



## Letters

# Lifestyle, progesterone, and risk of breast cancer

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## Causal association between progesterone concentrations and breast cancer has not been shown

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EDITOR—Increasing progesterone concentrations are not associated with increasing incidence of breast cancer, despite the neat correlation diagram by Jasienska and Thune, and they are wrong to infer causality.<sup>1</sup> Some points in their diagram are based on 20 or fewer samples, from which they draw conclusions about the whole country, and many of the progesterone values quoted do not coincide with their cited reference.<sup>2</sup> However, the main criticism is that they have ignored other scientific data that do not reinforce their hypothesis.

In some places high progesterone concentrations have been found in conjunction with a low incidence of breast cancer—for example, Shanghai, where the progesterone concentrations of small numbers of Chinese women were similar or even higher than women in Chicago or Harvard.<sup>3–5</sup> This is despite the fact that the incidence of breast cancer is 19.1 per 100 000 women with adjustment for age in Shanghai compared with about threefold in the United States.<sup>w1</sup> Determinations were not necessarily carried out by the same methods, which probably leads to some technical differences. Nevertheless, the values would not fit even close to the correlation by Jasienska and Thune. More importantly, if there were a causal association between high progesterone concentrations and cancer, women with breast cancer should have higher progesterone concentrations than normal controls, but they do not.<sup>w2 w3</sup>

Far from being a cause of breast cancer, progesterone (in the form of norethisterone acetate, a synthetic progesterone used because of oral availability) was until recently a treatment for disseminated breast cancer.<sup>w4</sup>

## Footnotes

-  References w1-4 are available on bmj.com.

## References

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## Authors' reply

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EDITOR—We documented a strong, positive relation between risk of breast cancer and mean progesterone concentrations in premenopausal women from five populations. We did not postulate a direct causal relation between progesterone concentration and risk of breast cancer, as asserted by Wiseman. However, data supporting a relation between “oestrogen plus progestagens” and breast cancer risk do exist, although the role of progesterone in the aetiology of breast cancer is more controversial than that of oestradiol.<sup>1</sup>

Firstly, epithelial cells of the breast have the highest mitotic activity in the luteal phase of the menstrual cycle, when progesterone production peaks.<sup>2</sup>

Secondly, combined oestrogen plus progestogen replacement therapy increases risk of breast cancer to a greater extent than does replacement of oestrogens alone.<sup>3</sup>

Thirdly, reduction in breast cancer risk among obese premenopausal women is most likely a result of frequent anovulatory cycles and impaired progesterone production. Thus, a causal link between progesterone and the risk of breast cancer is biologically plausible. In our analyses, however, progesterone concentrations were used only as reliable indicators of ovarian activity, without suggesting the dominant role of progesterone in the aetiology of cancer.

An evaluation of the relation between circulating concentrations of progesterone and oestradiol and risk