Home Testing: To Do or Not To Do?

One cannot enter a supermarket or drug store today without being aware that a home-use test kit can be placed in one's shopping basket along with fruits and vegetables or cough and cold remedies. I have even seen discount coupons offering $5.00 off the price of an ovulation test kit!

In the current issue of Clinical Chemistry, Daviaud et al. (1) discuss the reliability and feasibility of several home-use test kits for pregnancy. These authors have performed one of the most comprehensive studies to date on home testing. They evaluated the ability of 638 laywomen in France to carry out pregnancy tests using generally available home test kits unassisted by professional laboratory personnel. The main points made by these workers were that (a) only 11 of the 27 kits available on the market in France (1 of the 27 kits was made in the US) were sufficiently specific and sensitive to be used in the survey; (b) users of the pregnancy kits experienced considerable difficulty in understanding or following the instructions; (c) ~50% of 478 positive urine samples were falsely interpreted as negative; and (d) these problems were unrelated to the socioeconomic class of the user.

In a letter to the New England Journal of Medicine, Iosefsohn and I (2) noted similar results with the use of home test kits, but with several differences. First, in the hands of experienced technologists in our laboratory, all test kits used in our survey (all kits were made in the US) were sufficiently specific and sensitive to be used in the survey. Second, in a much smaller sample than in the French survey, we found only 10% false-negative results. Third, after watching laypersons perform the tests, our impression (not reported) was that the difficulty in interpreting the kit instructions was related to the educational level of users. It might be of interest to explore some of the reasons for the large differences in the percentage of false-negative results between the two studies.

Our group of laypersons included only hospital employees, and they may have been more motivated to do the test correctly than were the French subjects, who were from the general population. Therefore, our study may have been biased in a positive direction. Had we expanded it to include the general public, our false-negative results might have approached the 50% reported by the French group.

A second possible reason relates to differences between the US and France in the extent to which the respective governments exert premarket control on home-use test kits.

Home-use test kits for blood and urine glucose, pregnancy, ovulation, and fecal occult blood are currently on the market in the US. Kits for cholesterol testing at home are likely to be available soon, and there is much discussion now about the possibility that home testing for the AIDS virus, HIV, will be made available. Whatever the test, under the law it must be evaluated and approved, prior to marketing, by the US Food and Drug Administration (FDA), specifically by the Office of Device Evaluation. What form does this evaluation take? Is it possible that the FDA does not exert adequate supervision over manufacturers of test kits? Might such lack of supervision be responsible for the large number of false-negative results and for the difficulties experienced by kit users in performing and understanding the test instructions?

The rules promulgated by the FDA for ensuring that home-use test kits (in vitro devices, or IVDs in the parlance of the FDA) are of high quality appear to be stringent, at least on first glance. Manufacturers must submit documentary evidence that the tests are "safe and effective" and that the "risk:benefit" ratio is acceptably low. For example, in their premarket submissions to the FDA, manufacturers must supply evidence that (a) the test kits perform as well as their professional equivalents; (b) the device's performance will not be adversely affected by the anticipated variations in user techniques and intelligence; (c) a quality-control test is provided or built into the device; (d) the directions for use are simple, concise, and easy to use (with liberal use of pictorial explanations), and provide adequate warnings and precautions; (e) reagents are color-coded where practicable; and, (f) consumer field evaluations have been carried out. For requirement (f), the following must be submitted: the criteria used to select the study participants, with evidence that the selection was unbiased; and questionnaires answered by the participants, showing that they read and understood the directions and conditions for use of the test, understood the test's purpose and the meaning of the results, understood the test's limitations, and, after conducting the test, visited a health care professional.

In considering whether or not the FDA should be blamed for the failures of the kits or the failures of the users, one must keep in mind that the FDA is neither required nor equipped to conduct independent studies of the kits. As long as a manufacturer makes a proper premarket submission, the law requires that the FDA grant it permission to market the device. As with pharmaceuticals, the FDA relies on the integrity and veracity of the manufacturers of test kits, a reliance that history shows may sometimes be misplaced.
In sharp contrast, according to Daviaud et al. (1), home test kits in France are not regulated by any specific legislation other than by a general advisory published by the Ministry of Health. The French government plans to oblige manufacturers of home-use test kits to meet the same standards as for laboratory diagnostic kits, but I do not know whether these obligations, when they come into effect, will be as extensive as those promulgated by the FDA in the US. Because the test kits used in the French study were coded, it is not possible to evaluate the performance of individual kits. Such information might have been useful in understanding the reason for the high percentage of false-negative results.

Reading and understanding the instructions provided with home-use test kits are major factors in their success or failure. When we observed laypersons performing pregnancy tests, we found that steps were often omitted. Some tests were poorly designed from a psychological point of view. For example, in one kit a positive test was indicated by a colorless solution and a negative test by a colored solution; the person using this kit obtained the correct result but interpreted it in reverse, perhaps believing that anything colored had to be positive. It is important, therefore, that both negative and positive controls be included in such kits. Like the French group, we also found that the written instructions in the leaflets accompanying pregnancy tests are too long and too complicated for the typical layperson to follow. This might be a particular problem for inner-city teenagers using pregnancy test kits.

FDA rules require that home-use test kits provide a separate information sheet that discusses and lists any foods, medications, or other substances that could possibly interfere with the results. With pregnancy tests it is known that a false-negative result may be obtained if the kit user is concurrently taking carbamazepine and that the result may be falsely positive if the user is taking methadone, chloridiazepoxide, or promethazine. Proteinuria or hemoglobinuria may also lead to false-positive results. With fecal occult blood tests the results can be falsely negative as the result of vitamin C intake, and Young (3) lists over 100 substances that may lead to false-negative results.

Even when a test kit provides lists of medications or endogenous substances that might interfere with the test or produce false-positive or -negative results, a layperson using the kit might not know the name of the prescription drug that he or she is taking or understand the biochemistry of the test. It is unlikely that the user of such a kit would seek out professional advice about this potential because to do so would defeat the primary reason for doing the test at home.

Why should we be so concerned with the number of false-negative results? First, the French experience of 50% false-negative results suggests that the results from home test kits are no better than those obtained by flipping a coin. Second, from a practical viewpoint, it is more important to have no false-negative than no false-positive results, although one would prefer to have no false results at all. A false-positive result, although possibly alarming to the patient, would probably result in a visit to a physician. In contrast, a false-negative result could give the user a false sense of security, and he or she would be unlikely to seek medical advice until it was, perhaps, too late. For example, if a pregnancy test was falsely negative, it might result in delay to the point at which abortion could not be performed safely. However, even false-positive results can have serious consequences, ranging from the technical to the psychological.

The question of whether or not we, as professional clinical laboratorians, should condemn or endorse home testing is clearly complex, and the answer may depend on the test in question and public policy considerations. Are tests for HIV infection or the presence of drugs of abuse more fraught with difficulties than tests for urine glucose or pregnancy? Can the potential economic losses due to home testing and the psychological consequences of the results outweigh the convenience and cost savings of doing tests at home?

The marketing pressures are such that I see no reversal of the trend toward home testing. It therefore behooves manufacturers of home-use test kits to develop one-step methods, provide short and clear instructions with liberal use of pictorial examples, and include both positive and negative controls (preferably built-in). One might also expect colors to be used to represent positive reactions and a lack of color to indicate negative results, and methods to be developed that are free from interferences. This is a formidable task, and there may be a role for clinical chemists in assisting in such developments.

References

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