References

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Increases in CA-125 Concentrations in Children

To the Editor:
The glycoprotein CA-125 has been identified in epithelial ovarian carcinomas and in serum of women with this disorder (1). In addition, its presence has been demonstrated in the normal female genital tract; low concentrations of CA-125 (<65 arb. units/mL) have also been detected in the circulation in healthy women (2). The observation that serum concentrations of CA-125 in women exhibit characteristic changes during the menstrual cycle led us to suppose that these concentrations might reflect somehow the regular cyclic function of the uterus or ovary (3). To evaluate whether CA-125 is also produced before the onset of regular menstrual cycles, we studied the serum concentrations of CA-125 in girls before menarche. Boys of comparable age served as controls. We report here the surprising finding of increased CA-125 serum concentrations in some of these children.

Sera from 250 boys and girls between ages nine days and 16 years were analyzed for CA-125 with a sandwich-type solid-phase assay (CA-125 ELSA; ID-CIS, Dreieich, F.R.G.) based on the use of murine monoclonal antibody OC-125 as capture antibody bound to the solid phase and 125I-labeled OC-125 as tracer. After incubation and washings, the bound radioactivity was measured with a gamma-counter and actual concentrations were calculated from the standard curve and documented as arbitrary units/mL (1). The measuring range extended from 12.5 to 500 arb. units/mL. Based on measurements in healthy women during different phases of the menstrual cycle, the upper limit of normal CA-125 serum concentrations was determined to be 65 arb. units/mL (2).

The children were being treated in the children's hospital for the following disorders: various heart diseases or congenital heart abnormalities (70), infectious diseases (22), gastroenterological diseases (9), pulmonary diseases (11), liver diseases (3), neurological disorders (28), kidney diseases (18), malignancies (8), skin diseases (3), throat diseases (15), accidents (5), premature births (6), metabolic disorders (5), and miscellaneous (47).

Of the 250 children whose serum was available for analysis, 23 exhibited increased CA-125 serum concentrations (>65 arb. units/mL). The greatest percentage of increased CA-125 concentrations was observed in the group of 70 children (35 boys, 35 girls) with various heart diseases or congenital heart abnormalities: 16 children with severe heart failure (10 boys, six girls) had CA-125 concentrations between 65 and 459 arb. units/mL (mean 151, SD 106 arb. units/mL). Three of these 16 children also had above-normal values for liver enzymes. The remaining 54 of these children, who had stable cardiac function without decompensation, had CA-125 concentrations in the normal range (mean 14, SD 6.4 arb. units/mL). Among the 180 children with various other diseases, seven exhibited CA-125 concentrations between 73 and 276 arb. units/mL. Those children had liver cirrhosis, neonatal asphyxia, esophageal atresia, portal vein thrombosis with esophageal bleeding, and hydrocephaly with a peritoneal shunt. The remaining 173 boys and girls had CA-125 concentrations between 5 and 62 arb. units/mL (mean 18, SD 9.8 arb. units/mL), i.e., values within the normal range. We did not detect an age-dependent distribution (Figure 1).

Our pilot study demonstrates that CA-125 can be detected in the peripheral serum of girls before the onset of regular menstrual cycles. In most of the children, the serum concentrations of this glycoprotein did not surpass the range considered as normal in adult women.

We were, however, surprised to detect remarkably increased CA-125 serum concentrations in some of the boys and girls, because such increases had been reported only in adults predominantly having malignant diseases or endometriosis and ovarian hyperstimulation syndrome. We do not believe that these increases of CA-125 were iatrogenic effects. All infusions given to these children were measured for CA-125 content, which was always negative. In those children who had been connected to the heart–lung machine, sera were usually obtained when the children had already been disconnected from this equipment for several days. We cannot totally exclude the possibility that the CA-125 in these children was derived from the fresh-frozen plasma that had sometimes been infused; however, during a parallel study on tumor marker concentrations in male blood donors, nearly all of the donors' blood (from which the fresh-frozen plasma was prepared) during that period had normal concentrations of CA-125.

Figure 1. CA-125 serum concentrations (arbitrary units per milliliter, ordinate) in 130 boys (top) and 120 girls (bottom) of various ages.
period was also checked for CA-125 concentration, and only one (of >500) had an increased CA-125 concentration (60 arb. units/mL). The CA-125 concentrations of all other sera were always <35 arb. units/mL.

The ovary or the uterus, the most likely source of CA-125 in adult women, shows little functional activity in prepuberal girls. Although this does not exclude a gonadal origin of the increased serum concentrations of this glycoprotein in some of the girls, we favor extragonadal mechanisms as the main determinants of the increase of serum CA-125 concentrations. This view is strengthened by the observation of above-normal CA-125 concentrations in boys, where no relation between CA-125 serum concentrations and gonadal activity has ever been found (3). Although we were unable to identify a common cause for the increase of CA-125 in these children, there seemed to be an association with heart failures and cardiac diseases: 22.8% of these children exhibited CA-125 serum concentrations exceeding 65 arb. units/mL. Moreover, all of the patients with increased CA-125 concentrations were characterized by severe heart failures or had been connected to the heart–lung machine during heart surgery.

That the increased CA-125 concentrations were not caused by an impaired liver metabolism (as a consequence of right heart failure, as one could argue) is indicated by the observation that only three of the 16 patients with above-normal concentrations of CA-125 had above-normal concentrations of liver enzymes. To understand the significance and the cause of the increase in CA-125 in serum, we propose further studies that concentrate on function and regulatory mechanisms for this glycoprotein.

References

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Contamination of Breath Methane Samples in Sterilized Vacutainer Tubes

To the Editor:
In gas-chromatographic measurement of breath methane to investigate its relationship to various carbohydrate malabsorption conditions (1, 2), breath samples often have to be stored for considerable periods before analysis. Sterilized Vacutainer Tubes (Becton Dickinson, Rutherford, NJ 07070), filled with the breath sample under positive pressure and the stoppers secured with adhesive tape, have proved to be a dependable means for storage of breath samples (3, 4).

In investigation of the viability of Vacutainer Tubes for breath methane storage, extremely high methane concentrations for both control and study subjects were discovered and contamination was suspected. I then undertook a study for the presence of methane in Vacutainer Tubes. Methane was detected in sterilized tubes that were silicone coated (Table 1).

Methane was measured with a Model 16 Microlyzer equipped with a molecular-sieve chromatographic column (Quintron Instrument Co., Inc., Milwaukee, WI 53215). Dry air was used as the carrier gas at a flow rate of 35 ml/min. The chromatograph was calibrated with a methane reference mixture in compressed air (Quingas; Quintron Instrument Co.). The small-

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