Correlation between Glycosylated Hemoglobin in Specimens Containing Potassium EDTA and Fluoride/Oxalate

To the Editor:

We recently started estimating glycosylated hemoglobin (HbA1) by using an agarose electrophoresis system (Corning Medical and Scientific, Palo Alto, CA 94306). It is recommended in the manufacturer's literature that potassium EDTA-anticoagulated samples should be used. We routinely estimate glucose in fluoride/oxalate anti-coagulated samples, so we decided to compare results for HbA1 samples anticoagulated in the two ways.

Blood specimens from 80 patients who were attending the diabetic outpatient clinic were collected, part of each in a potassium EDTA-containing tube and another part in a fluoride/oxalate-containing tube. The samples were then analyzed as detailed by Corning. Each pair of samples was electrophoresed on the same gel to avoid between-batch variation. Comparison of the EDTA-containing samples (x) with the fluoride/oxalate-containing samples (y) gave the following linear regression equation: y = 0.97x + 0.59; r = 0.98. A pair difference t-test gave the following result: mean difference 0.26, S.E. of difference 0.07, t = 3.670 (p < .001). The difference is statistically significant, but too small to affect clinical interpretation of the results. Consequently, we have started estimating both glucose and HbA1 in fluoride/oxalate-treated samples. This has the obvious advantage to the patient of requiring the withdrawal of only one 5-ml sample.

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“Alpha” and “Beta” Errors

To the Editor:

Javier Fuentes (Clin. Chem. 28:2329, 1982) is correct when he questions what is meant by an alpha error and a beta error. The definition used by statisticians is the correct definition. An alpha error, or a Type I error, is a false-positive result.

In our book, Beyond Normality (1), we followed the teachings of Lee B. Lusted (2), who turned the classical statistical definition on its head and defined a false-positive result as a beta error!

Lusted now prefers not to use the terms “alpha” and “beta” errors. It is better to simply speak of “true-positive” fractions and “false-positive” fractions.

References


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Dehydroepiandrosterone Sulfate Concentrations in Plasma of Normal Ovulatory Women

To the Editor:

Internists and gynecologists utilize plasma dehydroepiandrosterone sulfate (DHEA-S) measurements widely in evaluating conditions involving adrenal androgen excess. In this application, DHEA-S measurements have largely replaced the traditional measurement of 24-h urinary 17-ketosteroid excretion (1). Because information on normal DHEA-S concentrations may be of major importance in the exclusion of serious endocrine disorders—including Cushings disease and syndrome, adrenal tumors, and congenital adrenal cortical hyperplasia (2)—it is important that the normal reference interval for DHEA-S concentrations be known as precisely as possible and that supranormal values be easily recognized in women of reproductive age.

DHEA-S concentrations may be increased or depressed under conditions that are unrelated to these serious diseases. They may be low in postmenopausal women, elderly men, patients taking glucocorticoids, underweight individuals, and in women of reproductive age who have had oophorectomies and are not taking estrogens (3). They may be high in reproductive-age women who are anovulatory and overweight in association with polycystic ovarian disease (3). Because DHEA-S concentrations are so easily effected by these conditions, it is difficult for reference laboratories to establish their own normal reference intervals by use of data on ostensibly normal women without first subjecting each of them to an expensive and impractical medical and gynecological screening. Consequently, reference laboratories are frequently finding “normal” values in excess of 5 µg/L, a range we believe to be excessively high.

We therefore evaluated a group of gynecologically normal, regularly ovulating women of normal body mass. We wanted to establish a normal reference interval in gynecologically healthy, nonobese, ovulating women that could be reproduced and used as a reference by other laboratories that are providing DHEA-S measurements.

The subjects were 17 healthy ovulating women of normal body mass, ranging in age from 20 through 35 years. Each woman had been studied during three to seven cycles with respect to daily basal body temperatures, serum estradiol concentrations, and serum luteinizing hormone concentrations, with careful documentation that each had long been normally ovulatory. None of the women had hirsutism, significant acne, or abnormal gynecological examinations.

DHEA-S concentrations were measured with a standard 125I radioimmunoassay kit obtained from Immucor Corp. (Division of Radioassay Systems Laboratories, Carson, CA 90746, cat. no. 11014). The assay was used as instructed. We compared results with this kit with those by a tritiated DHEA-S assay described by us previously (5). Seventeen samples were used in this comparison; the results, tabulated below, show no systematic difference (p = 0.19, signed-rank test).

\[
\begin{align*}
\text{Mean concn. µg/L} & = mx + b \\
\text{where} & \begin{cases} 
\text{y} & \text{x} \\
0.9555x + 0.107 & 2.056 \\
(r = 0.9722) & 1.932
\end{cases}
\end{align*}
\]

DHEA-S concentrations in the plasma of the 17 women ranged from 0.700 to 3.900 µg/L (mean 2.056, SD 0.859 µg/L).

