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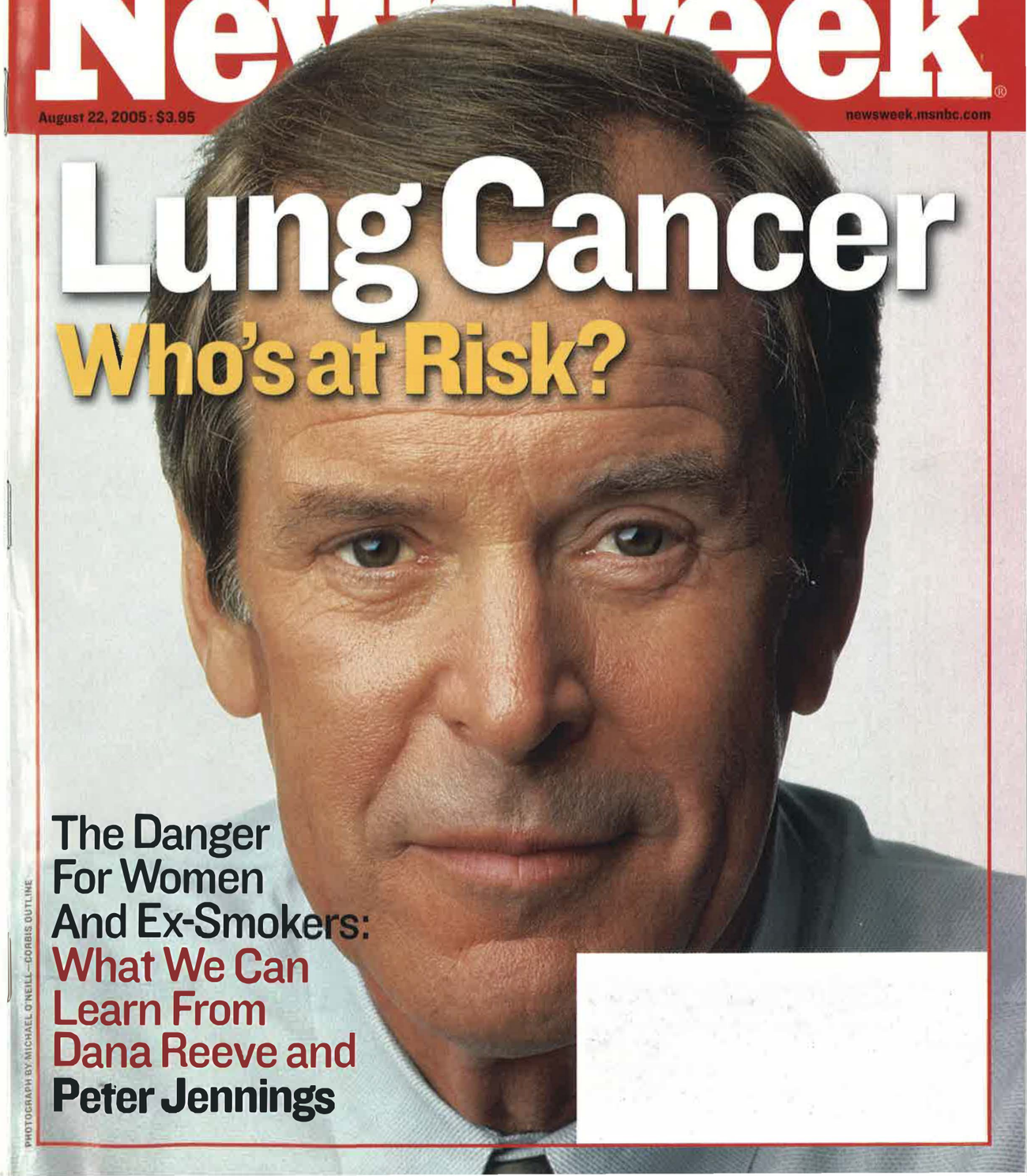
