Increased Polyamine Concentrations in the Hair of Cancer Patients

To the Editor:

Rapid tumor growth has been associated with markedly altered polyamine biosynthesis and accumulation *(1)*, and an increase in the concentrations of plasma and urinary polyamines might provide an independent biochemical marker of disease activity and response to therapy *(2–5)*. However, because the components of urine and plasma show variations throughout the day and because these two specimens are rather inconvenient to obtain and handle, another noninvasive method for measuring polyamine concentrations was required. According to recent reports, hair fibers may be used to obtain physiologic information *(6–8)*. Using hair samples, we have quantified biosynthetic steroids, which are converted from testosterone by 5α-reductase or cytochrome P-450 aromatase *(9, 10)*. We have now investigated whether hair polyamine concentrations are altered in cancer patients.

We obtained hair from 49 patients treated at Yonsei Medical Center from November 1998 to January 1999, including 13 individuals with invasive cervical cancers, 11 with ovarian carcinomas, and 25 who underwent hysterectomies for benign gynecological disease. The latter were matched with the cancer patients for age. None of the subjects had been treated with radiotherapy or chemotherapy before the hair sampling. The hair samples were obtained by collecting the portions that had been cut off during haircuts.

Hair polyamines, measured as described elsewhere *(11)*, were increased in cancer patients (Table 1). The magnitude of increase was similar to that reported previously for plasma and urine polyamines *(2–5)*. In the 25 controls, polyamine concentrations were <477 ng/g of hair. In cancer patients, polyamine concentrations were as high as 921 and 3998 ng/g in cervical and ovarian cases, respectively.

Particularly in the patients with ovarian cancer, the maximum spermine concentrations were ~10-fold higher than those of control subjects (Student two-tailed *t*-test, P <0.001). However, most of the patients were still within the range of values found in controls. Attention to this nonspecific type of low polyamine concentrations is particularly important for any planned use of polyamines in cancer diagnosis, differential diagnosis, or screening. Clinical processes leading to nonspecific polyamine alterations usually are obvious on routine physical examination or standard laboratory testing.

Our findings suggest that measuring polyamines in hair may be a simple, noninvasive technique to assist in the diagnosis and assessment of disease activity in patients with cancer. Hair, which grows at ~1 cm/month *(12)*, reflects long-term chronic nature with little fluctuation, whereas blood and urine reflect the acute status. This study may be the starting point for additional studies in the field of polyamine analysis, and a study on response to therapy is underway.

Table 1. Hair polyamine concentrations in controls and cancer patients.

	Mean age (range), years	Concentration,[a] ng/g	*P*
Controls (n = 25)	44 (31–66)		
Putrescine		51 ± 17 (50; 19–87)	NA[b]
Spermidine		219 ± 93 (202; 96–477)	NA
Spermine		120 ± 67 (100; 21–259)	NA
Patients with cervical cancer (n = 13)	40 (34–65)		
Putrescine		106 ± 40 (88; 76–189)	<0.001
Spermidine		499 ± 280 (478; 144–921)	<0.001
Spermine		246 ± 170 (281; 43–573)	<0.005
Patients with ovarian cancer (n = 11)	54 (37–75)		
Putrescine		99 ± 54 (105; 291–179)	<0.001
Spermidine		724 ± 697 (446; 90–1699)	<0.001
Spermine		1156 ± 1489 (379; 9–3998)	<0.001

[a] Data are expressed as mean ± SD (median; range)
[b] NA, not applicable, used as the control values.

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Diagnostic Accuracy of an Agarose Gel Electrophoretic Method in Multiple Sclerosis

To the Editor:

In >95% of patients suffering from clinically unambiguous multiple sclerosis (MS), oligoclonal IgG can be detected in cerebrospinal fluid (CSF) *(1, 2)*. Isoelectric focusing is the most sensitive method for detecting oligoclonal bands (OCBs) *(1)*, whereas agarose gel electrophoresis is reported to detect OCBs in ~80% of cases *(2)*. A commercial electrophoresis unit (Beckman Instruments) is commonly used in clinical laboratories. Laboratory support of a clinically probable diagnosis of MS in combination with brain magnetic resonance imaging is important to allow initiation of appropriate treatment as early as possible.

We evaluated the sensitivity of the Beckman modified agarose gel electrophoresis to detect OCB and estimated its diagnostic accuracy. We examined paired CSF and sera from 168 patients (122 females) with clinically unambiguous MS *(3)* for the presence of oligoclonal IgG.

We followed the manufacturer's instructions for application of samples to the buffered agarose gel (SPE-II gel). Electrophoresis was performed at 100 V for 40 min, followed by immobilization in a fixative solution and staining. All tests were done by the same technician and evaluated by the same experienced hematologist, both unaware of clinical or magnetic resonance imaging data.

OCB was detectable in 90 of the 168 patients (53%; 95% confidence interval, 52.9–53.1%). The mean IgG index [(CSF-IgG/serum-IgG)/(CSF-albumin/serum-albumin)] of OCB-negative patients was 0.87. Patients with detectable OCB had a mean IgG index of 1.28 (reference value <0.7).

This electrophoretic method does not appear to provide adequate clinical sensitivity because false-negative results in the detection of OCB may delay diagnosis and the start of treatment.

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More on Troponin Assays and Heparin

To the Editor:

A recent article [Troponin T and I Assays Show Decreased Concentrations in Heparin Plasma Compared with Serum: Lower Recoveries in Early than in Late Phases of Myocardial Injury (*Clin Chem* 2000;46:817–21)] concluded that "Until such methods [which are resistant to interference by both heparin and EDTA] are available, the sample of choice for cardiac troponin determinations is serum collected in tubes with or without gel, or in thrombin tubes with and without gel". We believe that the conclusion is not supported by the data presented in the article.

It is clear from the data presented in Table 1 of the article that a bias exists between plasma and serum measurements for the Elecsys 2010 and the Immulite systems. No data in the article, however, suggest that the measured bias is related to heparin. With specific reference to Table 1, the authors state that the heparin concentrations in the tubes range from 40 to 70 IU/mL. In their experimental design, they added heparin to serum tubes at concentrations of 50–450 IU/mL. The authors have erroneously calculated the concentrations of heparin in the plasma tubes as listed in Table 1. In fact, the total heparin in the tubes ranges from 40 to 70 IU to achieve a final concentration of 14–15 IU/mL *(1)*. In calculating the heparin concentration in the tube, the manufacturer does not consider that blood consists of red blood cells, which presumably may not take up heparin. Therefore, recalculation of the manufacturer's stated concentration, assuming a 40% hematocrit, gives final heparin concentrations in the plasma of between 24 and 25 IU/mL. The association made by the authors comparing troponin concentrations measured in serum with added heparin (50–450 IU/mL) and in plasma from heparin tubes with whole blood (24–25 IU/mL) should not be made because the heparin concentrations are very different and the sample matrix (serum vs plasma) is different. The authors state that "Therapeutic concen-