

CANCER

The best tests to find a killer

BY KATHERINE HOBSON

The perfect screening test for cancer? "Whatever finds my disease in time to treat it," most patients say. Doctors have a longer description: A good test has to be very well balanced. It must find early signs of the disease without mistakenly diagnosing illness in well people—or missing those signs in sick ones. It can't be so unpleasant that no one wants to be screened, and the test's expense has to be justified by how many cancers it catches. Only a handful of established procedures meet these criteria. Those include blood tests to find prostate cancer, mammograms for breast cancer, and colonoscopy for colorectal cancer.

But there are newer tests. Some are more sensitive or accurate than existing screens, according to studies released last week. Even more exciting: Some detect lung and ovarian cancers, for which there is currently no good screening. (Those two diseases alone will kill nearly 172,000 Americans this year.) They present a very real opportunity to save lives by catching cancer earlier.

As with any cutting-edge technology, not all the glitches have been worked out, making the decision to get a new test confusing, and many are not covered by insurance. "Saying 'I've got to have this test because it's the newest' isn't exactly right," says Bernard Levin, vice president of cancer prevention at M. D. Anderson Cancer Center in Houston. Doctors say the tests may be most appropriate for some people who are at especially high risk for cancer because of family history or some other factor.

LUNG CANCER

This is a disease crying out for an early warning: It kills more Americans than any other form of cancer, and five years after diagnosis, just 15 percent of suf-

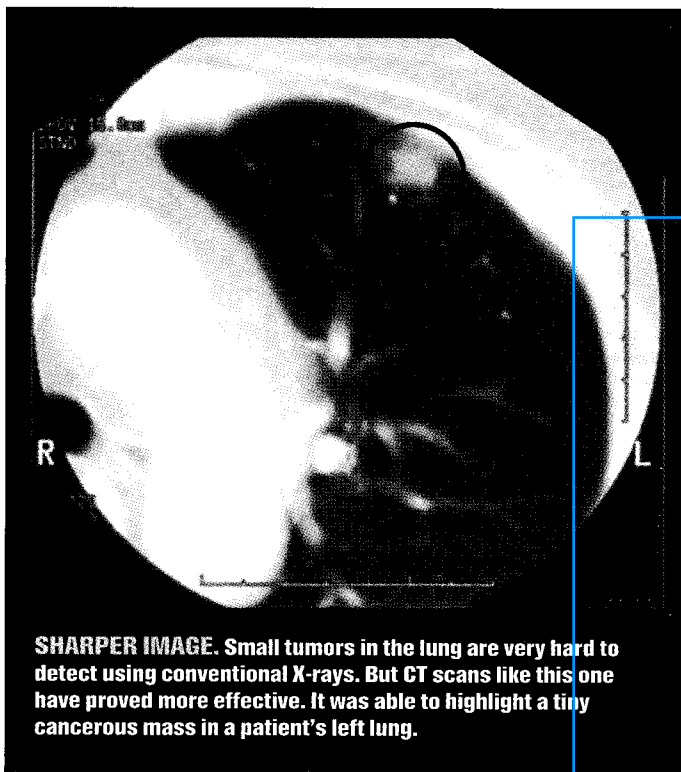
ferers are still alive. Currently, the American Cancer Society doesn't recommend any early detection tests, because none have been proved to enhance survival. But many think CT scans, which can pick up smaller tumors than can a regular X-ray, could be used to screen those most at risk—all smokers over age 50, and people that age who have quit within the past two decades. The test takes X-rays from many angles and combines

gressive disease. And such a sensitive test means that many noncancerous lesions will be picked up, prompting false alarms. (Last week, however, a study in the journal *Lancet* showed that positron emission tomography, another type of scan, can cut down on these false positives when used together with CT.) Patz says he's waiting for the results of a National Cancer Institute long-term trial of several screening methods before recommending CT. If you do opt for the test, doctors say, be sure you find a radiologist with lots of experience reading lung CTs, and don't go to the full body scan booth at the local mall; accuracy takes a practiced eye.

