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**In Reply.**—In addition to discovering a regrettable mistake in citation, Drs Fava and Lamon-Fava speculate that the elevation of WBC counts is an epiphenomenon and that the true risk factors are stress or the type A behavior pattern. In contrast, we postulate that high WBC counts are an independent risk factor for ischemic disease. In support of this hypothesis, our article cites a large number of epidemiologic and clinical trials. These seem to suggest that even when other conventional risk factors are taken into account, the WBC count emerges as an independent predictive variable. In the second part of the article, we summarize the mechanisms by which WBCs could harm the circulation. Essentially, leukocytes may block the microcirculation because of their rheological behavior. Once trapped there, they can cause damage by releasing free radicals and enzymes. Thus, our hypothesis is supported by epidemiologic, clinical, rheological, and biochemical research. While Drs Fava and Lamon-Fava think that high WBC counts are an epiphenomenon of stress or the type A behavior pattern, we have evidence that they represent one mechanism by which these and other risk factors affect the circulation and lead to the increase in cardiovascular morbidity.

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**Toxic Shock Syndrome**

**To the Editor.**—In relating influenza to toxic shock syndrome (TSS), Sperber and Francis' further diminish the prospect that barrier contraception will be a major determinant of TSS in this country. Even as multiple causes of TSS are identified, the number of recorded TSS hospital admissions is currently estimated to be less than 1500 nationally.<sup>2</sup>

Already, prior surveillance efforts have shown that 60% to 80% of all cases of TSS are associated with menstruation and the use of tampons. The remaining cases of nonmenstrual toxic

Total Additional Number of Cases (and Additional Number of Cases per Million Users) per Year of NMTSS\* due to Sponge Use, by Prevalence of Sponge Use and Relative Risk Based on 40 Million Women at Risk

Percent of Women Using Sponge	Relative Risk				
	2.5	5	10	20	40
1	2†	6†	16†	32†	56 (1.4)
2	6†	14†	28†	54 (1.4)	88 (2.2)
4	12†	28†	52 (1.3)	88 (2.2)	120 (3.0)
8	22†	48 (1.2)	84 (2.1)	120 (3.0)	152 (3.8)
16	40 (1.0)	78 (2.0)	118 (3.0)	150 (3.8)	168 (4.2)

\*NMTSS indicates nonmenstrual toxic shock syndrome.  
 †Additional number of cases per million users <1.

shock syndrome (NMTSS) occur post partum, in women with surgical wounds, or in women who use barrier contraceptives.<sup>3,4</sup> It now appears that a portion of these cases may be due to postinfluenzal staphylococcal superinfection.

A recent National Institutes of Health Center for Population Research workshop on TSS and contraception reviewed the National Institutes of Health-supported national case-finding effort by the Centers for Disease Control to provide estimates of the annual number of NMTSS cases. Despite the fact that only about a dozen sponge-related cases have been reported, most recent TSS publicity has focused on contraception generally and the contraceptive sponge specifically.<sup>5,6</sup> This aggressive surveillance effort will provide the requisite cases for a retrospective study of the relative risk of TSS in barrier-contraceptive users. Provisional TSS relative risk estimates for sponge users range anywhere from 2 to 40, and, if verified, would suggest that NMTSS is two to 40 times more likely to occur in sponge users than nonusers. But since the rate of NMTSS is thought to be only five cases per million US women per year, even a large relative risk may not do away with the sense that TSS arises only rarely among sponge users.

An interesting finding of the panels was that regardless of how high the relative risk might be, TSS in sponge users may remain a low priority among public health authorities because of the underlying rarity of NMTSS. This is demonstrated by the low attributable risk, expressed as the number of excess TSS cases per million (Table), for several relative risks and levels of sponge use. Thus, even if the relative risk were 20 and if 8% of women of reproductive age were using the sponge, only 120 new cases (three per million) would occur in this country because women use the sponge.

What do these figures indicate to clinicians considering the sponge for a young patient who does not require a daily contraceptive? The personal risk

of NMTSS developing in a sponge user, based on both the effect of the sponge and the underlying rate of NMTSS, ranges from one in 80 000 for a relative risk of 2.5 to one in 5000 for a relative risk of 40. Simply stated, even if sponge use is highly associated with NMTSS, users will have considerably less than a 0.1% chance of developing NMTSS. The health consequences of not using barrier contraceptives at all, expressed in terms of pregnancy, abortion, maternal mortality, and pelvic inflammatory disease, appear to be more of a concern presently in young women than the possible risk of TSS.<sup>7</sup>

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**Dietary Supplements**

**To the Editor.**—The recent report entitled "Vitamin Preparations as Dietary Supplements and as Therapeutic Agents" is described as an update of the one published 28 years ago.<sup>2</sup> This new version is an important document and undoubtedly will be widely read. We offer our comments with the hope that the report will be updated in the near future. Perhaps future versions could be published first in a preliminary form

with an invitation for comments from concerned health professionals at large.