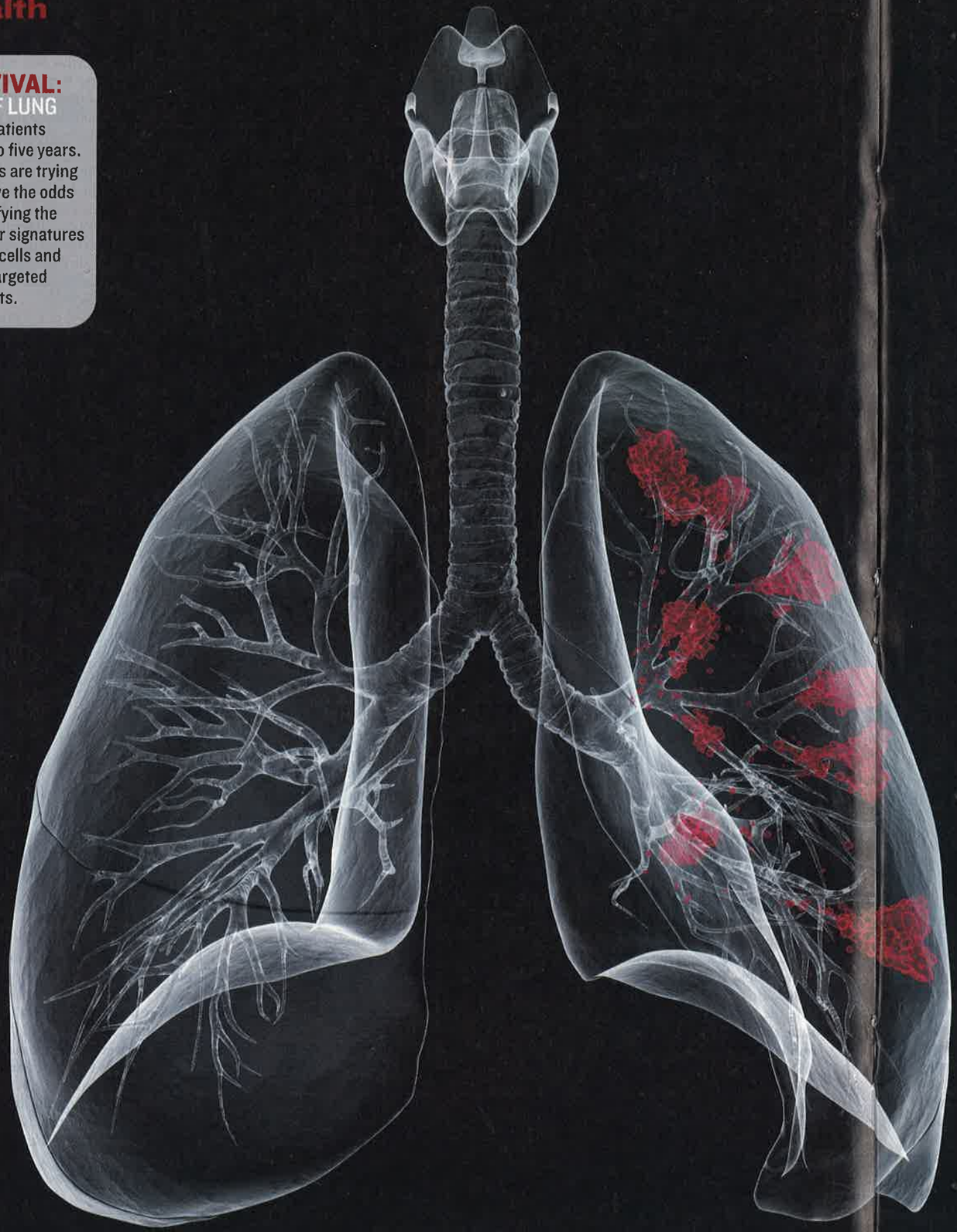
Lung Cancer
Who's at Risk?



