

might include an arm for treatment of asymptomatic patients who are concerned about possible long-term risks.

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#### [Two of the authors respond:]

The causes of hyperprolactinemia fall into 3 main categories: physiologic, pharmacologic and pathologic. Pathologic hyperprolactinemia is due to hypothalamo-pituitary lesions and secondary causes such as hypothyroidism or renal or adrenal insufficiency. Clearly, any secondary causes must be ruled out before imaging of the pituitary is considered. We proposed MRI of the pituitary as the next logical step after repeat determination of prolactin levels and exclusion of physiologic, pharmacologic and secondary causes of hyperprolactinemia, regardless of the extent of elevation of prolactin.<sup>1</sup> Any specific cutoff value below which MRI would not be performed (such as 100 µg/L) might miss some nonlactotrophic hypothalamic or pituitary lesions that would present with slight to moderate hyperprolactinemia. The latter condi-

tions require different management approaches from those for microprolactinomas.

Suckling in breast-feeding women is known to stimulate prolactin release. Moreover, breast stimulation in some non-breast-feeding normal women and rarely in some men may also cause an increase in serum prolactin levels.<sup>2,3</sup> Therefore, measurement of serum prolactin level should be avoided in the hours after breast stimulation or examination and ideally would be performed on another day.

We agree with Malvinder Parmar that metoclopramide and domperidone are potentially potent dopamine antagonists that can and frequently do result in significant hyperprolactinemia. Interruption or substitution of such agents, as indicated in our review,<sup>1</sup> should clarify their role in raising prolactin levels.

Christopher Kovacs raises a controversial issue that we did not address because of space limitations: the possible relation between increased prolactin levels and nonreproductive functions, including putative mitogenic and immune modulatory properties. Prolactin is a member of a family of growth factors that includes growth hormone, placental lactogen and placental growth hormone. These polypeptides can exert mitogenic effects in tissues expressing dedicated receptors. As indicated by experimental and animal models, mammary tissue expresses prolactin receptors and is positively influenced by prolactin.<sup>4</sup> However, prolactin is not a sufficient stimulus to cause malignant transformation. Furthermore, the data regarding the role of prolactin in human cancer have been conflicting. Some studies have suggested that higher circulating levels of prolactin are associated with an increased risk of radiographically dense breast tissue.<sup>5</sup> Others have noted that postsurgical hyperprolactinemia is associated with a significantly lower recurrence rate and longer disease-free and overall survival in node-negative breast cancer

patients.<sup>6</sup> In addition, in patients with chronically elevated prolactin levels (such as those with prolactinomas) no increase in neoplasia in general or breast cancer in particular has been noted.<sup>7</sup> We do not feel that the weight of evidence regarding the relation between excess prolactin and the risk of neoplasia is sufficient to form the sole basis for recommending inhibition of prolactin for postmenopausal women.

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