the presence of 19-norandrostenedione at the concentration of 7 μg/mg. This result was not challenged by the athlete. Nandrolone has also been identified by this laboratory in the hair of bodybuilders, in concentrations of 1–7 μg/mg (8). NA and noretiocholanolone were not detected in any hair.

The sensitive, specific, and reproducible method developed appears to be suitable for the detection and quantification of 19-norsteroids in human hair. The determination of one 19-norsteroid in hair may allow unambiguous confirmation of the exact nature of the abused agent.

Hair analysis may be a useful adjunct to conventional drug testing in sports because hair can provide a more accurate history of drug use than urine (9). This technology may find useful applications in doping control if accepted by the International Olympic Committee.

References

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Detection of Macroprolactin Causing Hyperprolactinemia in Commercial Assays for Prolactin

To the Editor:

John et al. (1) presented two clinical cases demonstrating the diagnostic confusion created by cases of hyperprolactinemia that are attributable to the presence of macroprolactin. The authors urged manufacturers of prolactin (PRL) reagents to (a) indicate in their product literature the extent to which macroprolactin interferes in their assays, and (b) have available a validated method to confirm the presence of macroprolactin. Considerable progress has been made in both of these issues since the distribution of serum from one of the cases presented by John et al. (1) by the United Kingdom National External Quality Assessment Scheme (UKNEQAS) (2); however, most of the data have been presented only in preliminary form. A more recent UKNEQAS distribution of a serum containing macroprolactin (2) provided data on more recently introduced assays, as well as on a wider range of assays (Table I), and showed a pattern of reactivity in PRL assays similar to that presented by John et al. (1). The Roche Elecsys PRL assay (2) reacted strongly with macroprolactin in this sample, as indicated by product literature.

Table 1. Method mean PRL results for PRL serum containing 93% macroprolactin and 7.1 μg/L monomeric PRL distributed through the UKNEQAS.

<table>
<thead>
<tr>
<th>Method</th>
<th>n</th>
<th>Mean PRL, μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beckman Access</td>
<td>5</td>
<td>22.5</td>
</tr>
<tr>
<td>Bayer/Chiron Centaur</td>
<td>7</td>
<td>24.6</td>
</tr>
<tr>
<td>Bayer/Chiron ACS:180</td>
<td>63</td>
<td>25.7</td>
</tr>
<tr>
<td>BioChem MAIAclone</td>
<td>2</td>
<td>36.8</td>
</tr>
<tr>
<td>Randox ELISA</td>
<td>1</td>
<td>32.8</td>
</tr>
<tr>
<td>Roche Cobas Core</td>
<td>2</td>
<td>46.5</td>
</tr>
<tr>
<td>J &amp; J Vitros ECI</td>
<td>1</td>
<td>53.4</td>
</tr>
<tr>
<td>Roche Enzymun</td>
<td>14</td>
<td>61</td>
</tr>
<tr>
<td>DPC Immulite 2000</td>
<td>2</td>
<td>62.1</td>
</tr>
<tr>
<td>DPC Immulite</td>
<td>9</td>
<td>62.5</td>
</tr>
<tr>
<td>Wallac DELFIA</td>
<td>22</td>
<td>72</td>
</tr>
<tr>
<td>Bayer Immuno-1</td>
<td>42</td>
<td>90.8</td>
</tr>
<tr>
<td>J &amp; J Amerlite</td>
<td>2</td>
<td>93.1</td>
</tr>
<tr>
<td>Abbott AxSYM</td>
<td>57</td>
<td>95.3</td>
</tr>
<tr>
<td>Abbott IMx</td>
<td>8</td>
<td>109</td>
</tr>
<tr>
<td>Tosoh AIA</td>
<td>4</td>
<td>119</td>
</tr>
<tr>
<td>Roche Elecsys</td>
<td>12</td>
<td>143.1</td>
</tr>
</tbody>
</table>

*Macroprolactin and monomeric PRL were determined by gel-filtration chromatography and the Wallac DELFIA PRL assay.

To method men.

PEG interferes in the Abbott AxSYM PRL assay, but preliminary communications (6,7) have described detection of macroprolactin by centrifugal ultrafiltration with this assay, and a full publication is in preparation. In the Wallac DELFIA assay, macroprolactin has been identified as the cause of hyperprolactinemia in 15–17% of patient samples with increased serum PRL (8). In the Elecsys and Architect assays, macroprolactin has been identified as the cause of hyperprolactinemia in 16–17% of patient samples with increased serum PRL (3,5). Preliminary results indicate a similar prevalence with the Immuno-1 (4), and it seems probable that this can be expected with all of the relatively strongly reacting assays in Table I.

The Bayer/Chiron PRL assays on the ACS:180 and Centaur analyzers have been considered low-reacting assays with regard to the presence of macroprolactin, as illustrated by the sera distributed through UKNEQAS (1,2). The differences be-
tween the results of relatively high-and low-reacting assays have been taken as an indication of the presence of macroprolactin in samples. Inspection of estimates of monomeric PRL by gel-filtration chromatography in these samples suggests that although the Bayer/Chiron PRL assays react with the macroprolactin present, these assays generally react to a lesser extent than others. The structure of macroprolactin is variable (9), and the reaction of PRL assays with macroprolactin is also variable (4, 10). The Bayer/Chiron PRL assays may react strongly with the macroprolactin in some patient samples, and concordance of results with other assays does not exclude macroprolactin as a cause of hyperprolactinemia. PEG interferes in the Bayer/Chiron PRL assays, and further work is needed to (a) establish the prevalence of macroprolactin as a cause of hyperprolactinemia with these assays, and (b) develop a method for detecting macroprolactin in these assays.

The distribution of specimens containing macroprolactin through UKNEQAS has provided valuable information on the response of PRL assays to macroprolactin. This distribution has also heightened awareness of macroprolactin and encouraged laboratories to consider and investigate macroprolactin as a possible cause of hyperprolactinemia. In the most recent distribution, 49% of respondents considered macroprolactin as a potential cause of hyperprolactinemia, and 5% of respondents who used assays that reacted strongly with the macroprolactin investigated and detected the presence of macroprolactin. Greater awareness of the problem is still required, but considerable progress has been made.

References

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Dr. John responds:

To the Editor:

Fahie-Wilson and major equipment manufacturers have done valuable work, but more than one-half of all participants failed to recognize that macroprolactin could be a cause of hyperprolactinemia. New assays are needed that react only with monomeric prolactin. Some prolactin assays are already minimally affected by the presence of macroprolactin (1). Interferences in immunoassays remain important and put patients at risk of unnecessary surgical intervention (2). Continued refinement of prolactin immunoassays is needed.

References

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MMP1 and MMP3 Polymorphisms in Promoter Regions and Cancer

To the Editor:

Tumors spread by way of a multistep process in which degradation of the extracellular matrix and basement membrane barriers is a key feature. The matrix metalloproteinases (MMPs) comprise a family of at least 16 proteolytic enzymes that degrade the extracellular matrix in a substrate-specific manner and are thought to have important roles in tumor invasion and metastasis (1).

Overexpression of MMPs is associated with tumor invasion and metastasis (2). Rutter et al. (3) recently investigated how insertion of a G nucleotide at −1607 bp in the MMP1 promoter sequence affects regulation of the transcription of the gene. Promoters containing this 2G sequence display substantially higher transcriptional activity than 1G promoters. In tumor cell lines, 2G homozygotes are found more often than in the general population (3). These data have been confirmed in patients affected by ovarian (4) and endometrial (5) cancer.

The MMP stromelysin-1 (MMP3) exhibits several activities that would make it a particularly good tumor...