Glaciologist Thompson cores ice from the world's loftiest glaciers, seeking to retrieve precious records of ancient climates before they melt away

Ice Man: Lonnie Thompson Scales the Peaks for Science

QUELCCAYA ICE CAP, PERU—As he neared the 5670-meter summit of Quelccaya ice cap in the high Andes, Lonnie Thompson appeared to be suffering. The 54-year-old glaciologist was sinking calf-high in loose snow with each step, gasping in the ever-thinning air, and hacking in violent coughing fits brought on by his chronic asthma. Every 100 paces or so he shoved the metal haft of his ice ax into the snow and hung his head between his knees—"gets blood to the brain," he explained. Then he straightened and started upward again, through dark clouds and whipping snow. "You know, in a way the weather today's a blessing," he said cheerfully. "When the sun's out, it bounces off the snow and blisters the roof of your mouth."

Thompson drills ice cores from Earth's most daunting peaks, a job that has given him an increasingly pivotal voice in how scientists think about climate. Over 3 decades, he has employed yaks, mountaineers, and sheer will power to virtually create the field of high-alpine tropical paleoclimatology. He first defied experts simply by showing it was possible to get deep cores from high peaks. Then he extracted records suggesting that much of the world is climatically more volatile than previously believed, especially the tropics, long regarded as set apart from wrenching polar and temperate-zone upheavals. Now Thompson faces his greatest challenge: Thanks in part to his data, it is clear that mountain glaciers worldwide are melting—fast. Last year he made global headlines by observing that the famous snows of Tanzania's Mt. Kilimanjaro—actually 11,700-year-old ice (see Perspective on page 548 and Report on page 589)—may be gone by 2015. Thus he is on a mission, racing through expeditions to Asia, South America, and Alaska to retrieve endangered samples.

Some researchers disagree with Thompson's interpretations, such as the exact timing and magnitude of ancient climate shifts, but all agree that his daring rescues of the ice and its records make him a rare old-fashioned pioneer. "He's the closest living thing to Indiana Jones, and just in time," says Harvard University geochemist Daniel Schrag. Paleoclimatologist Wallace Broecker of Columbia University's Lamont-Doherty Earth Observatory places him "in the ranks of our great explorers. You can argue about his interpretations, but the thing that will last is his data." Adds James Hansen, director of NASA's Goddard Institute for Space Studies: "If he wasn't doing it, we'd lose those records forever. He's a sort of hero."

In thin air. Thompson and team drilled the highest core ever on Tibet's Dasuopu glacier.

From Gassaway to the Andes

An unlikely sort. Pale and nondescript, unfailingly polite, quiet unless spoken to, Thompson looks like an encyclopedia salesman when he puts on a suit. In poor, rural Gassaway, West Virginia, his parents never made it past eighth grade; but Thompson loved science, setting up weather instruments in the barn and betting lunch money on the likelihood of rain. He met his wife, polar glaciologist Ellen Mosley-Thompson—now a partner in his work and top-ranked scientist in her own right—at their home state's Marshall University, where she was the lone female physics student. "I guess we both just grew up curious," says Mosley-Thompson in her still-craggy mountain drawl. And practical: Thompson planned to be a coal geologist. "I hated poverty," he says. "And West Virginia's full of coal."

Their horizons broadened during graduate work in the 1970s at Ohio State University (OSU) in Columbus, where he got a part-time job analyzing polar ice cores, a field then blossoming. Teams had recently drilled the first deep samples from Greenland and Antarctica, and founding fathers such as Willi Dansgaard of the University of Copenhagen were learning to study ancient precipitation, temperature, volcanic activity, and atmospheric composition from gases, isotopes, and other substances built up in thousands of yearly snow layers. The Thompsons were fascinated—"It started with atmospheric dust, but soon we were looking at all sorts of things," says Mosley-Thompson—and both ended up working on polar drilling operations while working toward doctorates at OSU. Most people ignored the modest, low-latitude alpine glaciers, which presumably had melted, slid downhill, or otherwise eroded too much to hold good records.