We suggest that manufacturers of DHEA-S kits supply user laboratories with a normal reference interval for a similarly screened group of subjects.

References


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Fetal Alcohol Syndrome and Lactic Acidosis

To the Editor:

We recently saw a newborn infant with the fetal alcohol syndrome and lactic acidosis. The mother was 32 years old, gravida 5, para 2, with one elective abortion. One previous infant had died in the perinatal period, of massive congenital anomalies; a second infant died with the sudden infant death syndrome. The mother had a long history of chronic alcohol abuse. After she learned of the current pregnancy, she became depressed and went on a drinking spree. She continued to drink to some extent during most of the pregnancy.

The baby was delivered at term by cesarean section because of fetal distress. It was a 2.74-kg male with Apgar scores of 4 and 7 at 1 and 5 min. Resuscitative efforts were required at birth, and the child developed transient tricuspid insufficiency due to asphyxia.

Tachypnea continued after birth and the infant had hypoglycemia (blood glucose concentration of 260 mg/dL). Arterial blood gas studies showed metabolic acidosis: arterial pH of 7.32, pCO2 of 16 mmHg, and [HCO3] 8.3 mmol/L. He was treated with bicarbonate and glucose, and over the next several days continued to have tachypnea and compensated acidosis. Six days after delivery, blood lactate concentration measured 7.6 mmol/L, pyruvate 10 μmol/L (760:1 ratio). The child was diagnosed as having fetal alcohol syndrome and an associated lactic acidosis. The next day the lactate concentration had declined to 4.3 mmol/L and both child and mother were discharged. Two weeks postpartum, the infant was seen in the outpatient department for failure to thrive and was referred to a medical geneticist for further studies.

Lactic acidosis is a common finding in adult alcoholism but apparently has not been frequently seen in the fetal alcohol syndrome. The metabolism of ethanol to acetaldehyde and acetate by the microsomal ethanol-oxidizing system leads to a stoichiometric increase in the NADH/NAD+ ratio. An increase in reducing equivalents in the form of NADH will lead to at least two metabolic abnormalities: increased lactate, due to a shift in the redox ratio of lactate to pyruvate mediated through the lactate dehydrogenase reaction, and a decrease in gluconeogenesis, probably secondary to decreased availability of pyruvate. These effects will result in a stoichiometric shift towards the formation of lactate.

Lactate measurement may be important to newborns with the fetal alcohol syndrome and metabolic acidosis.

References

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Chloride Interference with Use of an Iodide-Selective Electrode for Urinary I-

To the Editor:

In a recent study of urinary iodide excretion by subjects in Auckland, New Zealand, we evaluated an iodide-selective electrode (iodide electrode 94-53A with Digital Analyzer 701A; Orion Research Inc., Cambridge, MA 02139). We compared results with those obtained by a chemical method (1), using both aqueous standards (KI in distilled, de-ionized water) and a standard curve prepared by use of urine previously de-iodized with ion-exchange resin (Iobeads, Technicon Corp., Tarrytown, NY 10591).

Excellent results were obtained when the electrode was applied to aqueous iodide standards and the standard curve was linear to 1 × 10^{-6} mol of I- per liter. In contrast, the results were highly inconsistent when the electrode was used with dilutions of iodide in urine, where linearity was only achievable to 1 × 10^{-3} mol/L.

Subsequently, theoretical calculations were based on a modified Nernst equation (2): E = E _0 + 2.303 R T F log (a _ I⁻ + K _ I⁻ Cl⁻ a _ Cl⁻) where R is the gas constant, T the absolute temperature, F the Faraday constant, a _ I⁻ the activity of iodide in solution, and K _ I⁻ Cl⁻ the selectivity coefficient of the electrode for iodide with respect to chloride (for the electrode in question, the manufacturer's booklet gives a value of 1 × 10^{-6}).

These calculations revealed that at ratios of a _ Cl⁻: a _ I⁻ ≥ 10^8 there is a significant and increasing error caused by chloride.

At average urine concentrations of chloride and iodide (for example, chloride 0.2 mol/L, iodide 1.8 × 10^{-6} mol/L) the calculated chloride-induced error is 5%. This error rapidly increases with an increasing a _ Cl⁻: a _ I⁻ ratio.

Because the physiological concentration of chloride in urine may range from 50 to 600 mmol/L, we conclude that, on the basis of chloride error, the iodide-selective electrode is unsuitable for the accurate experimental determination of iodide in urine.

References

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Glucose Method Comparison Criticized

To the Editor:

Your recent publication of a three-page scientific note (Clin. Chem. 28: 2405, 1982) comparing four different methods for determining glucose may be misleading to some of your readers. Two of the four methods are currently obsolete in the United States. Of the 6100 laboratories reporting glucose values in the 1982 comprehensive surveys of the College of American Pathologists (1), fewer than 20 reported glucose values assayed by the neocuprone or alkaline ferricyanide methods—a slight decrease from the 24 or fewer laboratories reporting each of these two methods in 1981. Therefore,