

## Lab 'errors' often prove for the better

Each year, U.S. hospitals perform hundreds of millions of laboratory tests under physicians' orders. But a new study suggests that for approximately half the patients who undergo certain diagnostic blood tests, the tests performed by laboratory technologists aren't exactly what the doctor ordered.

The pattern would be more troubling, the researchers conclude, but for a second finding, perhaps even more surprising: In most cases, the tests performed were more appropriate than those the physician ordered.

"We were really quite surprised," says Albert F. Finn, a physician at the State University of New York at Stony Brook and coauthor of the study. The results, he says, reflect the increasingly complex world of laboratory medicine, in which many physicians may not take into account subtle differences between diagnostic tests. The study, Finn and others conclude, points to the need for improving the way physicians order lab tests and to the need for better communication among physicians, clerical staffers who transcribe doctors' orders, and laboratory personnel.

Finn and his colleagues report in the May 6 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION that they looked at changes made by ward clerks and laboratory personnel on orders for a variety of thyroid function tests on 181 patients at two hospitals. They chose to look at thyroid function because the tests are commonly ordered and because there is widespread agreement about which tests are appropriate for different clinical conditions.

In what the authors call "a disturbing finding," they report that nonphysician hospital staff added or deleted one or more tests from the original orders for 54 percent of the patients. However, the researchers report with surprise, "The net effect of changes to orders. . . was to reduce the number of inappropriately tested patients from 37 percent to 25 percent." Although the changes significantly improved the physicians' orders, Finn and his co-workers conclude that such "errors in the transmission of information" are "unacceptable." Virtually all state laws and hospital bylaws require that only physicians order lab tests.

Despite the apparent slap on the wrist, the finding provides a boost for medical technologists, who at times express frustration over a perceived lack of recognition for their role in the diagnostic process.

"At bottom, the laboratory professional and the attending physician are necessary collaborators, each relying on the other for their special roles in patient care," says Donna M. Meyer, president of the Washington, D.C.-based American So-

ciety for Medical Technology, which represents 22,000 nonphysician clinical laboratory specialists. Responding to the researchers' suggestion that "ancillary workers" be given guidelines to help them identify and inform physicians about "unorthodox laboratory test orders," Meyer said in a statement: "The real need, rather, is for the recognition that laboratory technologists are no longer the 'ancillary' workers of past decades, but are professionals whose body of knowledge is required for effective, efficient health care."

The researchers acknowledge in their report that laboratory technologists can in many cases improve on physicians' orders through their use of "informal, knowledge-based rules." They also credit computer-based ordering menus used at one of the hospitals for assisting clerks and technologists in their "reinterpretation" of doctors' orders. Previous research has shown that computer-based

ordering menus combining complementary tests under practical, diagnostic headings can improve physicians' selection and interpretation of laboratory tests.

Clerks using computer-based systems "were probably trying to make the best fit," Finn said in an interview. "Although unintentional, it resulted in them sometimes picking tests that were more acceptable or appropriate than [those] originally ordered."

Hospital accreditation commissions, the federal government and the media have voiced increasing concern about the accuracy of tests performed at clinical laboratories. However, Finn says, little has been said about the accuracy with which doctors' orders are followed.

"Things are getting incredibly complex, and I think physicians would gladly welcome well-designed test panels or other kinds of aids to ordering tests," Finn says. Meanwhile, he adds, "I think more attention now will be paid to what the physician actually orders and what . . . actually gets performed." — R. Weiss

## A *raison d'être* for heat-shock proteins

Cells of all organisms respond to heat or other stresses by making complex molecules called heat-shock proteins. Other heat-shock proteins exist in unstressed cells and seem to play a role in normal cell maintenance. Such a ubiquitous group of proteins, conserved through billions of years of evolution, must be important — yet no one has been able to say for sure just what purpose they serve.

Now, two separate groups of scientists have provided a partial answer. They report that one family of heat-shock proteins helps move other critical proteins across membranes inside the cell.

Proteins are essential to cell reproduction and functioning. But where these proteins are produced may not be where they are needed. Inside cells with nuclei are specialized structures called organelles that are separated from the rest of the cell by a membrane. For example, an organelle called the mitochondria requires protein and oxygen to produce the high-energy molecule ATP, one of the cell's basic fuels. Cellular protein, however, is created outside the organelles in the general area called the cytoplasm, and must cross a membrane to get into the organelle that needs it.

Just as it is difficult to thread a needle with tightly bunched-up string, it is difficult for globular proteins to pass through membranes. Sometimes, important proteins use heat-shock proteins to help get across the membrane and into the targeted organelle, report scientists from the University of California at Berkeley, the University of Wisconsin in Madison and Rockefeller University in New York

City, in two papers in the April 25 NATURE. The scientists speculate heat-shock proteins assist other proteins through membranes by grabbing them and unfolding them, thus presenting the organelle with a less globular, straightened protein.

Both groups of scientists looked at the same kind of heat-shock proteins, but one group studied those proteins in yeast cells while the other looked at an *in vitro* simulated cell system. Both found that without heat-shock proteins, other important proteins built up outside the organelles, unable to enter.

One of the proteins unable to cross membranes on its own is critical for making ATP in the mitochondria; without ATP a cell would die, and yeast cells unable to make heat-shock proteins don't last long, says Berkeley researcher Raymond Deshaies. His group looked at the buildup of only two proteins in yeast cells lacking heat-shock proteins, but he says many other proteins probably depend on heat-shock proteins to assist their movement across membranes, and heat-shock proteins probably perform many other functions as well.

Heat-shock proteins might also re-adjust incorrectly folded proteins by grabbing them, unfolding them and letting them fold back together in the correct way, says molecular biologist Hugh Pelham of Cambridge University, in an article accompanying the papers. Such proteins, he suggests, might be a boon to genetic engineers and others who are trying to pull individual protein molecules from the insoluble globs of protein often produced by engineered cells.

— C. Vaughan