Because there are only a few polar drilling operations, competition for jobs was stiff. Mosley-Thompson advanced, becoming a senior investigator on Antarctic drilling projects and chairing the National Science Foundation's (NSF's) Greenland science planning committee by 1985. Thompson, however, felt outcompeted for choice work. His fallback: tales of an unusual ice mass in the remote Peruvian Andes that sounded promising. It had plenty of annual snow to form thick, readable layers; an elevation so extreme they probably stayed frozen; and a flat base of basalt, so they probably never slid off. This was Quelccaya.

CREDIT: L. THOMPSON/BYRD POLAR RESEARCH CENTER/OSU

Its root in Quechua means "to inscribe."

Quelccaya was beautiful and dangerous. In 1974 Thompson and a colleague drove far above timberline to the end of a dirt track used by Quechua-speaking alpaca herders. Two days' walking over raw bedrock and rolling tundra brought them to the great ice dome, surrounded by giant moraines and boulder fields. Scattered herders ventured to the edge, but no recorded person had been on the ice itself; some native people see glaciers as purgatories for damned souls.

Indeed, between their 4900-meter-high off-ice base camp and the 4-kilometer hike to the summit, Thompson discovered the terrors of high altitude: waking up in the black night feeling as if you were suffocating, because you are; searing headaches aspirin can't touch; 21,000-meter thunderheads that drive lightning and loose rocks horizontally over the ground; unfiltered sun that fries flesh like bacon. "I've never sought extreme adventure," Thompson says earnestly. "It scares me. I only want the data."

He proposed drilling, but Dansgaard himself told NSF: "Quelccaya is too high for humans, and the technology [to drill it] does not exist." But Thompson kept at it, and finally in 1979 NSF funded him to fly up a heavy polar-style drill and generator by helicopter—a venture that failed in the first hour, when the pilot veered dangerously in the thin air and declared the trip over.

Thompson went home and talked University of Nebraska engineer Bruce Koci into designing a lighter drill that could be disassembled and powered by solar energy—the first such setup. Thompson slowly collected other collaborators and in 1983 mounted a new expedition with 40 mules, donkeys, and horses to ferry the drill parts to camp and 10 people to lug them over the ice—a low-tech approach that has become his trademark.

Among the members was Koci, who has since designed drills for many polar programs; a high-altitude climatologist aptly named Keith Mountain; and a rock-tough Quechua-speaking mountain guide, Felix Benjamin Vicencio. The core team is still together after 20-some years—a secret to its success, all agree. "We've all lost enough skin and blood that no one needs to be told what to do," says Mountain. "Something breaks, we fix it. Trouble comes, we know to get out of the way."

Mosley-Thompson does not go on the alpine trips, but she is central to the science. She and Thompson are co-principal investigators on all projects, and together they pick sites, write proposals, and analyze data. When he is gone, she directs logistics and their shared lab, still at OSU. Because she works in Antarctica and Greenland, their field seasons are reversed—November to May for her, June to September for him—a perfect arrangement after their daughter Regina was born in 1976, because they could each travel for months, yet always have one parent home. "We both like being captain," says Mosley-Thompson. "At home we have only two topics of conversation: our work and our family."

On top. Thompson's high-altitude adventures began near Peru's Qori Kalis glacier.

CREDITS: (TIMELINE PHOTOS) L. THOMPSON/BYRD POLAR RESEARCH CENTER/OSU; (BOTTOM) THOMAS NASH

The Thompson Record:

