directed against the modified protein part of the LDL lipoprotein, not
the lipid part. We agree that the peroxidation of lipids present in LDL
is not the only way to generate LDL oxidation. Direct oxidation of
the protein moiety of the lipoprotein also occurs. The process of LDL
oxidation leads to the modification of the protein moiety of LDL,
either directly—via aldehydes released from endothelial cells, as
Holvoet described, or via myeloperoxidase-derived hypochlorous
acid (1)—or indirectly—via peroxidation of polyunsaturated fatty
acids (2). In turn, direct and indirect pathways can be related. For
example, the tyrosyl radical generated by myeloperoxidase is also a
physiologic catalyst for the initiation of lipid peroxidation in lipoproteins
(3). The advantage of the antibody against oxidized LDL de-
developed by Holvoet and colleagues is that it is directed against the
most harmful of the LDLs, a modified apolipoprotein B–100 lipoprotein
that can be recognized by the scavenger receptor of the macrophages and,
and hence, promotes the development of atherosclerosis. It is
currently thought that oxidized LDL is more damaging to the
arterial wall than is native LDL (4).

Holvoet et al (5) showed that, with the exception of blood pres-
sure, all components of the metabolic syndrome were significantly
associated with high concentrations of oxidized LDL in US men and
women aged 70–79 y. Most importantly, high concentrations of
oxidized LDL increased the risk of myocardial infarction in this
population. The central role of abdominal obesity in the metabolic
syndrome and the increased risk of high waist circumferences with
high oxidized LDL concentrations (6) underscore the need for rou-
tine medical examination of waist circumferences.

None of the authors had a conflict of interest related to the letter.

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is associated with increased waist circumference independent of body

Whole-grain intake, metabolic syndrome, and
mortality in older adults

Dear Sir:

In an interesting study of older adults in a recent issue of the
Journal, Sahyoun et al (1) reported the association between whole-
and refined-grain intakes, the metabolic syndrome, and cardiovas-
cular disease (CVD) mortality. After control for some potential
confounding variables, the authors concluded that whole-grain in-
take is inversely associated with the metabolic syndrome and CVD
mortality in this age group.

Metabolic syndrome and CVD mortality in elderly people are
certainly worthwhile topics for study, particularly when the in-
take of whole grains is considered. Although whole grains contain
higher amounts of health-protective nutrients than do refined
grains (2), little research has been conducted on the physiologic
effects of a diet high in whole grains, particularly in older adults.
However, we think that there are some difficulties with the study
of Sahyoun et al that may confound the results. The authors
enrolled their subjects on the basis of their willingness to partici-
participate in the study, but they did not select the subjects randomly
from a population of older persons. We cannot, therefore, extrap-
olate the results to other older adults. It is not clear how the
authors treated underreporters and overreporters of energy intake
with respect to study participation. This point is important be-
cause the studied population is elderly; previous studies have
shown that underreporting of energy intake increases directly
with age (3). Although Sahyoun et al controlled for the effect of
energy intake in their analysis, it should be kept in mind that some
foods are underreported more than other foods (4), and simply
implementing a control for energy intake does not correct for the
confounding that may be caused by underreporting. Another im-
portant issue has to do with which foods are categorized as whole
grains and which ones as refined grains. Furthermore, the authors
did not mention whether there was any significant interaction
between sex and whole-grain intake. We showed that the asso-
ciation of whole-grain intake and the metabolic syndrome in
healthy Tehranian adults is similar in the 2 sexes (5), but it
remains to be shown whether similar associations exist between
whole-grain intake and the metabolic syndrome in elderly men
and women.

The independent association of whole- and refined-grain intakes
with chronic diseases should be assessed by control for the effect of
other food. For example, recent evidence from 2 parts of a study
showed the beneficial effects of dairy products, fruit, and vegetables
on body weight (6) and the metabolic syndrome (7). Lack of control
for the effects of other foods in the study of Sahyoun et al makes the
conclusion misleading. Another major weakness of their study of
Sahyoun et al is that they used a 3-d dietary record to collect dietary
data. This method of gathering data does not reflect the subjects’
usual dietary intake; because a 3-d dietary record measures short-
term intake, its use as a predictor of a long follow-up analysis is
problematic (8).