In the area of vitamins as dietary supplements, the point is made several times that "healthy adult men and . . . women consuming a usual, varied diet do not need vitamin supplements." This statement, which appears—unqualified—in the report's abstract, is not sufficient dietary advice. A varied diet is adequate only when "care is exercised in food selection."<sup>1</sup> The reason why we have registered dietitians, nutrition educators, school food-service programs, and other related professions and nutrition programs is to provide such care. That the "usual, varied" diets of many population subgroups within the United States do not always meet acceptable standards is supported by dietary surveys.<sup>2</sup> Vitamins A, B<sub>6</sub>, and C and the minerals calcium, magnesium, and iron pose the greatest dietary problems. Teenagers and the elderly are examples of subgroups particularly susceptible to nutritionally inadequate diets. Furthermore, the use of weight-loss diets, which an estimated 20% of Americans follow,<sup>3</sup> often makes it difficult to achieve recommended nutrient intakes.

We wonder if, in the desire to protect against the recognized hazards of irresponsible vitamin usage, we are not overlooking the potential value of vitamin-mineral supplements. Clearly, the emphasis should be placed on properly selected diets as the primary basis for good nutrition. Yet realistically, despite the availability of food-selection guidelines, eg, the *Daily Food Guide*, and despite the efforts of nutrition educators, proper food selection is not always possible or likely for many population groups. Perhaps the advice the Council on Scientific Affairs and other public health policymakers should be offering is that for the many people who cannot or do not select proper, well-balanced diets, a modest multivitamin-mineral supplement can be a safe, nutritious, and inexpensive part of a total health plan.

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5. *Health—United States*, publication (PHS) 80-1232. US Dept of Health, Education, and Welfare, 1979.

*To the Editor.*—In the April 10, 1987, issue of *JAMA*, there was an article entitled "Vitamin Preparations as Dietary Supplements and as Therapeutic Agents" by the Council on Scientific Affairs of the American Medical Association.<sup>1</sup> There is a statement in this article to the effect that there is no evidence that taking supplemental carotene will prevent cancer in man. This statement is incorrect; indeed, there are other benefits from a high intake of beta carotene.

First, there is epidemiologic evidence that low levels of beta carotene increase the risk of several types of cancer. The intake of dietary beta carotene was inversely related to the development of cancer of the lung in the Western Electric study<sup>2</sup> and several other studies.<sup>3,4</sup> Beta carotene may be protective against oral, gastrointestinal, and cervical cancer as well.

Currently, several studies in progress are testing the effects of supplemental beta carotene on cancer prevention. Most current data suggest that high doses of carotene in the diet will be beneficial in cancer prevention.

Furthermore, carotene is nontoxic and may have other benefits. Levels of beta carotene in serum and brain tissue directly correlate with mammalian life span.<sup>5</sup> Animal studies have not shown prolongation of life span with carotene supplementation. This has not been studied in humans.

Another possible benefit of beta carotene and other carotenoids is in the retardation of atherosclerosis. It has been shown that crocetin, a carotene derivative present in the spice saffron, can lower cholesterol levels and enhance the diffusion of oxygen into tissues.<sup>6</sup> Whether beta carotene and other carotenoids do this needs further study. Vegetarians have a lower incidence of atherosclerosis, and this may be one of the reasons.

At the present time, the advice to avoid beta carotene or other carotenoid supplements is not based on adequate scientific data. A diet high in beta carotene is advisable because of the benefits of carotenoids and because those foods high in beta carotene are high in other nutrients as well. Those people who are unable or unwilling to consume a diet high in beta carotene and other carotenoids might benefit from supplementing their diet with carotene pills.

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*In Reply.*—I appreciate Mr Jensen's and Dr Briggs' comments on the use of dietary vitamin supplements. The COUNCIL REPORT does state that (1) "if the total energy intake falls below 1200 kcal (5040 kJ), it becomes increasingly difficult to obtain all of the protective nutrients in adequate amounts, and supplements may be needed"; (2) "certain weight-reduction diets may lead to inadequate vitamin intakes . . . and hence a modest supplement may be recommended"; and (3) "socioeconomic conditions and reduced physical activity among the aged may lead to a curtailment in total food intake. Under such restriction, the use of a vitamin preparation in the prevention of deficiency may be indicated."

A recent national dietary survey does show inadequate intakes of vitamins A, B<sub>6</sub>, and C compared with the recommended dietary allowances (RDA)<sup>1</sup> for some segments of the population. However, this finding does not mean these groups are at high risk of developing vitamin deficiencies. As a former chairman of an RDA committee noted<sup>2</sup>:

The amounts of nutrients required by most people will be below the RDA and half the population should require less than half the RDA. Obviously a dietary standard of this type cannot be used to determine if the intakes of people who are consuming less than the RDA are inadequate.

Because of the nature of the RDA and of dietary surveys, it is not possible to assess nutritional status by comparing estimates of nutrient intakes with the RDA. The only way that vitamin status can be determined reliably is from clinical observations and measurements of blood or tissue concentrations or the rates of metabolic reactions for which the vitamins are needed. When this is done, a very small proportion of the population surveyed is found to have low, but seldom deficient, values.

Concerning Dr Kesden's comments on the benefits of beta carotene supplements for cancer prevention, the COUNCIL REPORT states as follows:

Several vitamins have been heralded as anti-cancer agents, supposedly preventing the development of many types of malignancies. Although epidemiological studies have suggested that certain types of cancer are associated with a low intake of yellow and green vegetables and low plasma vitamin A levels, there is no evidence that taking large doses of vitamin A or carotene will prevent cancer in man.

The National Cancer Institute has

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