One new test for lung cancer may not even require donning a hospital gown; simply breathe into a tube for two minutes, and a tabletop device collects and measures the presence of organic compounds in your breath. Developing tumors appear to trigger a certain pattern of these compounds. Test developer Michael Phillips, an internist at the New York Medical College, says the concept sounds wacky, but it works: A recent study in *Chest* showed that a pattern of nine compounds predicted 85 percent of lung cancers. Early studies also show the test can detect a different pattern that indicates breast cancer. But because the device needs Food and Drug Administration approval—something that may happen next year—before it can be used, the tests aren't currently available.

BREAST CANCER

Efforts to screen for breast disease focus on tests like mammograms, recommended annually for women over 40. Yet mammograms still miss as many as 30 percent of cancers; in high-risk women—who tend to have dense breasts—they do worse. But in June, researchers reported that magnetic resonance imaging, or



SHARPER IMAGE. Small tumors in the lung are very hard to detect using conventional X-rays. But CT scans like this one have proved more effective. It was able to highlight a tiny cancerous mass in a patient's left lung.

them in a computer into high-resolution images. Results from the ongoing federal Early Lung Cancer Action Project have shown that CT scans can find lung cancer earlier, at a presumably more curable stage. A recent study in the journal *Chest* reports the screening not only works but is cost-effective—it costs society about \$2,500 per year to save one life, much better than current screens for other cancers.

Not everyone thinks CT is a great solution, however. Skeptics like Duke University radiologist Edward Patz suspect that finding even tiny tumors comes too late to save people from the highly ag-

MRI, detected 96 percent of tumors in high-risk women without symptoms. A similar study on a different group also yielded encouraging results.

So should all women demand an annual MRI? Absolutely not, says David Dershaw, director of breast imaging at Memorial Sloan-Kettering Cancer Center in New York. In the general population, the vast majority of lesions found will be benign, which means a lot of unnecessary biopsies and anxiety.

But women who have already had a breast tumor, are carrying genes strongly associated with cancer called BRCA1 or BRCA2, or who have a strong family history of the illness might consider the test. "When we find something, the likelihood that it's cancer seems to be higher in the high-risk population," says Dershaw.

Neither MRI nor mammography, however, is sharp enough to detect abnormal cells before they lump together in a tumor. But another screening tool, ductal lavage, does seem able to do that for high-risk women. A doctor anesthetizes the nipple, then inserts a tiny flexible catheter into breast ducts and flushes out cells to be analyzed (graphic). If the cells are precancerous, women can take steps to prevent the disease, including more frequent monitoring and taking preventive drugs like tamoxifen. Because many abnormal cells never turn into cancer, the test is for high-risk women only. "A lot of women have an abnormal Pap smear that turns out fine, and you have the same problem with ductal lavage," says William Dooley, director of surgical oncology at the University of Oklahoma College of Medicine. False negatives are also a possibility, since not every duct is tested. But Dooley says despite the lack of big studies, high-risk women who show signs of breast abnormality, such as fluid from the nipples, should "think strongly" about the test.

