IN FOCUS

PRETESTING TUMORS

Long derided, test-tube screening for cancer-drug sensitivity slowly gains acceptance

On January 22, 1997, doctors diagnosed 40-year-old Randy Stein with pancreatic cancer and told him he had three months to live. Two years later, Stein is working out with a trainer twice a week, planning his next vacation and launching an Internet business to help cancer patients. "I'm doing fabulous," he declares. "It's a miracle." He beat the odds, he says, because his doctor used a test aimed at predicting which drugs would kill his tumor—"a test most oncologists don't order.

Conventionally, oncologists rely on clinical trials in choosing chemotherapy regimens. But the statistical results of these population-based studies might not apply to an individual. For many cancers, especially after a relapse, more than one standard treatment exists. "There is rarely a situation where you would get everyone to agree that there's only one form of therapy," says Larry Weisenthal, who runs Weisenthal Cancer Group, a private cancer-drug-testing laboratory in Huntington Beach, Calif. Physicians select drugs based on their personal experience, possible side effects and the patient's condition, among other factors. "The system is overloaded with drugs and underloaded with wisdom and expertise for using them," asserts David S. Alberts, director of prevention and control at the University of Arizona cancer center.

Given Stein's particularly poor prognosis and limited treatment options, his physician decided to look for drugs that might have a better chance of helping him than the "standard" regimens. So surgeons sent a part of his tumor to Weisenthal, who along with other researchers has developed a handful of techniques for assessing cancer "response" in
the test tube. They grow tumor cells in the presence of different drugs and assess whether the drugs kill the cells or inhibit their growth.

This idea of assaying cancer cells for drug sensitivity has been around since the 1950s. A 1970s technique sparked considerable enthusiasm until studies revealed numerous problems: fewer than 50 percent of tumors grew even with no drugs present, for example, and it took weeks to generate results.

“The rank-and-file oncologists drew the whole idea after the [1970s] assay proved to be a bust,” says Dwight McKee, a medical oncologist in Kalispell, Mont., adding that they equate all cancer-drug response tests with failure. Researchers have since improved the assays and can now obtain results in several days for many cancers.

If a drug allows cancer cells to grow in the test tube, even at exposure levels toxic to humans, chances are very good that it won't thwart the tumor in the body, according to John P. Fruehaufl, medical director of Oncotech, another cancer-drug-testing laboratory, in Irvine, Calif.

The idea is that physicians could rule out those treatments, and patients could avoid side effects from ineffective agents. “Current ways of treating people are almost as long as with what this test can do,” states Robert Fine, director of the experimental therapeutics program at Columbia University.

Such tests also provide information that enables physicians to devise unconventional therapies, emphasize Weisenthal and Robert A. Nagourney, medical director of Rational Therapeutics, a drug-testing company in Long Beach, Calif. In Rand Stein’s case, for example, Weisenthal suggested a drug combination not routinely used for pancreatic cancer. In other cases, Weisenthal and Nagourney abandon standard therapies entirely. Several dozen studies, most of which measured tumor shrinkage, have suggested that “patients treated with drugs that killed cells in the assay do better than patients in the overall population and much better than those treated with ‘assay-resistant’ drugs,” Weisenthal says.

But many physicians aren’t convinced of the tests’ utility, in part because for many cancers, they more accurately predict what won’t work rather than what will. Four of the five oncologists Stein consulted advised him against having them done. “They said, ‘Things react differently in the human body than they do in the test tube,’” Stein recalls. Indeed, the tests do mimic many aspects of human biology—drug delivery by the bloodstream, for example. “I’m thrilled for Randy, but what’s to say that the assay significantly affected his treatment course or outcome?” points out Lee S. Rosen of the University of California at Los Angeles Jonsson Comprehensive Cancer Center.

A revised national policy might eventually take the issue out of the hands of Medicare intermediaries. “We’re reexamining the current noncoverage policy and are developing a draft policy so we can get comment from the medical community,” comments Grant Bagley of the Health Care Financing Administration in Baltimore. “The existing medical evidence suggests that the tests are not experimental and may be medically reasonable and necessary in at least some situations. The question is under what circumstances we should pay for it.”

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