

cancer risk. Further work along the lines proposed by Hsieh and colleagues [1] should be undertaken.

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be conclusively stated whether the data of Kalache and colleagues [2] or our data are out of line. However, cessation of protection against breast cancer by a pregnancy that occurs after a certain age (perhaps around 35 years) has been given an adequate explanation even in the earlier paper by MacMahon and associates [3]. Experimental evidence has also shown that the mammary gland is particularly vulnerable to carcinogenic stimuli between puberty and the first pregnancy [4]. Thus, in comparison to subsequent pregnancies, the first birth in a multiparous woman represents a more significant biological event as it determines the duration of this period of increased susceptibility.

Many of the issues raised by Maguire and Kalache have been addressed in a recent paper of ours [5], and we cannot but agree with them that there are complex statistical issues and biological considerations that defy simple answers. A conceptual concern that we have with the notion that the last pregnancy has an overwhelming effect is that, contrary to first pregnancy which would always be the first, every pregnancy is the last until a new one occurs. In other words, no single pregnancy can be identified as the last in a fertile woman until much later. Hence, while unique biological effects on the breast are likely to occur during a first pregnancy, they are unlikely to occur during a last pregnancy. This duality requires that the effect of every pregnancy with respect to breast cancer risk should interact with time since that pregnancy, an issue that has only recently received attention [5-7].

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WE AGREE with Maguire and Kalache that age at any pregnancy including the first and the last should be carefully studied because nature may be hiding an important clue about the origin of breast cancer in the complex way that successive pregnancies affect human physiology. At this stage, given a recent large population-based study from Sweden that has reported almost exact findings as ours [1], it cannot