identify renal damage in these patients. In reviewing the patient data, we saw evidence of concern and confusion about the fluctuating results for urinary protein.

We conclude that aminoglycosides produce positive interference with the Dade Behring pyrogallol red–molybdate method for urinary protein estimation but not with other tested pyrogallol red–molybdate methods. Patients with essentially normal urinary protein concentrations but on aminoglycoside therapy had urinary aminoglycoside concentrations sufficiently high, even at the end of a 24-h dosing interval, to produce factually increased urinary protein results. The mechanism of the interference is unknown.

References

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False Hyperprolactinemia Corrected by the Use of Heterophilic Antibody-blocking Agent

To the Editor:
The prolactin immunometric assays (IMAs) that have replaced the old RIA for the diagnosis of hyperprolactinemia and for monitoring the effectiveness of subsequent treatment. Two pitfalls have frequently been reported for prolactin assays: the “hook” effect may yield false-negative results when the prolactin concentration is very high (1); and the presence in serum of a high proportion of a biologically inactive but immunologically reactive form of prolactin (macroprolactin) may yield false-positive results (2). Another source of false-positive prolactin measurements, i.e., interference from heterophilic antibodies, which was relatively frequent with RIAs (3–5), to our knowledge has been reported only once with IMAs (6). We describe here a case of antibody interference with a prolactin IMA, which led to unnecessary radiologic investigations and treatment.

In April 1999, a 45-year-old woman under contraceptive treatment (mini-pill) consulted her physician because of the onset of amenorrhea without galactorrhea. The physical examination was normal except for a small euthyroid goiter (normal thyrotropin). The serum prolactin concentration, determined with the automated VIDAS enzyme IMA (bioMérieux, Marcy-l’Etoile, France), which uses two mouse monoclonal antibodies, was increased [78 μg/L at the time of the examination (3rd International Standard 84/500 used as the standard)] and 121 μg/L several days later. Pituitary imaging by computed tomography revealed no evidence of prolactinoma. Nevertheless, despite the return of regular menstrual cycles after the pill was stopped, the woman was given antipro lactin treatment with a dopamine receptor agonist drug, Dostinex®.

In January 2000, the VIDAS prolactin value was still increased (111 μg/L). In February 2000, the patient, who complained of irregular menstrual periods, was referred to our university hospital. Her prolactin concentration, assayed with the Elecsys® electrochemiluminescent IMA from Roche Diagnostics, which uses two mouse monoclonal antibodies, was markedly decreased (<0.4 μg/L; 3rd International Standard 84/500 used as the standard). The antiprolactin therapy was stopped. In June 2000, the patient again had regular periods and a prolactin concentration (21.6 μg/L) within the reference interval, as measured by the Elecsys. The discrepancy between the results obtained by the assays of two manufacturers supported the interference hypothesis. In June 2001, the presence in our laboratory of a VIDAS system prompted us to undertake further investigations on the June 2000 serum sample (stored frozen at −20 ºC) to characterize the interference with the VIDAS assay.

The VIDAS prolactin result was >200 μg/L. The results obtained with the Vitros ECi assay (19.1 μg/L) from Ortho-Clinical Diagnostics, which uses a sheep polyclonal antibody and a mouse monoclonal antibody, and with the AxSYM assay (18.4 μg/L) from Abbott Laboratories, which uses a rabbit polyclonal antibody and a mouse monoclonal antibody, were in agreement with those of the Elecsys assay.

A false-positive result as a consequence of macroprolactinemia was ruled out by the normal recovery (76%) of Elecsys prolactin after the serum was treated with 25% polyethylene glycol (7). The hypothesis that an interfering antibody was present was supported by evidence of non-parallel behavior between the suspected sample and the assay calibrators. The 5- to 32-fold dilutions of the serum with the VIDAS prolactin diluent showed increasing recoveries (117–191%), whereas the 2- to 32-fold dilutions of a “normal” serum yielded recoveries of 83–97% (8). The addition of mouse, bovine, or rabbit serum (10% and 50%) to the patient’s serum was ineffective in decreasing the VIDAS prolactin result. Anti-iso typic human anti-mouse antibodies (HAMAs) were checked with the HAMA-ELISA assay from Medac, which uses mouse IgG immobilized on a plastic surface as the capture antigen and a mouse IgG-horseradish peroxidase conjugate to detect captured HAMAs (positivity threshold reported by the manufacturer, 40 μg/L). The result obtained with the patient’s serum was weakly positive.
chorionic gonadotropin assays (11), treatment with HBTs was able to obviate the interference. In similar cases of hyperprolactinemia without image of pituitary tumor, after macroprolactin screening prolactin should be assayed by two or more IMAs. The use of HBT blocking agents should also be encouraged to prevent unnecessary anxiety and costly medical procedures and to reinforce clinicians’ and patients’ confidence in diagnostic assays.

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Target Values and Method Evaluation in Proficiency Testing Programs

To the Editor:
A recent opinion article (1) in this journal presented sound metrologic principles and a plan of action to improve analytical accuracy in medical laboratories. In addition to the use of Certified Reference Materials outlined by Müller (1), use of proficiency testing and external quality-control programs can have a broader impact on interlaboratory comparability. Ideally, target values should be derived from reference methods and reference materials, but both are limited in their availability, and the mean (or other indicator of central tendency) of participant data is frequently used. This has been shown to provide a basis of comparison often comparable to reference methods (2).

The means of subsets of methods (peer-group means) are often reported as target values, a practice usually ascribed to method-dependent behavior of proficiency test specimens and so-called matrix effects (3, 4); this use of multiple “true values” in proficiency testing has been criticized (5, 6).