

## Mortality Attributable to Smoking in China

**TO THE EDITOR:** Gu and colleagues (Jan. 8 issue)<sup>1</sup> report that in 2005, an estimated 673,000 deaths in China were attributable to smoking. The study is of timely importance. But it did not include some important variables in the analysis. First, the effects of family income were not considered. In China, social deprivation is a major risk factor for ill health,<sup>2</sup> and data from a survey about household income and cigarette consumption<sup>3</sup> and from a study involving low-income employees<sup>4</sup> showed that smoking was associated with relatively high income. Without this adjustment, the association of mortality with smoking may have been attenuated. Second, the analysis did not include passive smoking. Nonsmokers may have been exposed to passive smoking, leading to the higher mortality in the reference group. Third, the number of deaths in rural China, where 70% of the population lives, may have been underestimated. It is interesting that the authors observed a lower relative risk of death associated with smoking in rural areas than in urban areas. In rural areas, persons who never smoked would be poorer and consume less nutritious foods than their counterparts who smoked and thus would have a higher mortality, reducing the association.

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**THE AUTHORS REPLY:** In response to Chen: as we discussed in our article, one limitation of our study

is that we were unable to adjust for some important potential confounding factors. Data on family income were not collected in our study. However, we collected data on and adjusted for levels of education and work-related physical activity, two important indexes of socioeconomic status that were highly related to family income.<sup>1</sup> Furthermore, relative risk, population attributable risk, and mortality were calculated separately for rural and urban residents; this should have eliminated the confounding effects of rural-urban differences in family income. We adjusted for the body-mass index, a measure of malnutrition in our study. In addition, only deaths from cardiovascular disease, cancer, and chronic respiratory disease were associated with cigarette smoking and included in the estimation of smoking-related deaths. There is no evidence that these diseases are caused by malnutrition. We agree that passive smoking has been associated with death from coronary heart disease and lung cancer,<sup>2,3</sup> and we noted that our study might have underestimated the deaths from these diseases that were attributable to smoking.

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## Endometriosis

**TO THE EDITOR:** In the review article on endometriosis, Bulun (Jan. 15 issue)<sup>1</sup> states that the presence of aromatase in endometriotic lesions appears to play an important role in the production of es-

tradiol, and it is considered to be a key factor for endometrial proliferation.

However, Delvoux et al. recently reported the absence of aromatase activity in endometriotic le-

sions,<sup>2</sup> and we also did not detect aromatase protein in the glandular and stromal compartments of ectopic endometrial tissue. We recently found that what was believed to be aromatase protein was mainly endogenous biotin labeling or iron deposits.<sup>3</sup> Using three different protocols, we found only barely detectable amounts of aromatase messenger RNA (mRNA). Among 21 peritoneal endometriotic lesions, 16 were aromatase-negative and 5 were near the limit of detection. Our results suggest that aromatase produced within endometriotic lesions might not be as important in endometriosis as postulated in Bulun's review.

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**THE AUTHOR REPLIES:** Biologically relevant levels of aromatase and its product estradiol in vertebrate tissues are lower by a factor of 100 to 100,000 than the levels of most other steroidogenic proteins and their products. Thus, the accurate evaluation of aromatase expression and enzyme levels in extraglandular cells and tissues is a complex task and requires a laboratory with substantial expertise and experience in making such

measurements. Since the mid-1990s, several laboratories in various parts of the world have consistently reported aromatase mRNA and enzyme activity in endometriotic tissues and cells.<sup>1-4</sup> My colleagues and I have reported the presence of aromatase in endometriosis, and we have described the signaling pathway responsible for coordinated induction of aromatase and other steroidogenic genes required for the production of estradiol from cholesterol in endometriotic tissue.<sup>1</sup> The letter by Colette and Donnez contradicts their recently published article in which they reported that aromatase mRNA was detected in all but 2 of the approximately 60 samples of ovarian, peritoneal, and deep endometriotic tissues they studied.<sup>5</sup>

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## Vitamin D Deficiency in Critically Ill Patients

**TO THE EDITOR:** Vitamin D deficiency is rarely considered or treated in critically ill patients. However, we recently reported three cases of life-threatening hypocalcemia secondary to vitamin D deficiency,<sup>1,2</sup> highlighting potential acute complications. The prevalence of vitamin D deficiency and its significance in the intensive care unit (ICU) are unknown.

We performed a prospective study of the vitamin D status in ICU patients (Table 1) referred to the Department of Endocrinology, St. Vincent's

Hospital, Sydney, between January 2007 and January 2008. Demographic, physiological, and biochemical variables were recorded, including the Simplified Acute Physiology Score II (SAPS II) (on a scale of 0 to 163, with higher scores indicating more severe organ dysfunction).<sup>3</sup>

Among approximately 1100 ICU patients per year, the mean ( $\pm$ SD) serum level of 25-hydroxyvitamin D in 42 referred patients was  $41 \pm 22$  nmol per liter ( $16 \pm 9$  ng per milliliter), with a high prevalence of hypovitaminosis D (Table 1). Moreover,