to what extent calcium antagonists will replace long-
acting nitrates remains to be determined. Unlike the
calcium antagonists, nitrates have no negative in-
tropic effects and may be the preferred drugs in
patients with significant ventricular dysfunction,
whereas nifedipine might be favored in patients with
adequate function and systemic arterial hypertension.

Thus, although nitrates have been used to treat
angina pectoris for at least 115 years and over 1,300
articles have been written about them in the past
decade,19 many questions remain about their mecha-
nisms of action and about the role of oral nitrates in
the longterm treatment of patients with exertional angina.

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Diet-Drug Treatment of
Hyperlipidemia in Coronary
Artery Disease

A Rational and Beneficial Approach

A close relationship between elevated plasma lipid
(cholesterol and triglyceride) and enhanced de-
velopment of coronary artery disease (CAD) has been
well-established by epidemiologic study, animal exper-
imentation and human premature atherosclerosis.
Clinically, however, the use of diet-drug treatment of
hyperlipidemia for primary or secondary CAD preven-
tion has not gained wide acceptance. Some of the
reasons for the reluctance include: (1) plasma lipid
levels of a significant number of patients with proven
CAD are considered to lie within an arbitrarily set
range of normal, (2) angiographically demonstrable
coronary arterial lesions are not consistently correlated
with hyperlipidemia or hyperlipoproteinemia, (3)
progression and development of new CAD are variable
and unpredictable. The inconsistent association of the
plasma lipid level with CAD is not surprising, in view
of the knowledge that atherosclerosis is a multifactorial
disease. A meaningful correlation between them can
only be consistently demonstrated in certain subsets of
patients, especially those with familial hyper-
cholesterolemia (primary type 2 hyperlipoprotein-
emia), who are known to have a strong predisposi-
tion to CAD.1,2

In human subjects, plasma lipid (cholesterol) levels
are delicately regulated by well-balanced compensa-
tory mechanisms of excretion, feedback regulation and
tissue storage. Disturbance in one or more homeosta-
tic mechanisms is manifested in one or the other types
of CAD-prone hyperlipoproteinemia or hyper-
lipidemia. Thus, the ongoing debate about the virtues
of imposing "prudent diet" on the population in general3
not only misses the point, but confuses the
patient and physician. Clearly, there is little need for
dietary or other forms of intervention in subjects who
can maintain normal lipid metabolism, but a specific
diet-drug treatment should be prescribed for a well-
defined type of disturbance in lipid metabolism.

Patients with familial hypercholesterolemia (pri-
mary type 2 hyperlipoproteinemia) exemplify the need
for and benefit from aggressive intervention with diet-
drug treatment. In this abnormality, a defect in the
Cellular low density lipoprotein (LDL) receptor sites
has been defined,4 and an effective combination of low
cholesterol-saturated fat diet with colestipol and nico-
tinic acid or probucol treatment has been developed5
6 to facilitate cholesterol elimination and to reduce
cholesterol (LDL) biosynthesis. Several groups of
investigators have reported encouraging data to sug-
gest that progression of CAD can be retarded and early
peripheral arterial lesions can be made to regress by successful longterm control of hypercholesterolemia (LDL elevation) and/or hypertriglyceridemia. 3-11 No detrimental harmful side effect has been infected on these patients who have been maintained on longterm diet-drug treatment.

Turning to primary prevention of CAD, the results of the Oslo Diet-Heart Study 12 showed that new CAD events were reduced significantly in subjects with highly elevated plasma cholesterol levels (mean = 328 mg/dl) through administration of high polyunsaturated diet. Although no genetic analysis was made in this study, the high serum cholesterol level of this selected group of subjects is strongly suggestive of familial hypercholesterolemia.

Observations on primary and secondary prevention of CAD cited above provide strong indications for concerted efforts to treat hyperlipidemic patients who are either at high risk of or already have CAD. They should not be interpreted as supporting the suggested broadly based use of the highly restrictive diet by the general public to prevent CAD.

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Mural Thrombi of the Left Ventricle

The diagnosis of left ventricular thrombus is of potential clinical importance in identifying patients at risk for systemic embolization. Over the past years, several sophisticated methods capable of detecting thrombus have been developed. Left ventricular thrombus can be detected by external imaging of radiolabeled blood components which are incorporated into thrombi, as with indium-III platelet imaging, 1,2 or by the definition of anatomic filling defects created by thrombi, as with radionuclide angiography, 3 x-ray computed tomographic scanning, 4 and two dimensional echocardiography. 1,2,4-12 These techniques provide somewhat complementary and overlapping clinical information and each has limitations. Indium-III platelet imaging, which is positive only if ongoing thrombosis is occurring, has the possible advantage over the other techniques of defining thrombus activity. In addition, it has a specificity approaching 100 percent but a lower sensitivity of approximately 70 percent. 3,12 The identification of thrombi by radionuclide ventriculography is probably inferior to the other noninvasive techniques because of the limited resolution of gamma imaging systems. 5 X-ray tomographic scanning can detect thrombi, but the sensitivity and specificity are not currently defined. 6

Two dimensional echocardiography has clear advantages over these other modalities since it is widely available, involves no radiation exposure, is relatively rapid, can be used at the bedside, and often gives valuable additional information. Moreover, as confirmed in this issue by Visser et al (see page 228), the sensitivity is relatively high, ranging from 77 percent to 95 percent, and the specificity is also high, ranging from 86 percent to 93 percent. 6,11 As Visser et al also note, the accuracy of echo is clearly superior to invasive contrast angiography, which had a sensitivity of 36 percent in their series.

Echocardiography has two principal limitations in the detection of left ventricular thrombus. Approximately 10 percent to 20 percent of patients have