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Formal Discussion of "Breast Cancer Incidence and Nutritional Status with Particular Reference to Body Weight and Height"[1]

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Dr. de Waard and his colleagues in Utrecht were among the first to bring together epidemiological and endocrinological expertise in the investigation of cancer of the breast. From its beginning their work has included consideration of the relationship of the disease to body form and nutrition. Anything they had told us would therefore have been of interest and relevance to this conference. It is, however, not sufficient for Dr. de Waard to be of historical interest. He has, once again, put new data before us that require us to look at our old concepts from a new perspective, and just when the old concepts seemed to be falling neatly into place.

In the 1974 analysis of their prospective study, de Waard and Halewijn (1) pointed once again to high body weight as a risk factor for breast cancer in postmenopausal women. While such a relationship had been demonstrated previously in several case-control studies, there are also several studies in which it had not been found. In addition, even in those studies in which the association was found, it seemed generally less strong than in the Dutch material. It seemed reasonable to take into consideration the fact that in most previous studies the women against whom the cases were compared were patients with other diseases, a group in which overweight women might well be overrepresented, therefore dampening any real difference existing between breast cancer cases and normal women of comparable age. Belief that the risk associated with overweight had been underestimated in the past was strengthened by the fact that knowledge was being developed of a mechanism that might account for the relationship. Most of the components of this knowledge have been referred to by Dr. de Waard in his present paper; these include the role of estrogens in breast cancer and specifically their role around the time of menopause as evidenced in the protective effect of surgical castration and the high risk associated with late menopause, de Waard's own work on the persistence of estrogenic cervical smears in overweight women, the demonstration of the production of estrone in adipose tissue of postmenopausal women, and the probable role of this process in the etiology of endometrial cancer.

However, de Waard's recent analysis suggested that the whole story did not lie in obesity or overweight. Indeed, although independent effects were found for both height and weight, the single best predictor of risk was total body mass (a combination of height and weight). The Friesland data, presented today, go further, suggesting that weight has no independent effect if there is an adjustment for its correlation with height. If this is true, the apple cart is well and truly overturned for, while body weight can be influenced by nutrition at any age (including the menopausal and postmenopausal ages in which the influence of adiposity on estrogen production has been demonstrated), maximum height has of course been determined long before that. While a relationship primarily with height does not rule out a role for nutritional factors, it suggests that such factors must operate in infancy and childhood rather than in adult life.

I must dissent from Dr. de Waard's statement that "A considerable proportion of the difference in incidence between the Netherlands and Japan can be explained by differences in body mass." While the data are consistent with such an explanation, it seems to me that the evidence is insufficient. While the difference in mean body mass between the women of the 2 countries is in the right direction, to give credibility to the explanation it would be necessary to show that Dutch and Japanese women of similar body mass have breast cancer rates substantially more similar than do Dutch and Japanese women overall. Such data would not be easy to come by. In any event, it seems unlikely to me that breast cancer is caused by a large body mass. It seems more likely that large body mass and high breast cancer rates are independent consequences of the same nutritional pattern, perhaps the same pattern that is responsible for the decline in age at menarche in Western countries between 1850 and 1950 and the greater height and earlier menarche of Japanese migrants to the United States.

One line of investigation is suggested by this viewpoint. Naturally we would like to know not only whether nutrition is related to breast cancer risk but also what specific nutritional patterns or factors are responsible for high risk. Meat protein, dairy products, and cholesterol all clearly come under suspicion; but to date we have only suspicions, and not very specific ones at that. It is difficult to study the role of nutrition on breast cancer risk directly; the long latent period and relative infrequency of the disease are obvious difficulties. If the nutritional factors leading to early maturation are the same as those influencing breast cancer risk, perhaps we could learn something of relevance

[1] This discussion of the paper by Fritz de Waard (Cancer Res., *35*: 3351-3356, 1975) was presented at the Conference on Nutrition in the Causation of Cancer, May 19 to 22, 1975, Key Biscayne, Fla.

by studying the specific nutritional determinants of age at menarche. Menarche is something that we can expect to occur sooner or later in almost all of any cohort of children and, at least relative to breast cancer, the observation of interest occurs sooner rather than later.

References

1. de Waard, F., and Halewijn, E. A. B. A Prospective Study in General Practice on Breast-Cancer Risk in Postmenopausal Women. Intern. J. Cancer *14:* 153–160, 1974.