CORRESPONDENCE

Breast Density and Cancer

The decrease in the radio-opaque density of mammograms by 6.1% in healthy, lean (body mass index <23) women, 30–65 years of age, who were fed a low-fat diet for 2 years (1) suggests that environmental factors modulate mammary parenchymal metabolism. However, it is unclear whether these findings are applicable to the individual woman in the detection of breast cancer.

In the Dom study of 23,311 postmenopausal Dutch women, which investigated the radiologic aspects of breast structure, de Waard (2) concluded that, from puberty on, breast abnormalities increase unless counteracted by pregnancy and that dysplasia in women with a pregnancy after 35 years of age involved luteal insufficiency. Furthermore, de Waard et al. (3) reported that a family history of breast cancer increased the positivity rate of mammary screening (relative risk [RR] = 2.2 positive/negative).

While the accuracy of screening varies among studies, it should be noted that 1) only 15% of the volume of breasts of premenopausal women consists of epidermal cells, 2) mammary dysplasia is not associated with estrogen receptor concentration (4), and 3) breast cancer develops in a large number of women who do not have radiologic abnormalities (5).

While mammary dysplasia is modified by fat intake (6), exercise (7), and diet (1), it is unclear how changes during pregnancy reverse adverse changes in mammary parenchyma.

Because the expression of estrogen receptors and mammary mitotic cycling are established at puberty (8,9), development of growth patterns of mammary tissue prior to puberty may “set” the future risk. Since the risk of breast cancer is associated with birth weight (10) and adult height (11), it is significant that 1) a low birth weight (<3000 g) increases the risk of preeclampsia later in life (12), 2) perinatal characteristics are associated with high-risk mammographic patterns (13), and 3) daughters born after an eclampsia/preeclampsia pregnancy have a lower risk of breast cancer (14), supporting the importance of fetal growth patterns. If cancer develops as a failure of the host organs to exercise growth control, mammary dysplasia should be associated with growth factor production (15).

While increasing density in breast parenchyma from none to more than 73% of the area in patients increases the RR by 6.05 (95% confidence interval = 2.82–12.97) (5), a large proportion of women with screening-detected breast cancers may experience no benefit from treatment because their disease may never progress or may even regress if left undetected (16,17).

With the more rapid tumor growth in women under 35 years with stage II node-positive disease (approximately 11% of breast cancer cases) (18), it would be of interest to determine the increase in mammary dysplasia and growth factor profile in such selected patients. Furthermore, in premenopausal, healthy women requesting a reductive mastectomy, measurement of ovarian and breast carcinoma during the menstrual cycle. Breast Cancer Res Treat 1987; 10:273–8.


Devitt JE. Breast cancer: have we missed the forest because of the tree? Lancet 1994;344:734–5.


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References


Note
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Re: Risk Factors for Lung Cancer and for Intervention Effects in CARET, the Beta-Carotene and Retinol Efficacy Trial

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study (1) and the Beta-Carotene and Retinol Efficacy Trial (CARET) (2) showed an excess of lung cancer in supplemented individuals at high risk of developing this complication (e.g., smokers). From a reanalysis of their data, Omenn et al. (2) concluded that these subjects should be discouraged from taking β-carotene; however, in their recommendation, they did not address the issue of alcohol consumption. Similarly, in a comment on their ATBC Study, Rautalahl et al. (3) mention six possible explanations for the complication, but they do not include alcohol as a possible contributory factor. It should be pointed out, however, that alcohol has been reported to increase β-carotene levels in men (4), women (5), nonhuman primates (6), and rats (7); this increase in β-carotene levels may be of relevance because of a possible dose effect for the above noted complication. Furthermore, in the nonhuman primates, there was associated hepatotoxicity, including striking ultrastructural lesions and an increase in circulating transaminases (7). Since heavy smokers are commonly also drinkers, we questioned (8) whether the complication could have been exacerbated by ethanol and, specifically, whether the excess of lung cancer might have occurred predominantly, or even exclusively, in those smokers who were also drinkers. Subsequently, this hypothesis was verified in a reanalysis of the ATBC Study (9); this reanalysis revealed the complication to be associated with alcohol drinking. Actually, the data of Omenn et al. (2) also showed a statistically significant difference between the nondrinkers and persons consuming substantial amounts of alcohol, albeit with a less consistent dose–response effect. Furthermore, in both of these clinical and experimental studies, a similar preparation of β-carotene was apparently used, i.e., β-carotene incorporated into beadlets. These beadlets were found to augment the hepatotoxic interactions between ethanol and β-carotene (7,10), with exacerbation of the ultrastructural changes in the mitochondria, the associated release of mitochondrial enzymes into the circulation, and the proliferation of the smooth endoplasmic reticulum. The beadlets contain various additives, but the compound responsible for the toxicity has not yet been identified.

Another postulated mechanism for toxicity is the oxidative attack of β-carotene by heavy smoking (11). It is interesting that ethanol is also known to cause significant oxidative stress (12), incriminated in many adverse effects, including promotion of carcinogenesis. Furthermore, in CARET, retinol was administered at the same time (1,9), and it may also have contributed to the toxicity, since studies in rats (13) and humans (14) revealed that the combination of ethanol and vitamin A results in hepatotoxicity not seen with the same dosage of either compound alone.

Contrasting with the findings of the ATBC Studies (1) and CARET (2), a study by Hennekken et al. (15) found no comparable complications. However, Hennielsen et al. used a lower dose and a different β-carotene preparation. Moreover, no alcohol consumption data were given, but there was a much lower incidence of smokers and, hence, presumably of drinkers. Obviously, further analysis is needed, but it is now appropriate, whenever supplementation of β-carotene is being considered, to warn of the possible hazards from concomitant drinking of substantial amounts of alcohol.

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References