The Trembling Edge of Science

Losing world-class chemist Karen Wetterhahn to mercury poisoning redrew the boundaries of safety and risk.

BY KAREN ENDICOTT

The mercury compound Karen Wetterhahn needed looked like a small vial of water. A mere drop or two proved lethal.

"Sometimes it's hard to predict the long-term consequences of doing something. You don't always have the knowledge you need. You have to make your best judgment."
—Karen Wetterhahn, 1995

"Karen had no idea she was in peril," says chemistry department chairman John Winn. "None of the chemists here would have felt in peril."

The Wednesday in August that stole Karen Wetterhahn's life seemed to be just another day in the lab. The chemist needed to transfer a small amount of a chemical from one container to another. As she always did when working in her lab, Wetterhahn donned her protective lab coat, goggles, and disposable latex gloves. Because the chemical she would be working with that day was dimethylmercury, a highly toxic and volatile liquid compound, the transfer would be done in a chemical fume hood. The ventilated hood would place a glass barrier between her and the mercury and create a convection current to draw vapors away from the air she would breathe.

Wetterhahn prudently asked her colleague David Lemal to help her with one part of the procedure—opening the sealed glass vial. Lemal chilled the vial in ice water to lower the vapor pressure of its contents. He scored around the top of the ampule with a file, cleanly snapped the top off, and left the lab. Using a syringe-like pipette, Wetterhahn drew a small amount of the dimethylmercury out of the vial, deposited it into a pencil-thin glass sample tube, then pipetted the rest into a small screw-top storage vial. In the process a drop or two of the liquid dripped from the pipette onto her left glove. She sealed and labeled the sample tube and storage vial—dimethylmercury 8/14/96 KEW—peeled off her gloves, left them in the fume hood, then thoroughly washed her hands. All standard procedures.

Karen Wetterhahn went home to her husband and two children. She should have gone straight to the hospital. For the dimethylmercury that had landed on her glove had penetrated the latex and then her skin and was already beginning a slow, unseen journey into her blood and into her brain.

But how could she have known this? There were no visible holes in her glove. The dimethylmercury, clear like water but three times as dense, hadn't burned or otherwise announced itself as it seeped into her skin. Even the wetness of the drop or two would have been indistinguishable from the clamminess that builds up inside rubber gloves. There was no reason for Karen Wetterhahn to think that she had been exposed to dimethylmercury.

Five months later the deliberate, focused, and precise scientist found herself stumbling into walls and slurring her speech. The woman who was never sick suddenly was asking her husband to pick her up from work because she didn't feel well enough to drive home. She finally heeded a friend's admonition to see a doctor. She was admitted to the hospital at the Dartmouth-Hitchcock Medical Center. When neurologist Richard Nordgren told her that her symptoms—nausea, weight loss, loss of balance, and trouble with speech—could be caused by exposure to mercury, Wetterhahn mentioned the small spill of dimethylmercury that had happened back in August. Samples of Wetterhahn's blood and urine were rushed to a lab for testing. By the time preliminary reports confirmed the possibility of mercury toxicity, she was having trouble with her hearing and eyesight. When more lab results confirmed the diagnosis—severe mercury toxicity—DHMC clinical pharmacologist David Nierenberg treated her with chelation therapy. Each day she ingested a medication that would act like a magnet, attracting the mercury and binding it into a substance her body could excrete.

As soon as the diagnosis was clear Wetterhahn's laboratory was closed. Nierenberg tested Wetterhahn's family and laboratory colleagues for mercury. All members of the chemistry department were given the opportunity to be tested. Wetterhahn asked John Winn, chairman of the chemistry department, to make sure that the people who had helped her with the dimethylmercury work were checked. Everyone who worked with her or had done any recent work with mercury compounds had the tests done. Everyone tested normal. The College's Office of Environmental Health and Safety arranged for a certified industrial hygiene firm to test the air and surfaces in Wetterhahn's lab, office, car, and home. Everything she might have touched was tested, even doorknobs, light switches, and telephones. The only place mercury was found was the canister that contained the vial of dimethylmercury Wetterhahn had used. She was keeping it, in the safety of the chemical fume hood, until the results of her experiments were accepted for publication. She was holding onto it in case she needed to repeat or replicate any part of the experiments. "Why don't you get rid of it," Wetterhahn now told Winn. She didn't want anyone else to face what she was facing.

The mercury in Wetterhahn's body was attacking her nervous system at an alarming rate. Her field of vision kept shrinking. Her hearing was shutting down. She had to struggle to speak, but she urged Winn and Nierenberg to do all they could to alert the scientific community to the dangers of dimethylmercury.
On February 6, barely three weeks from the moment she noticed anything was wrong, Karen Wetterhahn slipped into a coma.


Disposable latex gloves gave Wetterhahn needed dexterity. No one knew that dimethylmercury soaks through them.

The three weeks were long enough for the scientists to understand that their colleague was not coming back. "When we heard the diagnosis there was almost a sense of relief that we knew what it was," David Lemal says. "Then we realized the horror of the irreversibility of the damage." Worse still, they knew that Wetterhahn knew. "It was obvious that the chelation therapy wasn't working. She was a very good metal toxicologist. She knew what the mercury was doing to her," says Kent Sugden, a post-doctoral fellow in her research group on chromium. "When she went into a coma many of us saw it as merciful."

While Wetterhahn lay suspended in the immutable final symptom of mercury poisoning, her colleagues replayed the steps that had brought her to this most unforeseen of fates. They tried to make sense of the facts. They tried to understand how she could have done everything right but the outcome could have gone so horribly wrong. They kept bumping up against the limits of what anyone knew about dimethylmercury. The more they probed the more they realized that when it comes to dimethylmercury, the line between safety and risk had to be redrawn.

