Letters to the Editor should be typed double-spaced (including references) with conventional margins. The overall length is limited to five manuscript pages, including not more than one figure or one table.

Tandem Mass Spectrometry In Drug-Abuse Testing, Exemplified for Anabolic Steroids

To the Editor:

In a recent Special Report concerning the analytical and technical aspects of confirmation methods in drug-abuse testing (Clin Chem 1988;34:471–3), Peat commented that the application of tandem mass spectrometry to confirmatory analyses should be developed. We felt this important direction in such analyses merited further comment.

The primary advantage that tandem mass spectrometry offers the drug-testing laboratory is very high selectivity of detection. This selectivity is ideal because it provides the amount of information necessary for reliable confirmation. More-selective detection techniques can also speed analyses by allowing the use of less-rigorous chromatographic conditions (e.g., faster temperature ramps, higher flow rates, and shorter columns) or even direct analysis of mixtures without gas chromatography (1, 2). Faster procedures lead to higher sample throughput, which, in busy laboratories, can reduce the number of mass spectrometers needed. Some cost reduction can therefore be realized, especially for personnel. Cost reduction is particularly important, given that economic pressures are the primary obstacle to the use of mass-spectrometric confirmation techniques despite the consensus that mass-spectrometric confirmation is essential for legally defensible testing (3).

High sample throughputs also make possible large-scale testing entirely by gas chromatography/mass spectrometry (GC/MS) for analytes for which there are no good screening procedures. In the case of anabolic steroid testing, antisera with acceptable cross reactivity to all of the structurally varied analytes are not available. In addition, the intermittent availability, short shelf-life, and variable lot-to-lot performance of commercially available class-specific antisera make them inappropriate for routine screening in a laboratory with contract constraints. As a result, we found that GC/MS analysis of all specimens, without so-called screening, was the only reliable method of testing for abuse of anabolic steroids. However, such a program requires a high volume of samples to be put through the mass spectrometer, which we found can best be handled by tandem mass spectrometry.

As an example, Figure 1 illustrates the quantification by GC/tandem mass spectrometry of endogenous testosterone in a specimen of human urine in a selected reaction-monitoring experiment (4). Steroids isolated from urine by solid phase extraction were derivatized to form the methoxime, t-butyldimethylsilyl ether derivatives. For testosterone, the fragmentation of the molecular ion (m/z 431) by loss of C4H9· (to yield m/z 374) was monitored along with the corresponding fragmentation for the deuterated analog, d5-testosterone. As can be seen, testosterone can be detected and quantified in <6 min, clearly separated from epitestosterone. Fragmentations corresponding to the anabolic steroids of interest can be added to the fragmentations monitored. Because all the commercially available triple-quadrupole mass spectrometers we evaluated (5) allow many different transitions to be monitored in specific time windows, even minimal gas-chromatographic separation of the analytes can allow a large number of transitions to be monitored with acceptable dwell times. A GC/tandem mass spectrometry experiment can, therefore, be developed for the needed number of compounds in a chromatographic analysis that takes 5–8 min. Thus the use of tandem mass spectrometry allows, in a relatively high volume analysis scheme, reliable testing for anabolic steroid abuse entirely by GC/MS.

References
5. Finnigan-MAT Corporation, TSQ 70, San Jose, CA. VG Maaeslab, Trio-3, Altringham, U.K. Delai-Nermag Corporation, R 30-10, Houston, TX.

Michael Kinter
James R. Shipe
John Savory

Clin. Labs., Dept. of Pathol.
Box 168
Univ. of Virginia Med. Center
Charlottesville, VA 22908

Interpretative Reporting of Laboratory Results

To the Editor:

I read with great interest the editorial concerning interpretive reporting by Dr. Killingsworth in the May issue of Clinical Chemistry (1). Having directed a clinical endocrinology laboratory for 17 years, I agree with all of the points listed concerning the relevancy and use of the lists of numbers generated and reported. I believe that laboratory data can be interpreted by the clinical chemist, and in many cases more effectively so than by physicians who use the data as an aid in treating their patients.

Fig. 1. Quantification of testosterone by isotope dilution in a human urine specimen with GC/tandem mass spectrometry monitoring the fragmentations m/z 431–m/z 374 and m/z 433–m/z 376, where A is peak area in arbitrary units.

2178 CLINICAL CHEMISTRY, Vol. 34, No. 10, 1988