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been identified. Vitamin C is essential in the formation of adrenalin, collagen, the synthesis of neurotransmitters, and many other biochemical functions.

Some of the bone mineral losses smokers experience also may be a secondary effect of low vitamin C levels or other nutritional conditions. Two studies²⁰ found significantly more severe osteoporosis in smoking postmenopausal women than for their nonsmoking counterparts.

Some heavy smokers develop amblyopia which reverses after they either receive vitamin B₁₂ supplements or quit smoking. Smoking-related losses of this vitamin appear to be due to reaction of B₁₂ with cyanide in inhaled tobacco smoke.²¹ Research on the possibility that smoking induces vitamin B₆ deficiencies suggests that the loss of this vitamin may involve a reaction with carbon monoxide in smoke.²²

Smoking and Estrogen Use

An important adverse interaction between smoking and a drug is the well-established increased risk of myocardial infarction in smokers who take oral contraceptives. FDA has required since April 1978 that oral contraceptive labels and information leaflets for patients carry the boxed warning: "Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes a day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke."

FDA imposed this warning following Mann et al.'s²³ research reporting the association between cigarette smoking and oral contraceptives. Subsequent studies have confirmed the high risk of cigarette smoking for oral contraceptive users. Jain²⁴ determined that (1) the use of oral contraceptives among women aged 40 and over who are heavy smokers is substantially more hazardous than no fertility control; (2) the use of oral contraceptives among heavy smokers aged 30-39 may be slightly more hazardous than no fertility control, and is substantially more hazardous than any other method of birth control; and (3) the use of contraceptives among heavy smokers aged 15-29 may be more hazardous than any other method of birth control, but somewhat less hazardous than no fertility control.

A recent study by Sloane et al.²⁵ of women who suffered a myocardial infarction before age 50 found a dose-response relationship involving smoking. Demonstrating that smoking is a risk factor for myocardial infarction in healthy women, these investigators estimated that women who smoke 35 or more cigarettes a day have a rate of myocardial infarction 20 times higher than those who never smoked.

Jick et al.²⁶ have also shown that apparently healthy women aged 39 to 45 who were taking noncontraceptive estrogens have an estimated relative risk of 7.5 for nonfatal myocardial infarction compared to nonusers of estrogens. All but one of the nonfatal myocardial infarction patients were cigarette smokers, and about half (16/34) of the controls were smokers. It then appears that women aged 39-45 may have a substantial risk when they both smoke and take estrogens.

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