

Gauging the value of carcinogen assays

Long-term rodent studies to establish the potential human carcinogenicity of a chemical can take up to five years and generally cost well over \$1 million. Since the carcinogenic potential of an estimated 50,000 widely used chemicals has not yet been established, researchers often turn to quick, in-vitro assays, like the "Ames test," in deciding which chemicals to run through the expensive, but more conclusive animal tests first. These assays test a chemical's ability to induce DNA damage.

But how predictive are they of carcinogenicity—at least in rodents? Four of the most commonly used, including the Ames mutagenesis assay, are all about 60 percent predictive, according to researchers with the National Institute of Environmental Health Sciences (NIEHS) and Information Systems and Networks Corp., both in Research Triangle Park, N.C. Moreover, they report in the May 22 *SCIENCE*, little is gained by subjecting a chemical to a battery of more than one of these assays, even though each assay picked up somewhat different subsets of the chemicals shown to be carcinogenic in rodents. The reason, says NIEHS's Michael D. Shelby, is that while subsequent assays pick up some carcinogens missed by the first test, they also contribute additional false positives and false negatives.

"What you're really interested in," he says, "is not the number of carcinogens found, so much as [an accurate] discrimination between carcinogens and noncarcinogens." After testing 73 chemicals, the researchers conclude that "no battery of tests constructed from these assays improved substantially on the overall performance of the [Ames] . . . assay." The other assays tested for chromosome aberrations, for swapping between chromosomes of one of their paired strands of genetic material, and for lymphoma-cell mutagenesis.

While describing the *SCIENCE* paper as "very good," Carnegie Mellon University economist Lester B. Lave does challenge some of its conclusions. He and Gilbert S. Omenn, dean of the University of Washington School of Public Health in Seattle, have suggested the cost of a false-positive finding of chemical carcinogenicity might be \$1 million, and the cost of a false-negative, \$10 million — based on their estimates of costs associated with pulling a safe chemical from commerce or not protecting humans from one that is truly dangerous. If one weighs the four assays in the *SCIENCE* paper for their false-negative/false-positive rates, Lave says one can no longer conclude they all perform equally. While the Ames test still comes out ahead, he says, a battery of tests can now offer somewhat better discrimination of hazard risk than any one assay

alone.

Work by Fanny K. Ennever and Herbert S. Rosenkranz at Case Western Reserve University Medical School in Cleveland have used assay-misidentification rates to determine which assay results are inconclusive. Ennever says their data show that if these inconclusive results are eliminated, in contrast to the NIEHS findings, "the battery does indeed do

better than the Ames test alone."

The Case Western scientists have also found that identifying true carcinogens is not always an assay's most valued asset. If the cost of false negatives is very high — and it may be to a firm formulating a new consumer product — then the test that most reliably identifies true-negatives or noncarcinogens, would be most useful. On these grounds, Ennever says, the Ames test would not surpass the other three assays in the *SCIENCE* paper.

— J. Raloff

Is now the time for cholesterol screening?

Next to the now-familiar blood-pressure machine at your nearby shopping mall may soon be a cholesterol-screening device. Health officials met last week to discuss a proposed, massive nationwide cholesterol screening program — now spurred on by a recent study showing newly developed testing methods could make "shopping-mall" screening possible.

But medical experts say that nestled among the obvious benefits from knowing and, if results are abnormal, lowering your blood cholesterol are some troublesome aspects, such as the failure of many physicians to adequately counsel patients about cholesterol and the confusion as to what effects lowering cholesterol actually has on health. Abnormal cholesterol levels have been tied to increased heart disease and cancer risk (SN: 1/3/87, p.4), yet the magnitude of cholesterol's effects have been questioned (SN: 4/25/87, p.261).

Representatives from state and federal health departments, medical associations, and industry debated those issues last week in Washington, D.C. at a meeting hosted by Baylor College of Medicine in Houston and the George Washington University Medical Center in Washington, D.C. Discussion revolved around the concurrent release of results from a study by 11 lipid research clinics across the United States that evaluated a rapid, automated assay requiring only a fingerstick sample of blood.

After testing the assay on nearly 13,000 people at schools, work sites, shopping malls and other locations, researchers said last week that new technology has made mass screening for cholesterol a practical goal. The study used a \$4,000 desk-top machine developed by Boehringer Mannheim Diagnostics of Indianapolis, which sponsored the study. According to those reporting the results, the method determines cholesterol levels within three minutes, giving results that vary about 1 to 4 percent from rigorous, standardized laboratory tests used for comparison. With its accuracy, speed and lower test cost (about \$3 per test versus an average \$20 for current testing), the Boehringer machine — and similar equip-

ment from other companies — was touted as the technological vehicle for which mass screening has been waiting.

However, reducing the 550,000 U.S. deaths each year from coronary heart disease will take more than technology, say those who cite studies showing physicians may be reluctant to participate despite public enthusiasm. For that reason, the cholesterol-screening bandwagon may be slow to roll, say scientists and physicians who support a screening program as part of the 18-month-old National Cholesterol Education Program being coordinated by the National Institutes of Health. Baylor's Michael E. DeBakey says that screening for cholesterol "should be just as effective as screening for hypertension [blood pressure] in controlling a major risk factor for coronary heart disease."

Other anticipated problems of widespread screening would be maintaining machines in non-medical settings, as well as deciding who should be screened, and assuring that those with high cholesterol seek medical advice and adjust their diet.

— D.D. Edwards

Colorectal oncogenes found

Using new methods to find genetic mutations, two groups of scientists have found more evidence that genes called oncogenes are a significant cause of cancer. Oncogenes have been found to transform normal cells into cancerous cells. Scientists at the State University of Leiden in the Netherlands and Johns Hopkins University School of Medicine in Baltimore report that over one-third of the colon and rectal tumors they studied contain the *ras* oncogene. Another group at the State University of New York in Stony Brook and the University of Alabama at Birmingham found similar results using a different assay method that also detected gene mutations, which apparently convert normal *ras* genes into the oncogenes found in malignant cells. The two independent studies are reported in the May 28 *NATURE*. □