I. INTRODUCTION

Beta-carotene belongs to the chemical class of carotenoids responsible for most of the yellow, orange and red colors of fruits and vegetables. Of the over 50 carotenoids which are normal constituents of the blood and tissues of humans, beta-carotene is the major component. Transportation of carotene in the blood is primarily with LDL. Females have a consistently higher average plasma carotene concentration. The metabolism of circulating beta-carotene is only incompletely understood. Beta-carotene can be split into retinol in the small intestine. The process is relatively inefficient and self-limiting in that the conversion rate decreases with increased vitamin A status. Whether plasma beta-carotene can be converted into retinol or retinoic acid has not been established. Beta-carotene is safe, and even the long-term intake of 180 mg beta-carotene per day does not lead to hypervitaminosis A. Beta-carotene is deposited in adipose tissue and other lipid rich tissues. An intake of above 25 mg/day results in reversible yellowing of the skin.

Considerable attention is currently being given to beta-carotene as a promising disease preventing agent, the effect of which is to a large extent unrelated to its provitamin A activity.

II. CANCER

Since the suggestion was first made that carotenoids may protect against the development of cancer [1], numerous epidemiological studies have shown a strong and consistent association between a high consumption of carotene-containing vegetables and fruits, and a high beta-carotene status, with a lower risk of cancer [2]. The relationship is most evident for lung cancer as shown by the consistency of the epidemiological evidence from diverse populations, the graded nature and temporal sequence of the association, its independence from cigarette smoking, and its coherence with the evidence from animals [3-5]. Smokers have significantly decreased serum levels compared with those of non-smokers with similar food intake [6]. Based on these findings Stähelin et al.[7] has calculated a plasma level of 0.30 μmol/L (=16 μg/dl) as the lower limit for a cancer protecting effect of beta-carotene. In vitro experiments show beta-carotene to have antimutagenic and antitransformation activity at concentrations similar to those found in tissues. Animal studies have revealed a marked anticancer effect under various experimental conditions at a variety of sites and in several
species. Beta-carotene exerts its anticancer effect most likely independently of any retinol or retinoic acid formation by enhancing immunological function [8], or by quenching singlet oxygen [9] and trapping free radicals [10] - which may cause damage to DNA and other biomolecules. These properties enable beta-carotene to interfere in the stages of initiation and promotion of cancerogenesis.

In view of the convincing experimental and epidemiologic evidence, the preventive effect of supplemental beta-carotene on the incidence of various types of cancer is currently being studied in several long-term intervention trials. The only currently completed trials of carotene administration have reported a strong protective effect of beta-carotene, both alone and in combination with retinol, against chromosome breakage in the oral mucosal cells of tobacco-betel nut chewers. The twice weekly administration of beta-carotene (180 mg/week) induced the remission of oral leukoplakia in a certain percentage of treated individuals, prevented the formation of new leukoplakias within the 6-month trial period, and reduced the frequency of exfoliated buccal mucosal cells with micronuclei. All of these premalignant lesions are associated with increased oral cancer incidence [11]. A dose of 60 mg/week alone was adequate to maintain the low frequency of micronucleated cells. Among the clinical trials using cancer incidence as the clinical endpoint, is the prospective 5-year trial on the effect of 20 mg beta-carotene on lung cancer incidence in 29'000 Finnish smokers, a joint study by the NCI and the Finnish National Public Health Institute. The trial will run until mid 1993. The ongoing Harvard Physicians' Health Study involves about 22'000 US physicians, and is designed to investigate the effect of 50 mg of beta-carotene given every second day on cancer occurrence. Thus, in the next couple of years, the availability of data from these and other carefully designed and conducted randomized trials should provide definitive answers to the questions of whether supplementation of beta-carotene will, in fact, reduce the risk of cancer among humans.

III. CARDIOVASCULAR DISEASE

Recent evidence shows that beta-carotene may also have a role in the prevention of cardiovascular disease. As an unexpected preliminary result of the Physicians' Health Study in the U.S., 50 mg beta-carotene on alternate days led to a 44% reduction in all major coronary events, defined as cardiac death, MI, or revascularization in 333 men with coronary revascularization and/or angina pectoris prior to randomization [12]. These findings raise the possibility that, for people with angina pectoris or coronary bypass history, beta-carotene therapy may lessen the likelihood of a secondary major coronary event.

The above finding could well be in line with the new theory suggesting that oxidized LDL is linked to the development of atherosclerosis [13]. According to this hypothesis, oxidized LDL, which is cytotoxic to endothelial cells and chemotactic to circulating monocytes, opens up gaps in the endothelial lining and allows monocytes to accumulate in the arterial wall. Inside the wall the monocyte/macrophage avidly take up oxidized LDL by
the scavenger receptor pathway (which is not downregulated) and are transformed into destructive foam cells. Growth of the foam cells in size and number results in the formation of fatty streaks, the precursors of atherosclerotic plaques. LDLs contain, among other lipophilic antioxidants, beta-carotene which is consumed during free radical attack [14]. Thus, the development of atherosclerotic plaques could be prevented or slowed down by improving the antioxidant defence of the LDL. At least in animals, the approach has been shown to function in principle: BHT, a commonly used food preservative, and probucol, a cholesterol-lowering drug; both have been proven to act protectively as antioxidants in animal atherosclerotic models. Further evidence that beta-carotene may have a role in the prophylaxis of atherosclerosis is seen in the reduction of LDL oxidation by beta-carotene in vitro.

Taken together, there is promising evidence that beta-carotene (and other antioxidants) can prevent oxidation of LDL, and slow down the narrowing of the arteries and even prevent heart attacks and strokes. However, further laboratory and clinical studies are needed to confirm or refute these preliminary findings.

SUMMARY
Cancer and cardiovascular disease are still the number one and two killer diseases in most developed countries. There is justified hope that beta-carotene will be proven efficacious in the prevention and/or delaying of the onset of these chronic diseases. Chronic disease prevention through better nutrition, judicious use of supplements and better lifestyles will assume added importance in the coming years as the proportion of the population over 65 years increases.

REFERENCES


