup>2</sup>

It is true that the doses of cabergoline used in hyperprolactinemia are considerably lower than those used in Parkinson's disease,<sup>3</sup> so it would be reasonable to assume a lower risk of valvular lesions. However, higher doses of cabergoline, similar to those used in patients with Parkinson's disease, have been used in treating resistant hyperprolactinemia associated with giant prolactinomas.<sup>4</sup> In such cases, the risk of valvular disease may be greater.

Antonio Pinero, M.D.

Pedro Marcos-Alberca, M.D.

José Fortes, M.D.

Fundación Jiménez Díaz  
28040 Madrid, Spain  
pmarcos@fjd.es

1. Horvath J, Fross RD, Kleiner-Fisman G, et al. Severe multi-valvular heart disease: a new complication of the ergot derivative dopamine agonists. *Mov Disord* 2004;19:656-62.
2. Clarke CE, Deane KH. Cabergoline for levodopa-induced complications in Parkinson's disease. *Cochrane Database Syst Rev* 2001;1:CD001518.
3. Colao A, Di Sarno A, Cappabianca P, Di Somma C, Pivonello R, Lombardi G. Withdrawal of long-term cabergoline therapy for tumoral and nontumoral hyperprolactinemia. *N Engl J Med* 2003;349:2023-33.
4. Gillam MP, Middler S, Freed DJ, Molitch ME. The novel use of very high doses of cabergoline and a combination of testosterone and an aromatase inhibitor in the treatment of a giant prolactinoma. *J Clin Endocrinol Metab* 2002;87:4447-51.