Minimally invasive or noninvasive testing offers many advantages. It relieves the anxiety patients feel about needles, lowers the risk of exposing laboratory professionals to blood-borne diseases, and reduces the turnaround time for test results.

Researchers have directed much of their effort to blood glucose, finding ways for diabetic patients to monitor their levels easily and frequently. As devices for measuring other analytes are developed, factors that will determine their success or failure become apparent.

**Microbilirubin**

The handheld BiliCheck (SpectRx, Norcross, GA) measures the concentration of bilirubin in the forehead skin of 1- to 8-day-old newborns, says Phyllis Hlavac, RNC, MN, perinatal clinical nurse specialist at Atlanta’s Northside Hospital, which delivers 14,000 babies per year. “The system requires no reagents, and results are available in 15 seconds,” says Hlavac.

“The first step is to insert a disposable covered tip (one for each patient) into the battery-powered hand held device,” Hlavac says. “Then you press a button that causes the device to calibrate itself. When the calibration is done, you remove the cover to expose the clean tip used in the test. You place the device on the baby's forehead and apply a small amount of pressure to make light shine from the device onto the skin of the baby. The device prompts you until you have 5 readings, which the computer averages.”
Hlavac and her group participated in the BiliCheck FDA (Food and Drug Administration) trials and have used the system routinely since November 1999. Before implementing this device, they used a technique that allowed them to measure skin bilirubin levels only in white newborns or term newborns. "At that time, the technology could not differentiate skin thickness or skin color," says Hlavac. "We can use the BiliCheck on any race of baby of 34 to 42 weeks' gestation; this includes older premature babies [34-37 weeks]."

According to Hlavac, the BiliCheck device directs white light into the skin and measures the intensity of specific wavelengths returned to the device. From these data, the device determines the level of bilirubin in skin and uses this to calculate the concentration of bilirubin in the blood. "The system must first subtract the known interfering skin components," says Hlavac. "When we compared values obtained by a variety of nurses with those of traditional laboratory methods, we obtained a correlation coefficient of 0.96."

Hlavac says the main advantage of the BiliCheck is the speed with which it produces results. "The parents want to take the baby home, and they are thrilled that the test is noninvasive." She adds that the BiliCheck test costs 20% to 25% of what it costs to do a serum bilirubin level.

Hlavac cautions that the BiliCheck cannot give valid results for newborns undergoing phototherapy. "The incident light chemically changes the subcutaneous bilirubin (which the BiliCheck measures)," she says. "When this occurs, you can no longer relate the skin bilirubin level to the blood bilirubin level; the phototherapy changes the physiologic dynamics between the two." Hlavac adds that the system is also not designed to measure adult bilirubin levels and that measurements on newborns must be done only on the forehead. "Jaundice starts on the face of babies, then moves down the body," says Hlavac. "You get different bilirubin levels at other sites on the body, and only the readings taken on the forehead correlate to blood levels."

Hlavac does not use the BiliCheck if the newborn's forehead has hematomas or bruises resulting from a difficult delivery. In addition, a large birthmark or a lot of hair on the forehead invalidates the results, she says.

Hlavac uses the BiliCheck only if the newborn appears yellow. "You begin to see jaundice at 5 to 6 mg/dL (86 to 103 mmol/L) in serum for a thin-skinned Caucasian baby," she says. "If the serum bilirubin concentration ever exceeds 20 mg/dL (342 mmol/L), or after an exchange transfusion, you switch to serum bilirubin. Our physicians agreed to switch to serum bilirubin—the "gold standard"—when the meter reading exceeds 15 mg/dL (256 mmol/L) or when clinical outcome becomes an issue. That's why we will never get entirely away from serum bilirubin levels."
Prothrombin Time

The INRatio system (HemoSense, Milpitas, CA) for prothrombin time (PT) will soon be available for routine use, according to HemoSense CEO Larry Cohen. "The system is designed for use by people taking oral anticoagulants such as Coumadin (warfarin sodium)," he says. "The patient inserts a test strip into the battery-powered meter, lances a finger, places a drop of blood on the test strip, and reads the results on the display in 2 to 3 minutes." He adds that the user can read both the PT and the international normalized ratio (INR) on the display.

