B Vitamin Therapy Not Beneficial

Homocysteine from page 1

inexpensive, was thought safe, and could have turned out to have a big payoff in re-
duced clinical events, it might have been a reasonable strategy to use while await-
ing results of randomized treatment out-
come studies.

But now the Norwegian Vitamin Trial (NORVIT) has shown that such therapy doesn't prevent cardiovascular events; in-
deed, it may even increase the risk. And there was also a disturbing trend, albeit not statistically significant, for an increase in cancer, said Dr. Bonaa, professor of cardiology at the University of Tromso (Norway).

Dr. Bonaa was the principal investigator in NORVIT, a randomized, double-blind, multicenter trial in which 3,749 Norwe-
gian patients were followed for 3.5 years following assignment to 0.8 mg/day of
tiamine—that is, in excess of 13 mcg/L—
fared worst, with a 27% increase in car-
diovascular events regardless of whether or not they received B vitamins.

Studies are being planned to learn whether folate accelerates cancer cell
growth. Discusant Ian M. Graham, M.D., was unwilling to declare the homocysteine hy-
pothesis dead and buried.

Because of NORVIT's complex two-by-
two factorial design, the study was un-
derpowered to firmly conclude that B vi-
tamin therapy was without benefit or

indeed harmful. But there is cer-
tainly no evidence for this or any other source that the relationship be-
tween homocysteine and cardio-
vascular disease is causal, said Dr. Graham, profes-
sor of epidemiology and public health at the
Royal College of Surgeons, and a cardiologist at
Trinity College, Dublin.

He agreed that the NORVIT cancer findings warrant further study. While epi-
demiologic data suggest a diet rich in fo-
late protects against cancer, there is also evidence from in vivo studies to support the argument that folate promotes cancer cell
growth.

NORVIT was sponsored by the Nor-
wegian Research Council, the Norwegian Council on Cardiovascular Research, and other nonprofit institutions, with no in-
dustry support.

Good Prognosis for ‘Mild’ Coronary Artery Disease Discredited

STOCKHOLM — The progno-
sis of nonobstructive coronary artery disease may be far less be-
nign than generally assumed, ac-
cording to two studies presented at the annual congress of the Eu-
ropean Society of Cardiology.

Patients with less than 50% in-
cal stenosis upon diagnostic coro-
nary angiography aren’t considered candidates for percu-
taneous intervention; they are typ-
ically told they have “mild” CAD with a very good pro-
gnosis. For this reason, critical path-
ways for risk assessment and treatment of such patients have never been developed, accord-
ing to Raffaele Bugiardini, M.D., of the University of Bologna, Italy.

The assumption that nonobstructive CAD car-
rries a good prognosis is not based on hard data, and had not been examined in a large study until recently. And now that it has, the as-
sumption turns out to be incorrect, the cardiologist
said.

Dr. Bugiardini presented a secondary analysis of three published, random-
ized clinical trials from the Thrombolysis in Myocar-
dial Infarction (TIMI) pro-
gram involving 10,915 pa-
tients with acute coronary syndromes (ACS) for
whom angiographic data

were available. The studies were the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT–TIMI 22), Orbifolin in Patients With Unstable Coronary Syndromes (OPUS–TIMI 16), and TIMI II-B studies. The prevalence of nonobstructive CAD in this ACS population was 8.3%. Slightly more than half of the 910 affected patients had mild CAD as defined by a stenosis of less than 50%, whereas the re-
mainder had angiographically normal, smooth coronary arter-
yes.

The primary outcome mea-
sure in Dr. Bugiardini’s analysis was the combined 1-year rate of death, MI, stroke, coronary revascularization, and/or unsta-
table angina requiring rehospital-
ization. It occurred in 11.2% of patients with nonobstructive CAD. The incidence was 8.8% in ACS patients with angiographically normal arteries and 13.3% in those with less than 50% stenosis.

Those rates will strike most physicians as surprisingly high. Even more disturbing was the unexpectedly high rate of the most serious outcomes—death or nonfatal MI—in this suppos-
edly low-risk population. The overall incidence was 2% at 1 year, with a 2.8% rate of death or nonfatal MI among patients with mild CAD and 1.7% in those with angiographically normal coronary arteries, Dr. Bugiardini said.

Now that the prevailing as-
sumption—that mild CAD car-
rries a good prognosis—has been discredited, it becomes impor-
tant for physicians to risk-stratify patients with nonobstructive CAD so that their management can be tailored appropriately, he said. The validated and widely used TIMI risk score for patients with unstable angina/non–ST-
segment elevation MI can play a useful role here, he added.

When he applied the TIMI risk score to the 665 eligible patients, the associated 1-year risk of death or MI climbed from 0% (in those with a TIMI score of 0) to 4.1% (in those with a score of 4 or more). (See box.)

“The 0.0% death or MI rate seen with a TIMI score of 1 is the ex-
pected rate in the general pop-
elation of asymptomatic sub-
jects. But when you go to a score of 3 points, you see a completely unaccept-
able 2.8% rate of death or MI. That is not acceptable. So patients with a score of 3 or 4 are really at great risk,” said Dr. Bugiardini.

Separately, Sylvie Swales, M.D., presented data from the World Health Organi-
zation’s Monitoring Trends and Determinants in Car-
diovascular Disease project (MONICA) Belgian sub-
study. This prospective sur-
vey of the 130,000 residents of the Belgian province of Luxembourg identified all
those who underwent coronary angiography for

the first time in any Belgian hos-

The subsequent 5-year inci-
dence of coronary death among
274 subjects with mild CAD as defined by a less than 50% sten-
osiwas 7.8%, similar to the 8.1% rate among 377 others with an-
angiographically significant single-
 vessel disease not treated with an-
gioplasty or bypass surgery. The 5-year rate of coronary death or nonfatal MI was 10.3% in those with mild CAD and 14.8% in those with nonobstruc-
tive CAD as defined by a 50% or
greater stenosis.

The prognosis was far better for the 763 individuals whose an-
giogram showed smooth vessels. Their 5-year rate of coronary death was just 0.7%, while their rate of coronary death or nonfa-
tal MI was 1.2%, noted Dr. Swales of the Catholic University of 
Leuven (Belgium).

Dr. Bugiardini said that al-
though it is possible that cases that are labeled as “nonobstruc-
tive” CAD represent misclassifi-
cation of the angiogram, it has been his clinical observation that poor patient compliance with secondary prevention measures is a much bigger factor.

“When told they have nonob-
struc-tive coronary artery disease, patients relax more than the doc-
tors,” said Dr. Swales. “So often, after 6 months or maybe even 2 months, they are not taking their drugs. It’s going to be nec-
 essary to have a public education campaign.”