▲2002
MT. BONA-CHURCHILL, ALASKA, 4300 METERS

2000
PURUOGRANGRI ICE CAP, TIBET, 6072 METERS

2000
MT. KILIMANJARO, TANZANIA, 5893 METERS

▲1997
DASUOPU, TIBET, 7200 METERS; HIGHEST CORE; STUDENT SHAWN WIGHT DIES

1997
SAJAMA, BOLIVIA, 6542 METERS

▲1993
HUASCARÁN, PERU, 6048 METERS

1992
GULIYA ICE CAP, CHINA, 6200 METERS

1987
DUNDE ICE CAP, CHINA, 5325 METERS

1983
QUELCCAYA, PERU; 5670 METERS; FIRST DEEP CORE OF A TROPICAL GLACIER

1979
MOSLEY-THOMPSON EARNS PH.D., OSU

1976
THOMPSON EARNS PH.D., OSU

1974
FIRST EXPLORATION OF QUELCCAYA ICE CAP, PERU

1970
THOMPSONS GRADUATE FROM MARSHALL UNIVERSITY

Core Skill

On that 1983 Quelccaya expedition, Thompson's team spent 10 grueling weeks climbing daily from camp to the drill. At the end they had taken two cores to bedrock, some 160 meters down. Thompson was triumphant when the cores held what he had hoped: exquisite yearly dust and stable oxygen-isotope records documenting regional weather back to A.D. 470. It was nothing so vast as the 100,000-year-plus polar-ice archives, but it was still the first real tropical ice record. It showed major drying events indicated by thick swaths of dust and wet periods marked by thickened ice layers—probable indications of past El Niños.

Most surprising was that the oxygen isotopes, which vary in precipitation according to temperature, showed major shifts matching the Medieval Warm Period of about 1050–1375 and the 300-year Little Ice Age, which ended around 1880. Before this, nearly everyone had thought that the tropics did not see such swings, because cores of oceanic plankton taken during the massive Climate/Long-Range Investigation Mappings and Predictions Project (CLIMAP) of the mid-1970s suggested they were largely stable even in glacial times, cooling only 1 or 2 degrees C at low elevations.

Many researchers took intense interest. Archaeologists who had theoretically linked climate shifts with the rises and falls of pre-Inca civilizations were delighted; here were the shifts, recorded at the right times, including a 300-year drought starting around 1150 that many believe wrecked the Tiwanaku civilization around Lake Titicaca. "Quelccaya provided precision and time coverage we had never seen in this part of the world," says archaeologist Izumi Shimada of Southern Illinois University, Carbondale. "It was the first, most crucial evidence that such climate events were real."

However, a single 1500-year core was not enough to change all scientists' views of ancient tropical climate—or of the importance of tropical ice cores in general. Many doubted that any tropical ice dated back to the last glacial age, the acid test for a long-term climate record. Thompson needed more and older cores. And over the next 15 years, he got them, in feats that were as much physical as scientific. Ice taken from the Guliya ice cap in remote western China in 1991 and 1992 by Thompson and Chinese colleagues had to be hauled across the Gobi Desert in ancient trucks; once when a drive shaft fell off, the team used ice cream to cool the cores.

South American glaciers were equally daunting. Getting to the drill site on 6048-meter Huascarán, Peru's highest peak, meant dodging daily avalanches and crossing a 10-meter-wide crevasse on a narrow ladder. So in 1993 they hauled up 6 tons of equipment and camped next to the drill for 53 days straight—perhaps a world record for high-elevation living. A gale hurtled Thompson's tent, with him inside, toward a 3000-meter drop, until he jammed his ice ax through the floor. The drillers came back gaunt—and bearing 4 tons of 9-centimeter cores. In 1997 on Bolivia's 6542-meter Sajama, the indigenous Aymara people feared that drilling would anger mountain deities. So before ascending, Thompson and the others took part in a long ceremony that involved chanting, smoking cigarettes, drinking high-test alcohol, chewing coca leaves, and sacrificing a blindfolded white alpaca. Only 2 weeks after bringing down the Sajama cores, Thompson headed to Tibet to core the even higher Dasuopu glacier, at 7200 meters still the world's highest ice-core site (*Science*, 15 September 2000, p. 1916).

There, disaster struck. Like everyone else, 26-year-old OSU graduate student Shawn Wight developed altitude sickness on the climb. But then Wight forgot Thompson's name, and Thompson sent him down the mountain, where he coughed up blood; Thompson took him to a hospital in Lhasa, but complications multiplied. Wight was shuttled to Cleveland, where doctors determined that he had picked up a bacterial infection. Wight died two and half months after leaving Dasuopu. His parents sued OSU for $21 million, claiming that safety procedures were inadequate and that Thompson had reacted too slowly. Three years of legal battles revealed that the group lacked equipment such as oxygen tanks and satellite phones, which Thompson said were too cumbersome and would have made no difference. "The mountains are dangerous," he says. "You can reduce risk, but never eliminate it." In 2001 an Ohio state court ruled that Thompson had acted properly, and dismissed the case, but the affair left him shaken. A lengthy article in *The Chronicle of Higher Education* (27 July 2001) asked "Research at What Cost?"