PHOTOGRAPH BY MICHAEL O'NEILL—CORBIS OUTLINE

The Danger For Women And Ex-Smokers: What We Can Learn From Dana Reeve and Peter Jennings

SURVIVAL: 15% OF LUNG cancer patients make it to five years. Scientists are trying to improve the odds by identifying the molecular signatures of tumor cells and testing targeted treatments.



The Deadliest Cancer

Lung Cancer kills more Americans than any other type of malignancy—and some of the victims never smoked. But despite grim statistics there is some good news: fresh research offers hope for earlier diagnosis and more-effective treatments.

BY GEOFFREY COWLEY AND CLAUDIA KALB

WITH THE NEWS LAST WEEK THAT FORMER smoker Peter Jennings had succumbed to lung cancer at 67 and Dana Reeve, who never smoked, was diagnosed with the disease at 44, millions of Americans grasped a terrible truth—the deadliest form of cancer doesn't strike just the pack-a-day crowd. Suddenly lung cancer was everyone's concern. And rightly so. Lung cancer may not inspire walkathons or pink-ribbon awareness campaigns, but after three decades of the War on Cancer and four decades of surgeon generals' reports, it remains the most devastating of all malignancies. The disease kills some 160,000 Americans a year—more than breast cancer, colon cancer and prostate cancer combined. The burden has grown steadily in recent decades, thanks to the rising inci-

BRIAN SNYDER—REUTERS/LANDOV

NONSMOKER: Reeve is among an overlooked minority being diagnosed

ILLUSTRATION BY BRYAN CHRISTIE FOR NEWSWEEK

dence among women, and survival rates have scarcely budged. Nearly 60 percent of patients still die within a year of diagnosis, and 85 percent die within five.

The vast majority of cases are smoking-related, but curbing the use of tobacco isn't the only challenge we face. America's 46 million former smokers still constitute a huge reservoir of risk. And people who smoke don't all suffer the same consequences. Why do some stay healthy, even as nonsmokers are stricken? Are women more susceptible than men? And what are the prospects for earlier detection and more-effective treatment? Can science save other former smokers from Peter Jennings's fate? Researchers are the first to acknowledge the daunting challenges they face. But health officials are making new commitments—the National Cancer Institute unveiled a new research initiative last week—and after decades of discouragement, some researchers are voicing cautious optimism. Geneticists are zeroing in on mutations that may make some people vulnerable. Biologists and radiologists are devising new ways to detect small, localized tumors. And new treatments are beginning to extend survival times, even for advanced-stage patients. "That's not a home run," says Dr. David Johnson of the Vanderbilt-Ingram Cancer Center in Nashville, Tenn., "but it's hardly a bunt single."

SURGING: 80,660 WOMEN were diagnosed with lung cancer in the U.S. last year, as 68,510 women died from it. Smoking has caused a 600 percent increase in women's lung-cancer death rate since 1930.

The causes of lung cancer are no great mystery: some 87 percent of all cases result directly from smoking. Whatever your age, sex, race, occupation or family history, the surest way to protect yourself is to avoid smoking or to quit. Unfortunately, quitting doesn't completely negate the genetic damage that tobacco smoke causes in lung tissue, so former smokers remain more vulnerable than nonsmokers. How much more vulnerable? It depends on how long you smoked, and how heavily. "If you smoke a pack a day for 20 years or more, you have a 50 percent chance of dying from smoke-related disease," says Dr. Norman Edelman, the American Lung Association's chief medical officer. "There is a linear relationship between total smoke exposure and risk for cancer." But the risk declines markedly as healthy cells replace damaged ones in an ex-smoker's lungs. After 10 years of abstinence, a quitter is only half as vulnerable as someone who continues to smoke.

Even among smokers, the risk is not equally distributed. Nelson Mallary took up smoking at the ripe age of 9 and kept at it for more than six decades, burning through 60 butts a day and laughing off generations of friends and relatives who pestered him about quitting. "I was convinced I would never get cancer," he says. At 83, the Atlanta psychotherapist is still cancer-free (he finally gave up cigarettes in his 70s), but he has since learned a few things about the vagaries of the disease. The first blow came in 2000, when lung cancer killed his 43-year-old stepson. Just three years later, his biological son met the same fate. Both men shared their father's addiction. Unfortunately, neither shared his luck.

