Letters to the Editor

Maternal pregnancy hormone profiles in areas with a different incidence of breast cancer

Sir

In the January 1999 issue of the Journal, Lipworth et al (1999) reported that during the second and third trimester of pregnancy, Chinese women in Shanghai, China had significantly higher levels of several gestational hormones (oestrogens, prolactin, growth hormone) than Caucasian women in Boston, USA (Lipworth et al, 1999). The study indicates that women living in low-risk areas for breast cancer may have hormonal profiles during pregnancy that would stimulate the maturation of mammary cells to a fuller extent, as compared to women in high-risk areas.

A few aspects of the study make difficult its interpretation. Chinese women in the study were on average 6 years younger than American women (mean 25.1 vs 31.0 respectively). Although the literature on the relationships between maternal age, parity and pregnancy hormones is limited, existing evidence suggests that maternal age is an important predictor of pregnancy oestrogen levels. It has been shown that during the third trimester of pregnancy, total oestrogen and oestradiol levels are highest among women aged 20–24, intermediate among women older than 25, and lowest among women below age 20 (Panagiotopoulou et al, 1990). Lipworth et al stated that their results remained essentially unchanged after controlling for maternal age but these data were not reported. It would have been more informative if the results had been presented stratified by age.

Parity is another factor that could affect hormone levels during pregnancy. There is evidence that maternal levels of free oestradiol are higher in the first, as compared to the second, pregnancy (Bernstein et al, 1986). Therefore, reporting the results stratified by parity would have been more helpful, especially considering that 36.8% of American women in the study had a previous full-term pregnancy, as compared to only 3% of Chinese women.

If the authors could provide convincing evidence that the ample differences in maternal age and parity between the two populations have been taken into account appropriately, the study by

Lipworth et al raise the interesting possibility that women in an area with a low incidence of breast cancer have a distinct pregnancy hormone profile characterized by higher levels of oestrogens and other mammatrophic hormones. Such hormone profile could advance the development and full maturation of breast cells making them less susceptible to carcinogenesis, as postulated by Russo et al (1982; 1994). In this connection, it would have been of particular interest to have measured pregnancy hormones promoting breast differentiation, such as human chorionic gonadotropin (Russo et al, 1990) and relaxin (Bani et al, 1986).

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Maternal pregnancy hormone profiles in areas with a different incidence of breast cancer – reply

Sir

We thank Dr Akhmedkhanov and colleagues for their useful ideas about human chorionic gonadotropin and relaxin and their thoughtful and sensible biologic considerations. In particular, the idea that high levels of hormones during pregnancy might stimulate early breast cell maturation is one of the explanations we are considering for the intrauterine effects on cancer occurrence in the offspring. With respect to the issue of confounding by maternal age and parity, because the findings of higher hormone levels among Chinese women compared with Caucasian women were

unexpected for us, we evaluated in detail every possible confounder, including maternal age and parity. When the data were stratified by maternal age (Table 1) or parity (Table 2), Chinese women consistently displayed higher mean levels of the measured hormones at both visits, with the possible exception of progesterone during the second visit, as indicated in our earlier report. (Since confounding does not depend on statistical significance, and in the interest of saving space, we have not presented the confidence interval around the mean.) Thus, we can assure Dr Akhmedkhanov and colleagues, and Journal readers, that there

Table 1 Serum levels of studied hormones at 16 and 27 completed weeks of gestation among pregnant women in Boston, USA ($n = 304$) and in Shanghai, China ($n = 334$), stratified by maternal age

		Age ≤ 20		Age 20–24		Age 25–29		Age 30+	
Hormone		Sample 1 Mean	Sample 2 Mean	Sample 1 Mean	Sample 2 Mean	Sample 1 Mean	Sample 2 Mean	Sample 1 Mean	Sample 2 Mean
Estradiol (E2)	Boston	16.7	47.7	14.7	38.1	15.8	39.9	13.4	38.8
nmol l ⁻¹	Shanghai	17.0	–	20.7	49.5	20.3	46.9	21.9	44.8
Estriol (E3)	Boston	3.01	14.3	3.7	14.6	4.1	13.5	3.7	14.1
nmol l ⁻¹	Shanghai	5.0	–	6.1	22.6	6.4	20.8	6.7	21.2
Prolactin	Boston	25.9	80.1	39.2	65.2	47.2	89.6	44.0	92.4
$\mu\text{g l}^{-1}$	Shanghai	30.0	–	58.5	111.5	67.0	123.5	71.7	119.7
Progesterone	Boston	88.6	167.0	104.9	248.3	136.3	263.5	132.6	263.9
nmol l ⁻¹	Shanghai	129.0	–	143.1	249.5	141.5	237.2	148.4	262.5
Growth hormone	Boston	13.7	1.3	1.4	0.6	3.3	0.9	2.9	0.9
mU l ⁻¹	Shanghai	5.9	–	4.2	1.9	3.3	1.5	2.8	1.7
Albumin	Boston	37.4	32.5	41.6	37.4	40.5	37.0	40.1	36.3
g l ⁻¹	Shanghai	44.7	–	43.6	40.0	42.8	39.1	42.3	38.9
SHBG ^a	Boston	417.3	344.2	312.6	417.1	381.1	431.8	356.1	423.7
nmol l ⁻¹	Shanghai	447.1	–	437.7	496.4	416.0	446.9	428.4	475.0

^aSex hormone-binding globulin.**Table 2** Serum levels of studied hormones at 16 and 27 completed weeks of gestation among pregnant women in Boston, USA ($n = 304$) and in Shanghai, China ($n = 334$), stratified by maternal parity

		No previous livebirths		One previous livebirth	
Hormone		Sample 1 Mean	Sample 2 Mean	Sample 1 Mean	Sample 2 Mean
Estradiol (E2)	Boston	15.4	42.2	11.8	33.9
nmol l ⁻¹	Shanghai	20.8	48.4	17.6	39.7
Estriol (E3)	Boston	3.9	14.2	3.8	13.7
nmol l ⁻¹	Shanghai	6.3	22.0	4.8	19.3
Prolactin	Boston	50.4	95.9	35.0	83.5
$\mu\text{g l}^{-1}$	Shanghai	63.3	116.4	50.6	103.4
Progesterone	Boston	135.3	269.2	129.2	253.4
nmol l ⁻¹	Shanghai	143.4	248.3	138.2	231.6
Growth hormone	Boston	3.1	1.0	2.8	0.8
mU l ⁻¹	Shanghai	3.7	1.8	1.5	1.2
Albumin	Boston	40.5	36.7	39.7	36.1
g l ⁻¹	Shanghai	43.1	39.6	43.2	38.8
SHBG ^a	Boston	372.1	436.1	345.9	408.1
nmol l ⁻¹	Shanghai	429.7	478.2	414.6	518.6

^aSex hormone-binding globulin.

was no effect when our results were adjusted for maternal age and parity.

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Serum lactate dehydrogenase isoenzyme 1 as a prognostic predictor for metastatic testicular germ cell tumours

Sir

In a recent letter to the editor, Shamash et al (2000) argued that a raised serum lactate dehydrogenase catalytic concentration (S-LD) prior to induction chemotherapy for patients with germ cell tumours predicted a poor outcome. They referred to increasing evidence for a

raised S-LD before first-line chemotherapy being as good if not better than serum human chorionic gonadotropin concentration (S-hCG), as found in, e.g., International Germ Cell Cancer Collaboratory Group (IGCCCG) (von Eyben et al, 1983; Mead and Stenning, 1997). Correspondingly, the fifth edition of the TNM (T =