Friends fear as well that Thompson pushes himself too hard. Once when he was in a Columbus hospital with bloody sputum and blue feet following a trip to Ecuador, a doctor discovered a minor heart-valve defect and advised him never to go to high altitudes again. That was 20 years ago. Six years ago he was also diagnosed with severe asthma, which worsens when he ascends. "It's controlled by drugs," he insisted at Quelccaya, in between hacking bouts.

Ice preserver. Ellen Mosley-Thompson in the cold room at Ohio State.

CREDIT: L. THOMPSON/BYRD POLAR RESEARCH CENTER/OSU

Reading the record

Despite the costs the cores kept coming, and in the mid-1990s the data, published in leading journals including *Science*, began to turn climate scientists around. According to several indicators, Huascarán was 19,000 years old (*Science*, 7 July 1995, p. 46)—well into the last glacial age—and Sajama, 25,000 years old (*Science*, 4 December 1998, p. 1858). The latter date was particularly hard to assail because it was based on carbon-14 analysis of plant matter and insects swept in by snowstorms—a rarity in ice cores.

The oxygen isotopes suggested that South America had been 5 to 12 degrees C cooler back then. Dust concentrations 200 times above present levels showed it was far drier; low nitrate levels suggested the Amazon was probably largely deforested. The ice also showed big postglacial shifts including the dramatic cooling of the Younger Dryas period around 12,000 years ago. This was powerful evidence that the tropics, too, were swept by global climate changes. And similar findings were beginning to come in from paleotemperature records in fossil corals, Andean lake sediments, and Amazon groundwater. Many researchers reversed views and came around to the idea that the tropics are crucial for understanding the past and, therefore, the future.

The Thompsons have "left little doubt about whether long-term climate phenomena are really global," says Ted Scambos, a polar glaciologist at the National Snow and Ice Data Center in Boulder, Colorado. Thompson and others argue that the tropics may in fact drive climate; he points out that much of Earth's landmass, and thus much of its water cycling, resides there. Some speculate that ocean currents may transmit changes from pole to pole via the tropics, or perhaps vice versa, but it's still not clear what drives what.

Debate continues as well over the exact interpretations of the ice data. Whereas Thompson claims that some Himalayan ice is very old—Guliya more than 500,000 years based on radiometric dating of chlorine isotopes—many are skeptical, because there is little supporting evidence. And some researchers, such as glaciologist Gerald Holdsworth of the University of Calgary, complain that Thompson picks sites "for novelty, not science." He and others also question Thompson's interpretation of oxygen isotopes. This involves comparing the amount of ^{18}O versus ^{16}O in each layer and assuming that the heavier isotope is more common in precipitation during warm times, a method other glaciologists pioneered on polar cores. Few doubt that the isotopes represent some kind of temperature shift, but many specialists say that in the tropics the recipe may be affected by additional factors such as changes in moisture sources and seasonal precipitation shifts. "Overall, he's shown the tropics have big swings. It's just a matter of degree," says Geoff Seltzer, a glacial geologist at Syracuse University who works in the Andes.

The Thompsons are the first to admit that the picture is complex, with different regions showing shifts at different times or not showing them at all. But "it's unrealistic to think conditions will be the same everywhere at the same time. That's why we need cores from so many places," says Mosley-Thompson. Recently other groups have entered the field, coring alpine glaciers in the Yukon, Bolivia, and Ecuador, and their studies so far tend to bolster the Thompsons'. "Eventually there will be a coherent picture," says Thompson. "It's complicated, but it's knowable."