> "What was difficult was people automatically assumed I smoked. You'd never say 'How'd you get it?' to someone with breast cancer."
>
> —MELISSA ZAGON, 37, NONSMOKER WITH LUNG CANCER

What, aside from smoking, might shape a person's risk? Environmental pollutants are clearly part of the story. The most important ones are radon, an odorless natural gas that can seep into homes and buildings from the soil, and industrial substances such as asbestos and arsenic. Age is another important risk factor (incidence rises sharply after 50). And like most malignancies, lung cancer is strongly linked to family history. People with affected parents or siblings suffer two to three times the usual risk themselves, compared with other people with the same risk factors, and researchers are now homing in on at least two genes that could help explain that phenomenon. In a study completed last year, a team led by geneticist Marshall Anderson of the University of Cincinnati Medical Center analyzed blood and tissue samples from 52 high-risk families, and traced their shared risk to a small region of human chromosome 6. The goal is to pinpoint "susceptibility genes," inherited mutations that make some people especially vulnerable to the cancer-causing agents in cigarettes and the environment. If labs could test for those mutations—as they now do for breast- and colon-cancer genes—high-risk people could be singled out for special precautions, intensive screening and possibly even personalized treatments.

Genes aside, growing evidence suggests that women are uniquely vulnerable to lung cancer. Most of the 600 percent increase they've suffered over the past eight decades can be tied directly to smoking. But when researchers look at the minority of lung cancers involving nonsmokers, a curious disparity emerges. Whereas nonsmokers account for just 10 percent of lung cancer among men, they account for twice that fraction among women. What could explain the discrepancy? Hypotheses abound, but one of the most compelling centers on estrogen, a female reproductive hormone with well-known links to breast and ovarian cancer. Cells taken from lung tumors are covered with estrogen receptors, and the tumor cells proliferate faster when exposed to the hormone in test tubes. Jill Siegfried, a pharmacologist at the University of Pittsburgh Cancer Institute, has documented the same effect in lab mice, and she suspects that something similar is happening in young women's bodies. If she's right,

ALIVE: Lung-cancer survivor Anita Johnston, 75

NO PUFF: Kathleen Reding quit 14 years ago

CARRYING ON: Zagon (center), nonsmoker and lung-cancer survivor, with some fellow members of the LUNGevity Foundation

TOP TO BOTTOM: PHOTOGRAPH BY PETER YANG FOR NEWSWEEK, PHOTOGRAPH BY JUSTIN NEWHALL FOR NEWSWEEK

PHOTOGRAPH BY JACK BRIDGES FOR NEWSWEEK

On the Trail of a Stealthy Killer

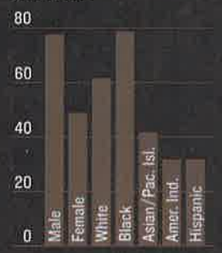
Lung cancer often isn't detected until it's too late for effective treatment. The disease, which is projected to strike 173,000 Americans this year, claims more lives than any other cancer. Researchers hope more funding will bring better therapy.

TAKING ITS TOLL

TOP CANCER KILLERS, IN THOUSANDS, 2005*

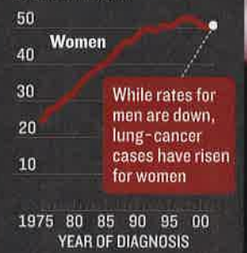
Lung/bronchus	**164**
Colorectal	56
Breast (female)	40
Pancreatic	32
Prostate	30
Leukemia	23
Non-Hodgkin's lymph.	19
Ovarian	16
Liver	15