OVARIAN CANCER

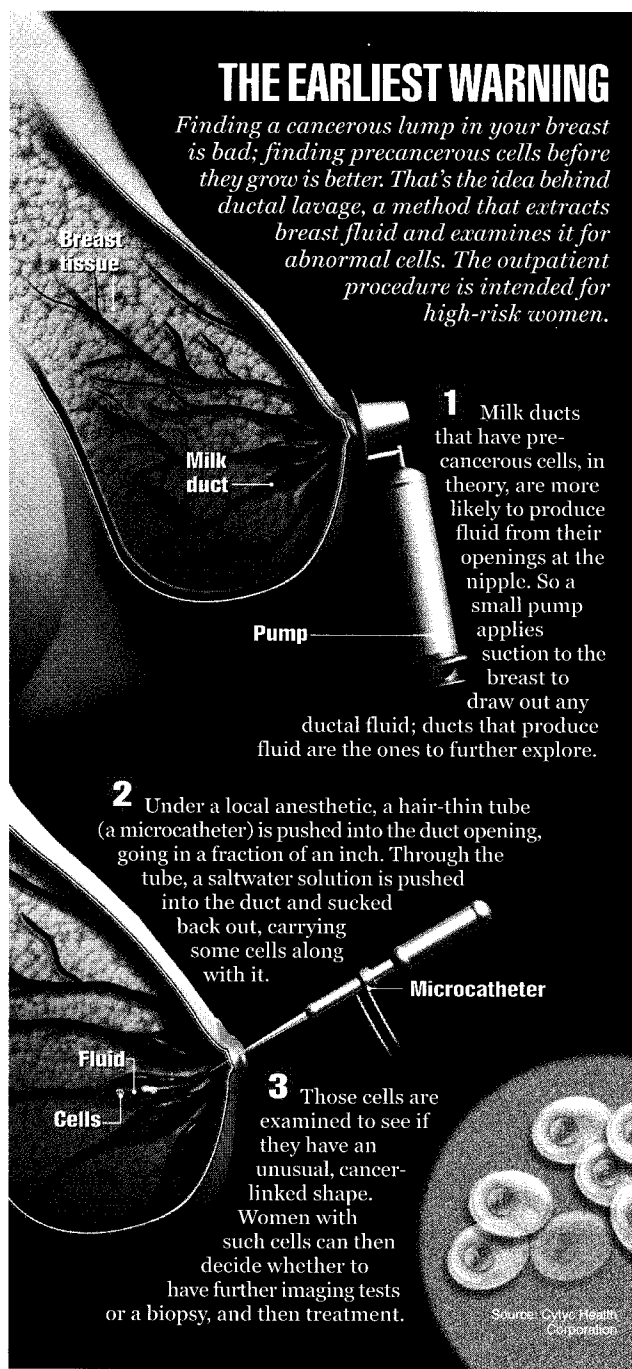
Unlike breast disease, there are no tests to screen for ovarian cancer, which has

few early symptoms and is especially deadly when caught late. (A blood test measuring a protein called CA-125, now used to monitor the progress of ovarian cancer patients, is not a good screening tool because it fails to pick up about half of the cancers.)

But researchers have higher hopes for a test called transvaginal ultrasound, which uses a narrow tamponlike probe inside the vagina to search out ovarian tumors. At the University of Kentucky Chandler Medical Center,

THE EARLIEST WARNING

Finding a cancerous lump in your breast is bad; finding precancerous cells before they grow is better. That's the idea behind breast fluid and examines it for abnormal cells. The outpatient procedure is intended for high-risk women.



where the technique has been studied for more than 15 years, researchers have shown that the screen is pretty good at picking up ovarian cancers. In a group of more than 20,000 women either over 50 or with a family history of ovarian cancer, the test identified tumors in 29 people. Most of those cancers were at the more treatable stage. Ever better, the five-year survival rate among those women was 88 percent, compared with the national average of 53 percent. (That may sound like a lot of screening to find a few cancers, but in fact it's in line with other screening tests like mammography.)

"In our view, it helps detect ovarian cancer, but we need large trials to prove that," says John van Nagell, director of gynecologic oncology at Kentucky. (The ultrasound technique is being evaluated in a large NCI study.) If you have a strong family history of ovarian cancer, speak with your doctor about ultrasound.

COLON CANCER

There's already a highly effective screening test for colorectal cancer: colonoscopy. It works; it's just not much fun to have a tube inserted through your rear and all the way up your colon. So people avoid it. Less intrusive tests, like one that detects blood in the stool, aren't as accurate.

But another option is coming to a lab near you later this year. PreGen-Plus is a different kind of stool test that doesn't find blood but instead detects mutated DNA shed

from tumors. It's not as accurate as colonoscopy, missing as many as a third of cancers, but it's better than the current stool test. And if the test is positive, a colonoscopy is the next step. This will, doctors hope, increase the total number of people being screened. "Not doing any test at all is tragic," says Sidney Winawer, a gastroenterologist at Sloan-Kettering and member of an advisory board for Exact Sciences, the test's developer. Anyone at risk for cancer would agree. ●