Thinning ice

Thompson captured his colleagues' attention with the South American cores, but Mt. Kilimanjaro, Africa's highest peak, made him famous. In early 2000, his team arrived for a month-long coring expedition, toting what some regarded as a suicidal new toy: a specially designed hot-air balloon for lifting cores off the windy 5893-meter summit. The Tanzanian government barred the balloon from the mountain, so Thompson hired 92 porters to carry the cores down. The ice is nearly 12,000 years old, and parts of it appear to align with major climate events shown in other cores. These include a heavy dust band indicating a disastrous drought about 4200 years ago, which also shows up on Peru's Huascarán. Ancient records report that at this time, the Nile stopped flooding and crops failed.

More immediately, in February 2001 Thompson announced that Kilimanjaro had lost 80% of its ice cover in the 20th century and predicted the ice would be gone in 15 or 20 years. This news appeared on the front pages of *The New York Times* and other newspapers, featured as a clarion call of drastic climate change. Thompson points out that the observation came from nothing more than archival images and his updated aerial survey. "All we did was connect the dots. The local people could have told you it's melting just as well as I can." He says that Africa's handful of other glaciers have already melted so much that data probably cannot be extracted from them. "Kilimanjaro is the first, and probably the last ice core from Africa," he mourns.

Going, going ... Thompson estimates that the snows of Mt. Kilimanjaro, seen in 1912 (*right*) and 2000, might be gone by 2015.

CREDITS: (TOP TO BOTTOM) L. THOMPSON/BYRD POLAR RESEARCH CENTER/OSU; E. OEHLER

The picture is the same for nearly all tropical and midlatitude glaciers. In the Himalayas, photos show that some 30 outlet glaciers on 6400-meter Puruograngri, which Thompson and Chinese colleagues cored in 2000, have retreated a kilometer or two since 1972. Highland Peru still has the world's largest concentration of tropical ice—1600 square kilometers—but Thompson estimates that's down from 2000 square kilometers in 1972. One study this year by glaciologist Mark Dyurgerov of the University of Colorado, Boulder, shows that the equilibrium-line altitude, below which glaciers generally lose mass, has risen about 200 meters worldwide in the last 40 years.

Quelccaya, where Thompson started, is a prime example. Aerial photos show that it has shrunk more than a fifth, to 44 square kilometers, since his first trip 28 years ago. This July Thompson made his 17th visit, with old hands including Felix Vicencio and glaciologist Vladimir Mikhalenko of the Russian Academy of Sciences in Moscow, and a *Science* reporter new to high altitude.

From their base camp, a stiff walk leads to a 150-ton granite boulder balanced on a nearby ridge. "First time I came, there was a whole valleyful of ice sticking 20 meters above this boulder, pushing on it," Thompson remembers. He pats the rock like an old friend. Now it sits balanced over an 80-meter drop to a brand-new lake. The ice is 400 meters away on the opposite shore, cracking and groaning in the midmorning sun.

The next day, a several-hour hike over rugged hills and desert takes the party to a wind-torn mesa overlooking Qori Kalis glacier—Thompson's favorite symbol of global climate change. This stupendous vertical ice mass pours into a wide valley from the icecap's edge, but it is wasting away. Survey photos show an exponentially increasing rate of retreat: 4.7 meters a year through 1978, and 205 meters in 2000–2001. "Sit here and you can practically watch it disappear," says Thompson. He has augered shallow cores periodically from the icecap's summit and found that in the past decade melting has percolated through the top layers. "I expect in 20 years I'll come back and see the marks where our drill punched through to bedrock in '83," he says. "Quelccaya will be gone."

All this has made the Thompsons into preachers. They tell anyone who will listen, from 5th-grade classes to Ph.D. colleagues, that humans are warming the Earth. "You have to be blind not to see the changes," says Mosley-Thompson. Says Harvard's Schrag, "[They have] absolutely the most central evidence. ... Nothing like this has happened for thousands of years. Many people have changed their tunes after seeing [their] results."