CASES PER 100,000 PEOPLE, 1998–2002



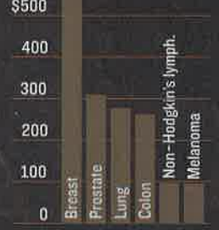
HARD HIT

LUNG-CANCER CASES PER 100,000 WOMEN



FUNDING

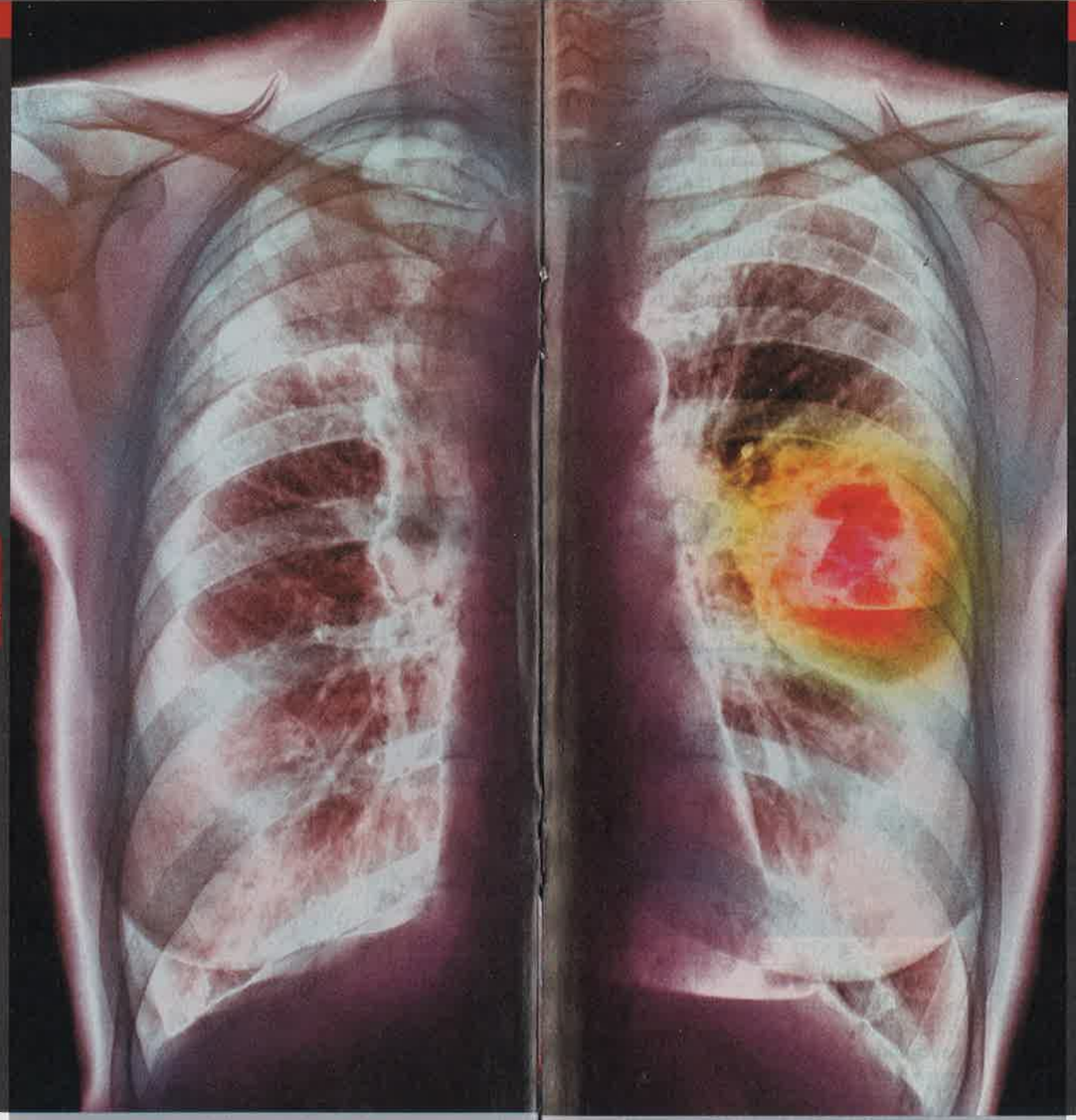
RESEARCH DOLLARS, IN MILLIONS, 2004†



CHANCES OF SURVIVAL

PERCENTAGE OF PEOPLE STILL LIVING FIVE YEARS AFTER A CANCER DIAGNOSIS, 1995–2000

Pancreatic	4%	Laryngeal	65%
Liver	8	Uterine cervical	73
Esophageal	14	Urinary bladder	82
Lung/bronchus	**15**	Uterine corpus	85
Stomach	23	Breast (female)	88
Ovarian	44	Melanoma	91
Oral cavity	59	Testicular	96
Colorectal	63	Thyroid	97
Kidney	64	Prostate	99



SCREENING: Colored chest X-ray showing a cancerous tumor (in red and yellow). Lung cancer is difficult to detect early.

drugs that suppress estrogen could open a new frontier in treatment and even prevention, just as they have in breast cancer.

For people at high risk of lung cancer, the more immediate challenge: to spot the disease at earlier, more-treatable stages. Even today, patients diagnosed with small, localized tumors enjoy a five-year survival rate of nearly 50 percent, but few are so lucky. Lung cancer tends to develop silently, causing none of the classic symptoms (hoarseness, wheezing, coughing, chest pain), until the tumors are large and dispersed. By the time they get a diagnosis, at least three out of four patients already have metastatic disease. Routine chest X-rays have never been found to improve survival rates, but experts are now hoping that a new technique—the so-called spiral CT scan—will succeed where old methods have failed. The machine itself is a wonder. Instead of simply snapping a flat picture of the lungs, it spins around the chest, assembling