decreased during pregnancy only for women who experienced nausea of pregnancy (p < 0.05). As seen in Figure 1, GGT declined only in early preg-
nancy and especially if the pregnancy was associated with nausea.

These data indicate that serum GGT activity is significantly lower during normal uncomplicated pregnancy than in heavy drinkers, and seems to be highest in early pregnancy, especially in women who are experiencing nausea.

Figures

1. Weekly decline of GGT during early pregnancy in emetic (—x—) and non-emetic (O—O) women

References

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Comparison of the EMIT Phenytoin Procedure with Old and New Antibodies

To the Editor:

Homogeneous enzyme immunoassay (EMIT®), currently the technique most commonly used for determining serum phenytoin (I), reportedly gives falsely high values for phenytoin in samples from azotemic patients (2–6). This interference appears to be ascribable to cross reactivity with 5-(4-hydroxyphenyl)-5-phenylhydantoin glucuronide (HPHP glucuronide), the major metabolite of phenytoin, which accumulates in the serum of patients with renal failure (2, 7). Recently, the Syva Company has developed a new antibody to phenytoin, which is said to be substantially less affected by interference from HPHP glucuronide (8). We evaluated this new antibody for phenytoin analysis, using samples from patients with normal or abnormal renal function.

We analyzed for phenytoin by EMIT according to the manufacturer's recommended procedure, in the AutoLab 6000 (Syva Co., Palo Alto, CA 94303), using Syva EMIT-AED Phenytoin Antibody kits. New antibody (reagent A) kits were from lots N01 and N01A. Old antibody kits were of lots L03C and L03D.

The gas-liquid chromatographic (GLC) comparison determinations were performed as described previously (2), except that the sample volume was decreased from 1.0 mL to 0.5 mL and ethyl acetate was used instead of anhydrous diethyl ether in the charcoal extraction step.

Serum creatinine was measured in the CentrifiChem 400 (Baker Instruments, Allen-town, PA 18001) by use of a kinetic alkaline picrate reaction (9).

Values from the two antibody procedures differed significantly (p < 0.001). Results show that both the new- and old-antibody procedures showed positive bias as compared with the GLC results, but the bias seemed to be less with the new antibody. The linear regression equations relating the GLC method and the two antibody kits were:

\[
\text{EMIT (old antibody)} = 1.687(\text{GLC}) - 0.417 \quad (r = 0.844, n = 33)
\]
\[
\text{EMIT (new antibody)} = 1.153(\text{GLC}) + 2.43 \quad (r = 0.830, n = 56)
\]

Figure 1 shows that when serum creatinine was <20 mg/L, the difference in phenytoin value between the new-antibody procedure and GLC was less than ±2 mg/L in more than 95% of the cases. However, when serum creatinine was >20 mg/L, the incidence of having a positive bias of at least 2 mg/L with the new-antibody assay increased substantially. This finding could not be accounted for by the inherent imprecision of the two procedures. A correlation of 0.489 existed between the degree of interference (new antibody minus GLC) and the degree of azotemia (as reflected in the creatinine value) but was too weak to allow creatinine values to be used to correct the phenytoin results. We conclude that:

- The new EMIT phenytoin antibody is not greatly superior to the old antibody.
- Values for samples from patients with azotemia still tend to be erroneously high, even with the new antibody.
- The incidence of falsely high phenytoin values does not increase until the serum creatinine exceeds 20 mg/L. This is in general agreement with the recent proposal of Apple et al. (2) based on the older antibody.

We recommend that for samples with a creatinine concentration >20 mg/L, the result with the EMIT procedure, even with the new antibody, should be reported only as an upper estimate, and a more nearly accurate result should be obtained with a GLC procedure.
References


Adrain C. McClellan Kwok-Ming Chan Donald A. Lichti Victor N. Meltzer Jack H. Ladenson

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Procedure for Discordant hCG Results

To the Editor:

Several recent reports (1–4) describe discordant results for human chorionic gonadotropin (hCG): serum specimens were positive in one assay but negative in one or more other procedures for hCG (1–4). Our laboratory interests have traditionally led us to analyze many serum specimens in several different hCG detection procedures. As a result, we have observed a substantial number of serum specimens that are discordant for hCG. In view of the above, it seemed timely and important to illustrate the phenomenon of discordant hCG results, to indicate how to recognize this phenomenon, and to recommend how to deal with the problem.

