blood groups. Two factors contribute to the probability of discrepancy and thus to the power of this method: the power will be higher if the number of blood groups is higher or if the frequencies are more similar.

References

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Guidelines and Recommendations in Laboratory Medicine

To the Editor:
Dr. Keffer (1) has provided a thought-provoking report on the noncompliance of physicians with most clinical practice guidelines (CPGs). He also refers to the Laboratory Medicine Practice Guidelines (LMPGs) produced by the National Academy of Clinical Biochemistry (NACB). As contributors to several LMPGs (2–4) and active participants in the NACB LMPG program, we offer some insights into the rationale of NACB and how the NACB LMPG process differs from that of CPGs authored by other professional societies. We discuss some reasons for the difficulty in assessing impact and suggest unrecognized impacts of these guidelines.

Most CPGs are aimed at physicians and have focused on clinical practices for a disease (e.g., asthma) or symptom (e.g., chest pain). By contrast, the intended audience for LMPGs includes not only physicians, but also clinical laboratorians and manufacturers of clinical assays. These guidelines include recommendations on the appropriateness of offering certain tests for particular clinical situations and for denying or limiting the availability of other assays. These changes and their effects may be difficult to document, but consensus recommendations can prompt manufacturers to construct new assays, such as the urine immunoassay for methylenedioxymethamphetamine (Ecstasy) as recommended (3).

Because of their potential impact, all NACB LMPGs are presented and thoroughly discussed in sessions at national meetings, and an estimation of the degree of consensus is sought. The proposed guidelines are also presented at other meetings where pertinent disciplines are represented (e.g., cardiologists, emergency medicine physicians, clinical toxicologists, and endocrinologists). This may be unlike some CPGs that are prepared and published by experts, but without open presentation.

Although traditional “evidence-based” documentation is noted for many NACB recommendations [e.g., randomized control trials (5,6)], other recommendations do not lend themselves to support by outcome studies. The NACB guideline for testing of newborns (7), for example, recommended that testing for alkaline phosphatase isoenzymes not be performed. It was impractical to perform a randomized trial to support this recommendation. In the NACB guideline for emergency toxicology testing (3), a 1-h turnaround time was recommended for reporting of test results. There are no outcome studies to show that this improves the clinical management of intoxicated patients or reduces length of stay in an emergency department. It is expected, nonetheless, that external expert opinion (in the consensus guidelines) will lend credence to the opinions of the local community of laboratory practitioners.

Dr. Keffer (1) attempted to show through a Medline search and other means that there are few, if any, published evaluations of the NACB guidelines. We suggest that the impact of guidelines can be better measured by citations in laboratory procedure manuals (in hospitals and commercial laboratories), manufacturers’ literature and product labeling, and internal documents used by industry to set performance requirements for their products. These occurrences are difficult to monitor, but we believe they are more accurate measures of the value of NACB LMPGs.

Clinical and laboratory guidelines are reached by consensus-building and may not alter practice in most settings because they are already based, at least in part, on what most practitioners feel should be the standard of practice. That standard is largely established based on the collective current practical experiences of those practitioners. This concept has recently been addressed in the area of clinical practice in an editorial by van Walraven (8). Guidelines of this nature thus are likely to change practices more drastically at the fringes than they are to move the central tendencies of practitioners. Indeed, it is our opinion that they may not be accepted as guidelines in the mainstream of clinical practice unless they represent the practices already in use by the mainstream and that the mainstream often has little to change to be in compliance with these guidelines.

The alternative view is that just because everyone is adhering to a particular practice does not make it optimal. Eventually, widely used but antiquated tests and methods must be replaced with new ones. Ultimately, recommendations must be a balance between consensus and an evidence-based approach. However recommendations are derived, codification can document and firmly establish a standard from which to build.

Dissemination of guideline information requires improvement. The
NACB recently conducted an informal e-mail survey of 2596 foreign and domestic doctoral members of AACC and NACB concerning familiarity with and use of the NACB guidelines. Overall, only 148 replies were received. This low response rate alerted the NACB leadership to a potential need for wider dissemination of these guidelines, and efforts are underway to use the Internet and other means to facilitate this.

In the NACB survey, although the numbers were small, there was an indication that when the guidelines were used, they were used in ways that met the original objectives of NACB. Among 57 clinical laboratorians who reported that they had used the guidelines, 60% indicated that they specifically selected tests, reagent sets, or products that followed the guidelines; 21% indicated they told their vendor representatives what their companies had to do to be in compliance; and 14% indicated that they had modified a vendor’s procedure to be in compliance with the guidelines. Among 16 industry laboratorians who responded to industry-focused questions, 6 indicated that their companies used the guidelines in product design (such as sensitivity, specificity, and choice of analytes), and 8 indicated that their companies use the guidelines in customer education.

One of the reasons for these somewhat less than ideal survey results is that the first four NACB guidelines were presented during satellite meetings of the AACC annual meetings, whereas more recently, the guidelines have been presented at EduTrak sessions at the AACC meeting in addition to meetings of cosponsoring medical societies. Moreover, the first four guidelines were published in monograph form only, whereas the latter guidelines have also been published in peer-reviewed journals (2, 5, 6). With the exception of the thyroid guidelines, of which >50 000 copies were distributed, <5000 copies of the monographs were usually printed. More recently, beginning with the guideline for cardiac markers (2), the NACB has posted preliminary versions of the guidelines on the NACB web page and invited e-mail commentaries. This combined approach has led to more widespread recognition of their existence and broader participation in formulating the recommendations made therein.

We applaud Dr. Keffer’s efforts in bringing this important issue to the forefront. The process of creating new guidelines warrants discussion to improve the products and assess their impact.

References

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α1-Microglobulin Is Stable in Human Urine ex Vivo

To the Editor:

Increased concentrations of urinary α1-microglobulin may imply proximal tubular damage (1). α1-Microglobulin has generally been considered to be stable in human urine (1, 2). Tencer et al. (2) observed good stability in 10 urine samples stored at room temperature for 7 days, at 4 °C for 30 days, and at −20 °C for 6 months. In contrast, Donaldson et al. (3) noted significant losses of α1-microglobulin in urine stored at −20 °C and that this problem was exacerbated in more acidic (pH <6.0) urines; they recommend that urine should be neutralized on receipt. The manufacturers of our assay recommend that urines be assayed fresh or stored at 4 °C for a period of less than 1 week and warm against freezing samples. Urine samples are often stored before batch analysis. To clarify the appropriate storage conditions for urinary α1-microglobulin, we studied stability under standardized conditions.

Random unpreserved urine samples were collected from 19 patients at a single nephrology clinic, and urinary pH was determined (mean pH 5.87; range, 5.08–6.85). Samples were then divided into two aliquots, one of which was neutralized (mean pH 7.58; range, 7.23–7.94) by drop-wise addition of 5 mol/L NaOH. Within 6 h of collection, α1-microglobulin and creatinine were measured in both aliquots. Ten (~1 mL) each aliquot of both the untreated and neutralized urines were stored in capped polystyrene tubes at room temperature, 4 °C, −20 °C, or −80 °C.