It seems that the proportion of women in the highest quartile of
whole-grain intake is less than that in the lower quartiles. This find-
ing that more men than women are eating whole grain is unusual,
and it may be confounded with energy intake, because men probably
eat more food in general than do women. However, energy intake
increases with the quartiles of both refined-grain and whole-grain
intake. Do the sex-specific data shed any light on this issue? The
finding that energy intake increases significantly across quartiles of
whole-grain intake, whereas BMI decreases, is also somewhat ques-
tionable. Identifying diet-disease relations is extremely important in

LETTERS TO THE EDITOR 1439
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Dear Sir:

We read with interest the study of Sahyoun et al (1) reporting a lower prevalence of the metabolic syndrome and a reduced risk of cardiovascular disease (CVD) mortality in older people consuming diets high in whole-grain foods. Although these results are for the most part confirmatory, adding to the existing evidence that whole-grain intake may confer protection against the metabolic syndrome and CVD risk, the message about the healthy benefits conferred by increasing whole-grain intake in an older population is important. One problem with the study is the use of body mass index (BMI) as a measure of waist circumference. BMI may not be equivalent to waist, either in terms of measurement (cm) or in predicting CV risk. The recent data from the INTERHEART Study (2) clearly showed that, worldwide, waist is superior to BMI in relation to the risk of myocardial infarction. Therefore, the results of Sahyoun et al must be viewed with caution, because their report does not specify how many subjects with abdominal obesity (men with BMI < 27) escaped evaluation or what was the frequency of abdominal obesity (with BMI used as a surrogate measure) in the definition of the syndrome.

Among the biologically plausible mechanisms of the beneficial effects of whole-grain intake on CVD risk, the authors failed to include inflammation. Recent evidence suggests that inflammation may be an important mediator in the association between the consumption of dietary fiber, one important constituent of whole-grain foods, and CVD. In a nationally representative sample of 4900 adults aged 40–65 years, the likelihood of elevation of C-reactive protein (CRP) was significantly lower in subjects in the highest fiber quartile than in those in the lowest quartile (odds ratio: 0.51; 95% CI: 0.27, 0.95), regardless of age and BMI (3). A cross-sectional analysis of 780 diabetic men from the Health Professionals’ Follow-up Study (4) showed that high intakes of cereal fiber were associated with higher plasma concentrations of adiponectin, an insulin-sensitizing adipocytokine with anti-inflammatory properties. Meal modulation of circulating inflammatory and anti-inflammatory cytokines may also play a role in the detrimental or beneficial effects of different types of carbohydrates. For instance, the fiber content of a high-carbohydrate meal may influence plasma concentrations of adiponectin and interleukin 18 (IL-18): the greater the quantity of fiber in the load, the greater the inhibition of plasma IL-18 and the stimulation of adiponectin (5). IL-18 is a potent proinflammatory cytokine that may be important in the process of plaque destabilization and hence in predicting cardiovascular death in patients with acute coronary syndromes (6). It is interesting that, in the study by Sahyoun et al, fasting glucose concentrations decreased across increasing quartile categories of whole-grain intake, a finding consistent with a proinflammatory effect of increasing glucose concentrations (7). Increased consumption of high-density and low-quality foods, such as those rich in refined grains and poor in natural antioxidants and fiber, may cause an activation of the innate immune system, most likely by excessive production of proinflammatory cytokines associated with a reduced production of anti-inflammatory cytokines. This imbalance may favor the generation of an inflammatory milieu, which in turn may predispose susceptible persons to a greater incidence of the metabolic syndrome (8).

Neither of the authors had a personal or financial conflict of interest.

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