Serum specimens were analyzed in two or more of the following quantitative procedures (in parentheses are the source of reagents; the hCG standard used, either Second International Standard, 2nd IS, or First International Reference Preparation for hCG, 1st IRP; and the sensitivity of each assay in int. units/L): Assay A, "GammaDab beta-hCG" RIA (Clinical Assays, Cambridge, MA; 1st IRP; 3); Assay B, an RIA with rabbit antiserum H2 raised against complete hCG and adsorbed with hLH-Sepharose to reduce cross reaction with lutropin (luteinizing hormone, LH) to <0.2% (5); Assay C, an RIA with rabbit antiserum H2 raised in this laboratory against free beta-subunit of hCG (2nd IS; 2); Assay D, "Concep-7-beta-hCG" RIA (Leuco Diagnostics, Southfield, MI; 1st IRP; 0.5); Assay E, "Beta-Tec" RIA (Wampole Labs, Cranbury, NJ; 2nd IS; 3); Assay F, an RIA with antiserum SB6 (provided by the National Hormone and Pituitary Distribution Program, NICHD, Bethesda, MD) raised against the free beta-subunit of hCG (6) (2nd IS; 7); and Assay G, "Tandem-R hCG" two-site immunoradiometric assay (IRMA) that utilizes two different monoclonal antibodies of hCG (7) (Hybritech, Inc., San Diego, CA; 2nd IS; 4).

For RIAs A, D, and E, the precipitation agent was second antibody along with polyethylene glycol; these assays and Assay G were performed as recommended by the suppliers. Assays B, C, and F were double-antibody RIAs. Assays A–F recognize complete hCG and also the free beta-subunit of hCG, whereas Assay G recognizes complete hCG but not the free beta-subunit.

Patient 1 was a 40-year-old woman with endometriosis and marked decidualization, who underwent total hysterectomy and bilateral ovariectomy in April 1982. As shown in Table 1, positive results for hCG were obtained with Assays A–D on all occasions studied, and on two of the four dates studied with Assay F. There was no significant trend in hCG during the 20 months of sampling. The positive results were confirmed by replicate analysis on several occasions with Assays B and F. In contrast, hCG was undetectable on all occasions studied with Assays E and G. There has been no clinical evidence of a tumor or other abnormality in Patient 1 since the time of hysterectomy, suggesting that the positive hCG responses are not clinically relevant.

Patient 2, a 30-year-old woman with one previous child, had a presumed spontaneous abortion in the fourth or fifth week of her second pregnancy. Dilatation and curettage (D&C) was performed, and during the next two months the hCG titer decreased from 50 to 28 (Assay B). This was followed by a gradual decline over the next two months to a plateau of 12 to 16 int. units/L in Assay B. The titer remained in this range for another eight months, during which time Patient 2 resumed normal menstruation. Serum specimens drawn more than two months after the D&C gave discordant results in different hCG detection procedures. For example, for the specimen drawn 10 months after the D&C the hCG values were 34, 11, 12, 3, <3, <7, and <4 int. units/L in Assays A–G, respectively. In month 11 after the D&C, Patient 2 became pregnant, after which all procedures became positive for hCG. Patient 2 ultimately delivered a healthy child.

Patient 3 had a tubal ligation at another institution three months after delivery of her second child. Two months after the tubal ligation, a slide test on urine for pregnancy was positive. A quantitative RIA for serum hCG was performed at the other institution, which used the "125I-hCG-beta radioimmunoassay" from Bio-RIA (Montreal, Canada), and a value of 110 int. units/L was obtained. Analysis of serum specimens drawn two and five weeks later with the Bio-RIA hCG kit gave hCG values of 194 and 191, respectively. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and left oophorectomy were performed, but no evidence of tumor or trophoblastic tissue was found in the surgical specimens. When serum specimens collect-

| Table 1. Discordant hCG Results (Int. units/L) on Patient 1
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