The latter may be related to a common origin and closer links between the population of Iraq (including Baghdad) and that of the Arabian Peninsula throughout history.

References


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Serum Testosterone in Women as Measured by an Automated Immunoassay and a RIA

To the Editor:
Taieb et al. (1) in their recent report in Clinical Chemistry described the relationship of serum testosterone concentrations measured by 10 immunoassays and by isotope-dilution gas chromatography–mass spectrometry (ID/GC-MS). Automated immunoassays fared badly, but RIAs agreed well with the ID/GC-MS.

In contrast to our findings, Taieb et al. (1) reported, in women, increased serum testosterone as assayed in the AutoDelfia immunoassay system (Perkin-Elmer). Between November 1, 2002, and February 28, 2003, we found for 2057 women a mean (median) testosterone of 2.1 (1.6) nmol/L by AutoDelfia, similar to the values of 1.7 (1.4) nmol/L for 2180 different female samples assayed consecutively in our routine using the Orion Diagnostica RIA between November 1, 2001, and February 28, 2002. By contrast, Taieb et al. (1) reported mean concentrations of ~5 nmol/L in the female samples measured by the AutoDelfia.

In the same time periods, consecutive male samples had mean (median) values of 16.7 (14.8) nmol/L by AutoDelfia (n = 1447) and 13.9 (12.9) nmol/L by the Orion (n = 1505). Again, the difference between the automated immunoassay and RIA values was much smaller than reported by Taieb et al. (1).

In our hands the main difference between the automated immunoassay and the RIA for the determination of testosterone in female samples was a much higher frequency of increased concentrations in individual samples caused by interfering substances in the AutoDelfia. This led us to resume use of the RIA. Although interference in RIAs for testosterone does happen (2), interferences appeared to be less frequent than in the automated immunoassay systems we have tested. It would be of great interest if Taieb et al. (1) could report the rate of interference leading to increased concentrations in individual samples in the different immunoassay methods they used in their study with ID/GC-MS as the reference.

References


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Dr. Boudou responds for the authors of the article cited above:

To the Editor:
Torjesen and Sandnes briefly summarize our study (1) that compared testosterone immunoassays with an isotope-dilution gas chromatography–mass spectrometry (ID/GC-MS) method. They report mean concentrations in female samples lower than ours for the AutoDelfia system and describe two indirect personal observations to explain our 2.5-fold higher values: One is a very rare IgG that reacted with the labeled analyte that compared the values to previously described criteria (1).

These samples were not problematic in immunoassays but were evaluated because they corresponded to our daily recruitment.

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As noted in our report (1), in 25 of 55 female samples testosterone was <2.06 nmol/L by ID/GC-MS. These women could be similar to the female patients of Torjesen and Sandnes. The testosterone concentrations measured by the AutoDelfia system were clearly overestimated, as shown in Fig. 3 of our report (1). In addition, in 42 of 55 females, testosterone was lower than the upper limit of the ID/GC-MS range (0.50–2.55 nmol/L) as measured in normally menstruating women 19–35 years of age with no evidence of hirsutism, acne, or alopecia and taking no oral contraceptives for at least 6 months before being tested. Hyperandrogenism has been diagnosed in 24 of these 42 females based on an increase in at least one serum androgen concentration at baseline: dehydroepiandrosterone sulfate >9.50 μmol/L; 17-hydroxypregnenolone >11.50 nmol/L; dehydroepiandrosterone >38.00 nmol/L; or androstenedione >7.85 nmol/L. Eighteen of 42 were “normoandrogenic” females. These 42 females had 17-hydroxyprogesterone concentrations within the reference interval. Mean (SD) testosterone measured by ID/GC-MS was 1.37 (0.56) nmol/L in normoandroenic females and 1.93 (0.33) nmol/L in females with hyperandrogenism, whereas it was 2.94 (1.77) and 5.30 (1.74) nmol/L, respectively, for these two groups when measured by AutoDelfia. One would expect that if some particular interfering substances were present in the female samples there would be an intriguing individual serum response in some, if not all, of the direct assays tested, but we did not observe this.

AutoDelfia with Immulite 2000 gives the highest mean testosterone values, widely dispersed results, and the highest overestimation, as shown in Fig. 3 of our report (1). This observation confirmed a previous report (3) in which serum pools were tested. The use of pools is more favorable to assay performance because interferences in individual samples are diluted. In that study, the testosterone concentrations in the two female pools tested by ID/GC-MS were 0.74 and 2.67 nmol/L, whereas they were 1.99 and 4.99 nmol/L, respectively, when measured by AutoDelfia (differences of 169% and 87%). In a dilution test, AutoDelfia results were high by 13–176% (3).

We accept the possibility of a change in the assay’s reagents between our two studies. Many relevant reports have highlighted interferences in immunoassays (4–7). Interfering substances and factors relating to blood collection (8) have been identified by the manufacturers and considered limitations of the assay procedure. We think that most of the sources of errors involved in direct steroid assays are directly related to the assay format, such as the matrix (9), the preparation and the purity of the labeled molecule, the specificity of the antibody, the flexibility of the labeled analyte–antibody complex, and assay optimization.

References

Cell-Free Fetal DNA Is Not Present in Plasma of Nonpregnant Mothers

To the Editor:
Fetal DNA sequences are present in the plasma of pregnant women (1) and can be studied to determine fetal sex (1) and RhD type (2). Unlike fetal cells, fetal cell-free DNA is cleared rapidly from plasma after delivery (3), with a half-life of 16–28 min. Even when clearance is slowed, as in preeclampsia (4), the mean half-life for clearance of fetal DNA is 114 min (5).

Recently, Invernizzi et al. (6) reported positive PCR results for a Y-chromosome-specific sequence in 36 of 160 (22%) women who had given birth to a son up to several years previously. By contrast, other published studies on pregnant women have described no false-positive results (1, 2, 7–14). It is conceivable that fetal cells remain and proliferate in the maternal circulation or are engrafted in maternal organs after delivery and that this proliferation is suppressed again in a subsequent pregnancy. Lambert et al. (15) also recently reported the presence of fetal DNA in plasma of nonpregnant women. They also found male DNA sequences in 8 of 22 (36%) healthy nonpregnant women who had previously given birth to sons, but filtration studies showed that this DNA was not cell free.

We recruited 120 nonpregnant women, with their consent, do-