as many as 400 images into a 3-D model that can illuminate even the tiniest lesions in lung tissue. "On a chest X-ray you can see tumors when they're one to two centimeters," says Dr. Claudia Henschke of New York Weill Cornell Medical Center. "On a CT scan, you can see them as small as two millimeters."

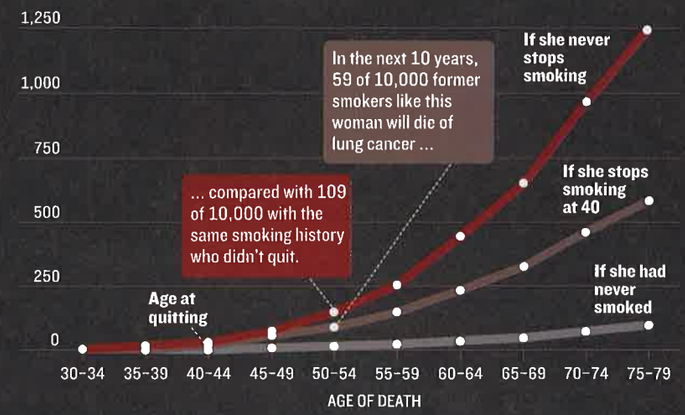
Talk to
Geoffrey Cowley about lung cancer, Aug. 17, at noon, ET, at **Newsweek.com**

The spiral CT has performed well in early trials, picking up operable tumors that traditional X-rays missed and enabling doctors to excise them safely. In a recent international study, Henschke and her colleagues reported that 81 percent of the lung tumors detected through spiral CT screening were successfully removed at early stages—and that 96 percent of the treated patients were still alive eight years later. So why not start screening everyone? With more than 90 million current and former smokers in the United States alone, isn't this a clear opportunity to save lives? In truth, it's too early to tell. No one knows exactly how the tiny tumors detected by spiral CT would behave if they were left untreated. As two NIH experts observed in The New England Journal of Medicine recently, "the apparently longer survival with screening may represent the indolent nature of the tumors that were detected rather than a benefit of screening itself."

CALCULATING YOUR RISK

Prevention is the best medicine for lung cancer. A 40-year-old who smokes a pack a day and started before the age of 18 can reduce her chances by more than half if she stops smoking now. Determine your own risk level at cancercontrol.cancer.gov/tcrb/smokersrisk.