According to Cohen, the INRatio system measures PT electrochemically. "There are tiny silver electrodes on the strips," he says. "Each strip contains dried reagents in 3 test areas—1 for the patient blood sample, 1 for the high control, and 1 for the low control. When the patient puts a drop of whole blood on the test strip, the blood flows to the 3 test areas, and the coagulation reactions begin. Because blood conducts electrical current, the conductivity changes as the clot develops. The instrument converts the change in electrical signal to PT."

"The controls ensure the integrity of each strip," says Cohen. "Although the INRatio does not display control values, it displays an error message if the control values fall outside the acceptable range (as determined by the device)." Cohen says HemoSense has filed with the FDA for professional point-of-care use and will soon file for self-testing approval.

According to Cohen, the INRatio is also sensitive to heparin anticoagulant in its assessment of PT. "Heparin is given intravenously in hospitals, and warfarin is given orally," says Cohen. "The sensitivity to heparin is an issue only during the crossover period when the patient is being prepared for discharge from the hospital. The doctor will not permit the outpatient use of the INRatio until the patient is taking only warfarin orally and is stable; by this time, the heparin will have left the circulation."

Cohen says the new system will dramatically improve care for patients taking oral anticoagulants because the patients can determine their INR more frequently from the measured PT. "The data show that patients who test PT frequently are in the therapeutic range for warfarin more often than those who test their PT infrequently," he says.

Helicobacter pylori

The Meretek UBT [urea breath test] Breath Test for Helicobacter pylori (Meretek, Nashville, TN) offers a noninvasive and economical alternative to endoscopy in diagnosing and monitoring peptic ulcers, says Connie DeHaan, RN, clinical researcher for Enrique Carter, MD, owner of Advanced Medical Diagnostics, Pasco, WA.

DeHaan says she can obtain the necessary breath samples from a patient suspected of having H pylori infection in 35 minutes. "The patient fasts for 4 hours to empty the stomach," says DeHaan. "Then we give a high-carbohydrate
pudding that delays gastric emptying. Five minutes later we take a breath sample and give the patient a dose of Pranactin, a synthetic urea labeled with nonradioactive carbon 13. After 30 minutes, we take another breath sample. If H pylori is present in the stomach, it will act on the urea to produce the enzyme urease, which the stomach breaks down to ammonia and carbon dioxide. DeHaan adds that the carbon dioxide travels through the bloodstream to the lungs, where it is expelled and collected for analysis by mass spectrometry.

According to DeHaan, the mass spectrometer allows her to measure the ratio of carbon 12 to carbon 13 in the first breath sample (baseline) and compare it with the ratio in the second breath sample. “If the second ratio is 2.4 units or more above the baseline level, we consider the test positive for H pylori,” says DeHaan. DeHaan has used the Meretek UBT test since June 1999.

To give a breath sample, according to DeHaan, the patient must breathe into one end of a balloon-like plastic bag. “The bag has a port on the other end that fits into a blood-collection tube,” says DeHaan. “The patient blows up the bag, then we seal the bag and concentrate the sample in the blood collection tube. The sample can be tested in-house or sent to a laboratory with a mass spectrometer.”

Peptic Ulcers and Helicobacter pylori

Although traditional view holds that peptic ulcers arise from hypersecretion of acids (typically in the stomach), Helicobacter pylori is thought to alter the normal mucosal activity, making the mucosa more vulnerable to damage by acids. One theory proposes that urease synthesized by H pylori converts urea to ammonia, which may wear away the mucous layer, leading to epithelial damage. Another suggests that cytotoxins and enzymes produced by H pylori may degrade the mucous layer, also leading to epithelial damage.

