dislipidaemia associated with atherosclerotic disease systemically alters the DC function. As highlighted in the review, the accumulated evidence indicates that DCs might be importantly involved in plaque destabilization. I agree with Bauriedel and co-workers that the impact of DCs on plaque destabilization requires clarification.

References

1. Bobryshev YV, Lord RS, Parsson H. Immunophenotypic analysis of the aortic aneurysm wall suggests that vascular dendritic cells are involved in immune responses. *Cardiovasc Surg* 1998;**6**:240–249.
2. Krupa WM, Dewan M, Jeon MS, Kurtin PJ, Younge BR, Goronzy JJ, Weyand CM. Trapping of misdirected dendritic cells in the granulomatous lesions of giant cell arteritis. *Am J Pathol* 2002;**161**:1815–1823.
3. Inder SJ, Bobryshev YV, Cherian SM, Wang AY, Lord RS, Masuda K, Yutani C. Immunophenotypic analysis of the aortic wall in Takayasu's arteritis: involvement of lymphocytes, dendritic cells and granulocytes in immuno-inflammatory reactions. *Cardiovasc Surg* 2000;**8**:141–148.
4. Inder SJ, Bobryshev YV, Cherian SM, Lord RS, Wang AY. Identification of dendritic cells in ePTFE grafts explanted from humans. *Cardiovasc Surg* 2000;**8**:265–273.
5. Skowasch D, Jabs A, Andrie R, Dinkelbach S, Luderitz B, Bauriedel G. Presence of bone-marrow- and neural-crest-derived cells in intimal hyperplasia at the time of clinical in-stent restenosis. *Cardiovasc Res* 2003;**60**: 684–691.
6. Bauriedel G, Jabs A, Skowasch D, Hutter R, Badimon JJ, Fuster V, Welsch U, Luderitz B. Dendritic cells in neointima formation after rat carotid balloon injury: coordinated expression withanti-apoptotic Bcl-2 and HSP47 in arterial repair. *J Am Coll Cardiol* 2003; **42**:930–938.

Yuri V. Bobryshev
St Vincent's Hospital
School of Medical Sciences
University of New South Wales
Sydney
NSW 2052
Australia
Tel: +612 8382 2395
Fax: +612 9314 7654
E-mail address: y.bobryshev@unsw.edu.au

doi: 10.1093/eurheartj/ehi634

Online publish-ahead-of-print 2 November 2005

Heart failure improvement from a supplement containing copper

Witte *et al.*[1] improved ventricular function and quality of life in septuagenarian patients with chronic heart failure and ischaemic heart disease by supplementation with multiple micronutrients.The authors suggested that their regimen may provide relief from multiple deficiencies, reduction in oxidative stress, and be a first step towards identifying elements that can be eliminated from the supplement without loss of benefit. Copper is an antioxidant nutrient for cardiovascular health[2] that may have contributed to their success.

The Western diet is often low in copper,[3] according to the pooled data from several articles on more than 900 diets chemically analysed. About 62 and 36% of diets of 80 randomly selected adults in Baltimore[4] were below the recommended dietary allowance and the estimated average requirement for adults, respectively, 0.9 and 0.7 mg daily.[5]

Copper deficiency is the only nutritional insult that elevates cholesterol, blood pressure, homocysteine, and uric acid, has adverse effects on electrocardiograms and arteries, impairs glucose tolerance, and promotes thrombosis and oxidative damage. More than 80 anatomical, chemical, and physiological similarities between animals deficient in copper and people with ischaemic heart disease have been identified.[6,7] Copper deficiency in animals can induce cardiac enlargement,[8] pleural effusion,[9] and heart failure[10] that are reversible with copper supplementation.

Dietary supplements including copper in this context may be inexpensive therapy rather than expensive placebos. The small size of this trial reveals that a follow-up trial can be relatively inexpensive and need not involve hundreds or thousands of people common in heart disease research. Perhaps, a trial with two to three times as much copper and a decrease in vitamins to nearer international recommended intakes will produce benefit in a shorter time.

References

1. Witte KKA, Nikitin NP, Parker AC, von Haehling S, Volk HD, AnkerSD, Clark AL, Cleland JGF. The effect of micronutrient supplementation on quality-of-life and left ventricular function in elderly patients with chronic heart failure. *Eur Heart J* 2005;**26**:2238–2244.
2. Allen KG, Klevay LM. Copper: an antioxidant nutrient for cardiovascular health. *Curr Opin Lipidol* 1994;**5**:22–28.
3. Klevay, LM. Lack of a recommended dietary allowance for copper may be hazardous to your health. *J Am Coll Nutr* 1998;**17**:322–326.
4. Pang Y, MacIntosh DL, Ryan PB. A longitudinal investigation of aggregate oral intake of copper. *J Nutr* 2001;**131**:2171–2176.
5. Anon. Copper. In: *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Chapter 7. National Academy of Sciences: Washington, DC; 2001. p1–27.
6. Klevay LM. Ischemic heart disease. In: Bogden JD, Klevay LM, eds. *Clinical Nutrition of the Essential Trace Elements and Minerals: The Guide for Health Professionals*. Totowa, NJ: Humana Press Inc.; 2000. p251–271.
7. Klevay LM. Advances in cardiovascular-copper research. In: Schrauzer GN, ed. *Trace Elements in Nutrition, Health and Disease*. Montreal, Canada, Salt Lake City: Institut Rosell; 2002. p64–71.
8. Dallman PR. Cytochrome oxidase repair during treatment of copper deficiency: relation to mitochondrial turnover. *J Clin Invest* 1967; **46**:1819–1827.
9. Viestenz KE, Klevay LM. A randomized trial of copper therapy in rats with electrocardiographic abnormalities due to copper deficiency. *Am J Clin Nutr* 1982;**35**:258–266.
10. Elsherif L, Ortines RV, Saari JT, Kang YJ. Congestive heart failure in copper-deficient mice. *Exp Biol Med* 2003;**228**:811–817.

Leslie M. Klevay
University of North Dakota
223 27th Avenue South
Grand Forks
ND 58201
USA
Tel: +1 701 772 6960
Fax: +1 701 777 4490
E-mail address:
leslie_klevay@und.nodak.edu

doi: 10.1093/eurheartj/ehi635

Online publish-ahead-of-print 2 November 2005

Heart failure improvement from a supplement containing copper: reply

We are grateful for the comments by Prof. Klevay and we agree that copper supplementation in a population of elderly heart failure patients could have significant benefits. Our choice of agents and daily intakes in the study[1] were generally made on the basis of previous animal and human work.[2] However, although there are data on the prevalence and potential effects of copper deficiency,[3] there are few about supplemental doses in humans at risk of deficiency.[4] We were therefore cautious, choosing 1.2 mg per day based on recommended daily intakes.

The recent MAVIS study has demonstrated that multiple micronutrient supplementation is not of benefit in reducing morbidity from infections in otherwise well ambulatory elderly patients.[5] However, patients with long-term multi-system illnesses, such as chronic heart failure (CHF), might be more likely to have important relative deficiencies in multiple micronutrients due to reduced intake, increased degradation because of