DEATHS PER 10,000 PEOPLE (ONE WOMAN'S ODDS)



CAUSES AND SYMPTOMS

About 87 percent of cases are caused by smoking. But thousands of nonsmokers succumb to the disease each year. Symptoms may be confused with other respiratory ailments.

CAUSES & RISK FACTORS
- Smoking
- Secondhand smoke
- Radon
- Asbestos
- Air pollution
- Lung diseases such as tuberculosis
- Certain genes seem to make people more susceptible

WARNING SIGNS
- Chronic cough
- Hoarseness
- Coughing up blood
- Weight loss
- Loss of appetite
- Fever
- Wheezing
- Repeated bouts of bronchitis/pneumonia
- Chest pain

TREATMENTS

Interventions depend on the type of lung cancer and how far it has progressed.

- **Surgery:** Doctors may remove a portion or an entire lung, depending on the tumor's size.
- **Chemotherapy:** Can target cancer cells that have spread outside the lungs.
- **Radiation:** An option for non-operable tumors. New technologies reduce damage to healthy tissue.

*PROJECTED. †BASED ON NATL. CANCER INSTITUTE FUNDING. SOURCES: NATL. CANCER INSTITUTE, AMER. CANCER SOCIETY, MEMORIAL SLOAN-KETTERING, AMER. LUNG ASSOC. PHOTOGRAPH BY S. FRASER—PHOTO RESEARCHERS, INC.

—JOSH ULICK

You might argue that it's better to be safe than sorry, but widespread screening could pose hazards of its own. A test this sensitive turns up all kinds of suspicious lesions, but it can't readily distinguish the 10 percent that are cancerous from the 90 percent that are not. That can require invasive follow-up tests, in which doctors use needles or scopes to excise lung tissue for analysis. "You end up finding a lot of noise," says Dr. Nasser Altorki, one of Henschke's colleagues at Cornell. "We have to figure out how to zero in on those 10 percent of patients who actually have the problem, without doing harm to the large majority of other patients." One solution is for radiologists to perform a follow-up scan when they find a suspicious lesion, and for doctors to biopsy only those that change or grow over time.

Some physicians now urge the highest-risk patients to consider annual CT exams. At Vanderbilt, for example, Johnson recommends annual screenings for people over 50 who have smoked a pack a day for 30 years (or two packs a day for 15) and who have an underlying lung condition. But health agencies and professional groups have yet to endorse routine screening. They're awaiting the results of a large federal study, launched in 2002 and scheduled to wrap up in 2009, that is designed to clarify the risks and benefits. Early results could come out as soon as next year.

Timely detection is a critical step toward saving lives, but it's only part of the challenge. Though patients diagnosed early fare better than those diagnosed late, half of them still suffer hard-to-treat recurrences within five years. Fortunately, their odds are improving. Recent studies suggest that traditional chemotherapy, administered after surgery, can boost five-year survival to nearly 70 percent. In the past, says Dr. Frances Shepherd of Toronto's Princess Margaret Hospital, patients were sent home after surgery to hope for the best. Today the best cancer centers are urging them to consider chemo.

Meanwhile, newer drugs are targeting tumors in more specific ways. Melissa Zagon—a nonsmoking, 37-year-old mother, wife and lawyer—had little cause for hope when her cancer was diagnosed in 2000. The tumor in her lung had already seeded three more in her brain, one of them the size of a golf ball. But after enduring surgery, radiation and

survival rates will require time, money and commitment—provisions that this disease has traditionally lacked. Unlike the people with AIDS or breast cancer, those affected by lung cancer have struggled vainly to mobilize public opinion—partly because there are too few survivors to take to the streets. Only a handful of charities, most of them local, have focused on raising money for research. "It's not like going out and raising money for a kids' cause," says Joel Massel of the Chicago-based LUNGevity Foundation, a group that Zagon founded with six other lung-cancer patients in 2000. "We've tried desperately to get a celebrity spokesman, but it's been extremely difficult." After more than 30 attempts, the group still lacks one. Public funding has been skewed, too. Last year the National Cancer Institute spent twice as much on breast cancer as on lung cancer—even though lung cancer took four times the toll. But change is in the wind. Late last week the NCI unveiled a new $80 million research initiative aimed at improving early detection, developing new therapies and combating the use of tobacco. "There's been a blame-the-victim mentality for lung cancer," says Dr. Margaret Spitz, the outside adviser who spearheaded the new initiative. "Obviously, we have to do more."