According to DeHaan, the mass spectrometer is calibrated with 4 internal quality control gases. “We calibrate the mass spectrometer every day,” she says. “We use our own breath in a blood collection tube and our quality control gases that have known values. When our values fall within the acceptable range, we are ready to run patient samples. After every 10 patients we run a set of quality control gases.” She adds that if she runs more than 30 samples in 1 day, she calibrates the mass spectrometer a second time.

DeHaan says the breath test has 97.8% specificity and accuracy as shown in the clinical trials conducted in the United States, Europe, and Canada. “Some people measure antibodies to H pylori in the blood,” says DeHaan. “But that test can come up positive 3 to 5 years after the disease has been treated and the bacterium is destroyed.”

According to DeHaan, recently taken antibiotics, Pepto-Bismol, and proton-pump inhibitor medications interfere with the results. “If a patient comes in with symptoms, Dr Carter does an initial endoscopy, because even if the patient tests positive for H pylori, there may be other conditions present,” she cautions.
The Fate of Point-of-Care Devices
According to Robert Sunheimer, MS, MT(ASCP)SC, SLS, a variety of factors will determine the success or failure of minimally invasive devices. As associate professor, Department of Clinical Laboratory Science, Program in Medical Technology, State University of New York, Upstate Medical University, Syracuse, NY, Sunheimer teaches courses that include such point-of-care technologies.

Physician Acceptance
"Physicians are slow to change," says Sunheimer, "particularly to methods with limitations such as those of the handheld bilirubin devices." Sunheimer states that traditional methods don't have these limitations, and physicians will continue to rely on these methods, which they trust. "We've seen this reluctance even with point-of-care instruments that have been on the market for awhile," he says. "In our laboratory, improvements in turnaround time of traditional test methods have discouraged their use." Sunheimer also suggests that regulations in some states may require that these devices be used under the laboratory state license, even though federal regulations permit their use by nonlaboratory personnel.

Profit Margins
Sunheimer has doubts that manufacturers of the new devices can turn a profit by the time physicians accept them. "They are expensive to operate, especially in volume," he says. "Not only that, other manufacturers have..."

Hemoglobin, Hematocrit, and WBCs in the Microcirculation
According to Ted Voboril, marketing analyst of Cytometrics (Philadelphia), Cytometrics’ Hemoscan provides a noninvasive way to determine the key components of a CBC—hemoglobin level, hematocrit, and WBC count.

"The Hemoscan is a portable instrument with a hand held probe" says Voboril. "The technologist places the probe under the tongue of the patient, like a thermometer. The probe emits light that reflects from the target (tissue) to a tiny camera." The result, according to Voboril, is an image of blood flowing through the capillaries. "The image is similar to what we would see if the light were shining from behind the tissue," says Voboril. The data gathered by the probe are used to determine the hematocrit, hemoglobin level, and WBC count.

According to Voboril, the system uses orthogonal polarization spectral (OPS) imaging to produce these real-time images of the microcirculation—arterioles, capillaries, and venules—..."
designed random access, high-throughput instruments that will do many different tests, and with consistently short turnaround times.” Sunheimer also questions what market share these new devices will capture. “So far I’ve not seen any laboratory altering its 5-year plan for equipment or staffing in response to these devices,” he says. “Laboratory managers are looking at volume, automation, and efficiency within the traditional laboratory, and this force is in competition with bedside testing. We also have new ways of communicating results through tube systems that permit turnaround times of less than an hour to the emergency department or operating room.”

**Conclusion**

Sunheimer sees opportunities for medical technologists, but not with the use of noninvasive testing devices. “I can’t see technologists or technicians running from the laboratory to the bedside and back,” he says. “There is already a shortage of qualified people in laboratories because so many medical technology schools have closed down. Supervisors just can’t spare them to leave the laboratory.”

Despite his skepticism, Sunheimer admits that minimally invasive or noninvasive testing will improve patient care. “Pain is a patient-driven factor;” he says, “and patients with diabetes or coagulation problems will be much more willing to do frequent home testing if they can do it without pain.”

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