Melting ice may be not only a sign, but a disaster in itself. The loss of data is "like a great library on fire," says Keith Alverson, director of the Bern-based nonprofit Past Climate Changes, which promotes paleoclimate research. Last month's collapse of a Russian glacier, which killed 120 people, may have been due to rapid melting; the United Nations has identified 44 new meltwater lakes in Bhutan and Nepal that may endanger communities downstream. And glacial meltwater supplies drinking water and hydropower to many nations such as Peru and Bolivia. "You deal with [climate change] or you adapt to it, but either way you have to know what's happening," says Thompson.

The Thompsons have a plan for finding out—they have their eyes on 13 sites worldwide to drill immediately. But it's a daunting list, including peaks in former Soviet republics close to ongoing wars; a 7400-meter Tibetan site even higher than Dasuopu; and Heard Island, a rarely visited speck in the southern Indian Ocean with weather so bad scientists would probably have to work and live under the ice surface. Government bureaucracies are slow with funds, says Thompson, and some ice may melt before he gets to it. So he is soliciting private donors such as media magnate Ted Turner and considering commercial endorsements for say, camping-equipment companies.

His growing celebrity makes this suddenly sound feasible. Until recently, he had never won a big award; after the Kilimanjaro expedition, he was named fellow of the American Geophysical Union, Distinguished Scholar at OSU, and one of America's top scientists by CNN and *Time*. This year so far he has won the $150,000 Heineken Prize from the Royal Netherlands Academy of Arts and Sciences; the Swedish Vega Medal; and, along with Mosley-Thompson (and Julie Andrews and Fred "Mister" Rogers), the Common Wealth Award from PNC Bank. He is the hero of two new books, *El Niño*, by J. Madeleine Nash (Warner, 2002) and the forthcoming *Thin Ice* by Mark Bowen

(Henry Holt, 2003). This summer he returned in triumph to Gassaway as grand marshal of the town's annual parade.

Meanwhile the field work and its risks continue. On the third day at Quelccaya in July, Thompson wanted to hand-augur another short core from the summit, but blowing snow and clouds kept the crew in camp until 9:30 a.m. Then sun appeared and they headed up. They used to race up the ice in 45 minutes, but that was with weeks of acclimatization and 20-some fewer years of age. This day, hindered by snowfall, it took closer to 6 hours. When the top came into view through the bad weather, Vicencio and Mikhalenko, who had arrived first, were turning the light fiberglass drill like a giant corkscrew. Thompson fell on his knees beside Mikhalenko and started logging samples. Presently someone noticed the time. "We started too late," cried Mikhalenko. They stuck the augur upright in the snow without finishing and scrambled to get down before dark; dark can kill in a place like this.

An hour later Vicencio and Mikhalenko emerged from the clouds just in time to see the last glimmers of sun on lakes far below. Thompson was ahead this time and had already disappeared in the gloom. Everyone was headed for a potentially deadly precipice at the ice edge. Vicencio and Mikhalenko are experts, though; reporter in tow, they located the danger zone, skirted it, and descended onto solid ground. There was no sign of Thompson—and they were now in a boulder field laced with dangerous holes nearly invisible in the blackness. Suddenly several bright lights appeared about 100 meters away. It was Thompson. Although he had bashed one leg hard on an unseen rock, he had felt his way down a streambed, found camp, and rifled the tents for flashlights. Then he had come back for his friends.

Next morning, the weather cleared, and Thompson headed straight back up to finish taking the core. –KEVIN KRAJICK

Kevin Krajick is the author of Barren Lands: An Epic Search for Diamonds in the North American Arctic. *He lives in New York City.*