Improving life for today's patients is of course critical. But the world's deadliest cancer won't be beaten by CT scanners and targeted therapies alone. In a tobacco-free world, lung cancer would be an orphan disease, not a pandemic. The ultimate challenge, says Cheryl Healton of the American Legacy Foundation, "is to create a world in which young people reject tobacco, and anyone who wants to quit can." Though smoking rates have declined in recent decades, a quarter of America's kids are still getting hooked by the time they leave high school. Critics insist it's no accident. Last week, just days before the NCI announced its new lung-cancer initiative, the Federal Trade Commission reported that the tobacco industry spent $15.2 billion marketing cigarettes in the United States in 2003 (the most recent year on record)—up from $12.7 billion in 2002 and $6.7 billion in 1998. Studies suggest the money is all too effective, and health advocates despair of countering its impact. "We're spending at best a thousandth of what they are," says Healton, whose tobacco-control foundation grew out of the industry's 1998 settlement of lawsuits brought by the states. The misfortunes of an anchorman and a celebrity widow won't change that dynamic, but giving lung cancer an overdue moment in the spotlight is a start.

With KAREN SPRINGEN, ANNA KUCHMENT and VANESSA JUAREZ

ABC NEWS—AP

LEGACY: Jennings, in Moscow in 1986, championed international news

APPRECIATION

July 29, 1938 - Aug. 7, 2005

Peter Jennings

BY JONATHAN ALTER

The obituaries around the world all had the same basic lead: Peter Jennings of ABC News dies of lung cancer. Jennings himself had a way of getting to the nut of any story. He might have cut to its brutal truth more quickly: "Peter Jennings, a smoker for three and a half decades, was done in on Aug. 7 by a partly self-inflicted wound." For all of his achievements, Jennings's death may prove as influential as his life.

The brief story of Jennings's life is this: Born in Toronto, the son of a well-known Canadian broadcaster, he debuted on the radio at age 9. After dropping out of high school, he went on the air immediately and landed the job of "ABC Evening News" anchor at the preposterous age of 26. He left New York to learn his craft as a foreign correspondent for 15 years and never stopped reporting after he became an anchor again. He combined dashing James Bond looks and a calm anchor style with the best of old-fashioned journalistic values—the search for truth in a world that doesn't always want to hear it. For a quarter century, he covered every big story in the world and often championed international reporting, even when the ratings showed that viewers wanted something less distant. His brave reporting was credited with bringing world attention to war crimes in Bosnia, which eventually helped hasten intervention and end the genocide.

The brief story of Jennings's death is this: He started smoking at age 11 when he stole a pack from his grandmother and showed his sister how to puff. Like many reporters, he became a heavy smoker. During the 1990s, he helped ABC News cover the tobacco story aggressively. He caught tobacco executives in lies, most memorably when one claimed that the "Joe Camel" ad campaign was not targeted at children. On April 5, 2005, he appeared, haggard and hoarse, for the final time on television and explained what happened. "Yes, I was a smoker until about 20 years ago and I was weak and I smoked over 9/11." It is unclear how much he relapsed in the years since but he was still addicted and known to retreat into the bathroom for a furtive smoke. He began coughing and feeling fatigued last fall, but was not diagnosed until March. His cancer was inoperable, though he tried chemotherapy and experimental radiation.

After all the old video deteriorates, Peter Jennings will be remembered most for two things: standing up for international reporting and driving home the risks of smoking. Each, in its own way, has the power to save people's lives. He did, and he will.