Letters to the Editor

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

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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

| Hormone  | Sample 1 | Sample 2 | Sample 1 | Sample 2 | Sample 1 | Sample 2 | Sample 1 | Sample 2 |
|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Estradiol (E2) | Boston | 16.7 | 47.7 | 14.7 | 38.1 | 15.8 | 39.9 | 13.4 | 38.8 |
| Shanghai | 17.0 | – | 20.7 | 49.5 | 20.3 | 46.9 | 21.9 | 44.8 |
| Estriol (E3) | Boston | 3.0 | 14.3 | 3.7 | 14.6 | 4.1 | 13.5 | 3.7 | 14.1 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| Shanghai | 447.1 | – | 437.7 | 496.4 | 416.0 | 446.9 | 428.4 | 475.0 |

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

| Hormone  | Sample 1 | Sample 2 | Sample 1 | Sample 2 |
|----------|----------|----------|----------|----------|
| Estradiol (E2) | Boston | 15.4 | 42.2 | 11.8 | 33.9 |
| Shanghai | 20.8 | 48.4 | 3.8 | 13.7 |
| Estriol (E3) | Boston | 3.9 | 14.2 | 3.8 | 13.7 |
| Shanghai | 6.3 | 22.0 | 4.8 | 19.3 |
| Prolactin | Boston | 50.4 | 95.9 | 35.0 | 83.5 |
| Shanghai | 63.3 | 116.4 | 50.6 | 103.4 |
| Progesterone | Boston | 135.3 | 269.2 | 129.2 | 253.4 |
| Shanghai | 143.4 | 248.3 | 138.2 | 231.6 |
| Growth hormone | Boston | 3.1 | 1.0 | 2.8 | 1.2 |
| Shanghai | 3.7 | 1.8 | 1.5 | 1.2 |
| Albumin | Boston | 40.5 | 36.7 | 39.7 | 36.1 |
| Shanghai | 43.1 | 39.6 | 43.2 | 38.8 |
| SHBG a | Boston | 372.1 | 436.1 | 345.9 | 408.1 |
| Shanghai | 429.7 | 478.2 | 414.6 | 516.0 |

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 =

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primary tumour, N = lymph node, M = distant metastases) classification included S-LD, serum alpha fetoprotein concentration, and S-hCG as serum tumour markers for testicular germ cell tumours (TGCT) (Sobin and Wittekind, 1997). The TNM classification is well documented and has been validated repeatedly.

LD consists of five LD isoenzymes. The characteristic S-LD isoenzyme pattern in patients with TGCT and a raised S-LD: they predominantly have a raised S-LD isoenzyme 1 catalytic concentration (S-LD-1) (von Eyben et al, 1983). In contrast, patients with a raised S-LD due predominantly to S-LD isoenzyme 5 catalytic concentration most likely have presence of another disease, not TGCT. The S-LD-1 pattern in patients with TGCT reflects a characteristic chromosomal abnormality in the tumours: a high copy number of the short arms of chromosome 12, 12p, often with an isochromosome of 12p, i(12p) (von Eyben et al, 1992a).

We combined the results of two published series of patients with metastatic TGCT monitored with S-LD in Table 1 (von Eyben et al, 1992b; 2000). Even though the patients were treated at two institutions using different staging systems and treatments, the two series showed consistent findings. 42 of 81 patients (52%) had a raised S-LD-1 and 41 of the 42 also had a raised S-LD. However, eight patients had a discordant pattern with a normal S-LD-1 and a raised S-LD (Figure 1). Separated in three subgroups according to the S-LD-1 level, the 81 patients differed markedly regarding the survival (P < 0.0001, log-rank test, chi square for trend) (Figure 2A). Overall S-LD, S-hCG, and the prognostic classification of the IGCCCG study also predicted the survival (P = 0.00032, 0.02, and 0.0005, respectively, Figure 2B and 2C) whereas S-AFP did not (P = 0.68) (Figure 2D). The subgroup of 39 patients with a normal S-LD-1 had the best survival and this favourable survival was not influenced whether S-LD was normal (31 patients) or raised (eight patients) (P = 0.56) (Figure 2E). Eight patients with an S-LD-1/S-LD fraction > 0.375 had a poorer survival than the 73 with a lower fraction (P = 0.002) (Figure 2F). So S-LD-1 might add prognostic information even for the TGCT survival than the 73 with a lower fraction (52 patients with an S-LD-1/S-LD fraction > 0.375 had a poorer survival than the 73 with a lower fraction (31 patients) or raised (eight patients) (P = 0.56) (Figure 2E). Eight patients with an S-LD-1/S-LD fraction > 0.375 had a poorer survival than the 73 with a lower fraction (P = 0.002) (Figure 2F). Eight patients with an S-LD-1/S-LD fraction > 0.375 had a poorer survival than the 73 with a lower fraction (P = 0.002) (Figure 2F).

We welcome interested oncologists to participate in a multicentre study of this question.

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Figure 1 Venn diagram shows the association between raised levels of S-LD and S-LD-1 for 81 patients with metastatic TGCT. LD1n&LDr denotes 31 patients with a raised S-LD-1 and S-LD and LD1n&LDn denotes 31 patients with a normal S-LD-1 and S-LD

![Figure 1](image)

Table 1 Subgroups of the patients with metastatic TGCT according to S-LD-1 and the serum S category of the serum marker levels in the fifth edition of the TNM classification

| Serum tumour marker | S categories | Number of patients (n %) |
|---------------------|-------------|------------------------|
| S-LD-1              | < 12 U l–1  | 39 (48%)               |
|                     | 112–120 U l–1 | 37 (46%)              |
|                     | > 1120 U l–1 | 5 (6%)                 |
| S-LD                | < 675 U l–1  | 53 (65%)               |
|                     | 675–4500 U l–1 | 22 (29%)             |
|                     | > 4500 U l–1 | 5 (6%)                 |
| S-AFP               | < 999 µg l–1 | 76 (94%)               |
|                     | 1000–10 000 µg l–1 | 4 (5%)     |
|                     | > 10 000 µg l–1 | 1 (1%)               |
| S-hCG               | < 4999 IU l–1 | 72 (91%)             |
|                     | 5000–50 000 IU l–1 | 4 (5%)   |
|                     | > 50 000 IU l–1 | 5 (6%)              |
| IGCCCG              | Good prognosis | 49 (60%)            |
|                     | Intermediate prognosis | 16 (20%) |
|                     | Poor prognosis  | 16 (20%)             |

Serum categories cover normal, raised and very raised S-LD-1 and the serum marker prognostic categories of the fifth edition of the TNM classification for S-LD, S-AFP and S-hCG. The TNM classification did not include S-LD-1.

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

Sir

von Eyben et al describe their experience of splitting total LDH into its various isoenzymes and have identified LDH isoenzyme 1 (S-LD-1) as having prognostic significance in untreated patients with metastatic germ cell tumours. The evidence they present is clearly impressive and S-LD-1 appears to be able to identify patients with a poor outcome as effectively as the IGCCCG specification or serum HCG alone.

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