CANCER DRUGS

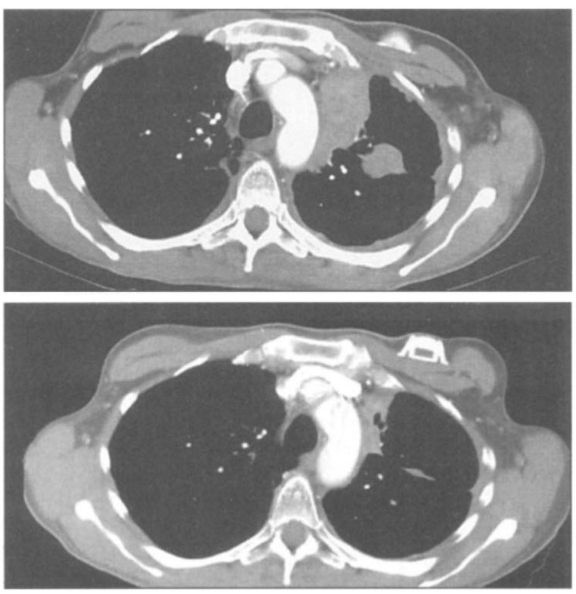
Smart Weapons Prove Tough to Design

Gleevec demonstrated the power of targeted cancer drugs, but applying similar strategies to the treatment of common cancers hasn't been easy

Physicians treating lung cancer grasp at every straw of optimism they can find, as the straws are few and far between: Many patients are diagnosed when their disease has spread and the prognosis is grim. But in a packed hotel conference room in a Maryland suburb last month, optimism occupied roughly two dozen seats near the front—a cluster of patients whose doctors had expected them to die long ago. One, Adriane Riddle, had traveled from San Bernardino, California, to tell the assembled doctors, drug company representatives, and regulators about the miracle drug she believed saved her life when she was diagnosed with metastatic lung cancer two summers ago at a startlingly young age. "It has given me a chance to turn 20," she said of Iressa, an experimental drug in a new class of targeted cancer therapies.

Although Riddle radiated good health, Iressa's future is far from ensured. Data from several clinical trials have been inconsistent, and some have been flatly disappointing. Iressa's creators at AstraZeneca, in London, frankly admit that they have no idea who will benefit from the drug or why—but some clearly do. Even so, Iressa edged a step closer to the market at the 24 September meeting, when the Food and Drug Administration's (FDA's) Oncology Drug Advisory Committee voted 11 to 3 to recommend that the agency approve the drug to treat a common form of lung cancer, known as non–small cell lung cancer.

FDA normally follows its advisory council's suggestions. But at the meeting, the agency voiced concerns about ambiguous clinical trial results, questioning whether the drug works as well as AstraZeneca claims. The agency now has less than 6 months to decide whether to allow Iressa on the market. The lobbying has been intense. Some oncologists, having watched the drug shrink tumors in some patients, inundated the FDA with letters begging it to approve Iressa. And the day the council met, an editorial in the normally staid *Wall Street Journal* attacked the FDA for its reluctance to endorse Iressa and other cancer drugs. The article's title: "FDA to Patients: Drop Dead."



Miracle drug? In scattered cases, Iressa's impact is remarkable: Here, a lung tumor (*top*, right side) nearly disappears after treatment (*bottom*).

Iressa is one in a new breed of cancer therapies: targeted drugs that home in on molecules critical to cancer. Unlike old-style chemotherapy that inflicts major collateral damage on healthy cells, these drugs should act like laser-guided missiles. For more than a decade, researchers and drug companies alike have been heralding their imminent arrival. Now, with a half-dozen drugs in late-stage clinical trials and some already on the market, such as the breast cancer drug Herceptin, the future has arrived. But it's not quite as rosy as some predicted. As the experience with Iressa demonstrates, designing, testing, and evaluating these therapies are proving more challenging than many expected.

The most celebrated new drug in this class is Gleevec, designed by Basel, Switzerland–based Novartis to treat chronic myeloid leukemia (CML). Approved in May 2001, Gleevec, used in ongoing therapy, sends nearly 100% of recently diagnosed patients into remission, and without the tortuous side effects of chemotherapy. Although not without problems, the drug has become the poster child for targeted cancer therapies, providing proof of principle that this approach—identifying and then disabling the molecular mechanisms that give rise to a cancer—is indeed a potent weapon.

But as other targeted drugs wend their way through clinical trials, it is becoming increasingly clear that few will enjoy the smooth passage of Gleevec. Gleevec attacks a relatively rare cancer that arises from a single molecular defect. More prevalent (and, from a company perspective, more lu-

CREDITS: ROY HERBST/M. D. ANDERSON CANCER CENTER