At the beginning nothing made sense. The accident seemed so improbable as to be impossible. "We're having professional shock," Winn said shortly after the diagnosis. "She was doing routine manipulations." His colleague Russell Hughes was equally mystified. "She was a careful experimentalist operating in new labs in a state-of-the-art facility," he says. She had not done anything unusual or foolish. She had taken the standard precautions: protective clothing and goggles, working in a chemical fume hood. She had worn rubber gloves, as standardly recommended. She had chosen the close-fitting disposable latex kind, like surgeons wear, so she would have maximum dexterity. "She had no idea she was in peril," says Winn. "None of the chemists here would have felt in peril." What no one knew at the time was that latex gloves are no match for dimethylmercury.

Chemists routinely consult material safety data sheets compiled by chemical manufacturer and suppliers for information about protections against specific chemicals. Three material safety data sheets (MSDS) were available for dimethylmercury. Alfa Aesar, the chemical supplier from whom Wetterhahn bought the dimethylmercury, recommended "rubber gloves." Organometallics, the company that manufactured the dimethylmercury, recommended gloves made of the synthetic rubber neoprene. Sigma Aldrich, the chemical supplier that produced the third MSDS, recommended wearing "chemically impervious gloves." However, "there is no such thing," says the College's health and safety director, Michael Blayney. "No glove is completely impermeable." The rates of permeability vary according to the glove type and the chemical involved. Despite the recommendations on the material safety data sheets, Blayney says, no one had actually tested any kind of protective gloves to see how they stood up to dimethylmercury.

After Wetterhahn's diagnosis, Blayney and Winn initiated such testing. They approached the National Institute for Occupational Safety and Health to find out where dimethylmercury permeability testing could be done, then sent the seven types of disposable gloves found in Wetterhahn’s lab to Intertek Testing Services for analysis. The results were shocking. **Dimethylmercury raced through latex gloves in 15 seconds or less, possibly even instantaneously.** The other types of disposable gloves from the lab failed as quickly. Only a specialized multi-layer plastic laminate glove fared well, providing more than four hours of protection. Blayney, Winn, and Nierenberg rushed to warn other scientists. In the May 12 , 1997, edition of the American Chemical Society’s weekly magazine, Chemical and Engineering News, they published an account of Wetterhahn’s accident and the results of the glove tests. They included the first empirically based recommendation for protection when handling dimethylmercury: "Rubber gloves" were not enough. Instead, "a highly resistant laminate glove (SilverShield or 4H) should be worn under a pair of long-cuffed, unsupported neoprene, nitrile, or similar heavy-duty gloves." Soon sites across the World Wide Web were repeating the warning.

But back on that day in August Wetterhahn had no idea that she was unprotected. Until the accident no one realized that merely a drop or two of dimethylmercury could prove fatal. "I looked at the amount of dimethylmercury left in the vial after the transfer and I assumed there was no way she could have gotten enough of it on her," group member Sugden recalls. "I thought the poisoning was from her previous work with mercury salts."

All mercury is toxic, but each form is toxic in its own way. "You can hold the silvery liquid mercury from a thermometer in your hand and nothing would happen," says John Winn. "The danger of liquid mercury is in its vapor." That’s why the mercury from a broken thermometer should be sponged up, sealed inside a plastic bag, and taken to a hazardous waste facility rather than vacuumed—vacuuming disperses the vapors. Other forms of mercury used in industry—for dyes, in various electronic devices like switches—readily contaminate waste sites or waterways they enter. The mercury accumulates in fish and can cause mercury poisoning in anyone who consumes them.

Wetterhahn’s accident showed that dimethylmercury was far more toxic than anyone thought. "We’re all exposed to mercury just by being alive," Winn says. "A usual mercury concentration would be ten micrograms per liter of blood or less. If the level rises to 50 micrograms per liter you’ve hit the toxic threshold, the beginning of toxicity. You would begin chelation therapy. A concentration of 200 micrograms per liter is toxic, but not necessarily lethal. Karen had 4,000 micrograms per liter. That’s 80 times the toxic threshold." Merely absorbing a drop or two placed her in the lethal range. "Everyone knew dimethylmercury was bad," says Sugden. "No one knew it was this bad." "On a scale of one to ten, dimethylmercury was a 15," says chemistry professor Dean Wilcox. "Before Karen’s accident we thought it was a ten. Now we know it is off the scale."

Scientists have been willing to work around dimethylmercury’s dangers because the compound happens to be invaluable in various areas of research, including experiments into how toxic metals damage living cells. Building on the idea that structure is related to function, researchers reason that if they want to know how a toxin interferes with the normal functioning of a cell, they need to know two things: the structure of the normal cell and the structure of the cell after a toxin binds to it. By pinpointing which part of the cell structure binds the toxin, they hope to learn how the toxin changes the cell functioning—and how that process might be turned off.

If you’ve ever had an MRI, a magnetic resonance image, to get a three-dimensional fix on a tumor or other medical problem, you are already acquainted with the kind of spectroscopic technology researchers like Wetterhahn use to learn about the components of cells. Two nuclear magnetic resonance spectrometers, research cousins to the MRI, reside in a first-floor lab at the College’s Burke Laboratory. Like MRIs, these NMR spectrometers use magnetic fields to detect differences in the molecular materials they scan. MRIs process the data into recognizable photographic images of the body. NMR spectrometers are a bit more cryptic, providing data that can be used to infer rather than photograph molecular structures. But then, they are measuring differences at the atomic rather than human level.

"The sample sits in a large magnet," explains chemistry professor John Bushweller, who regularly uses NMR spectroscopy in his research on how damage to proteins causes cancer. "You shine radio frequencies onto the sample to excite the molecules and see how different atoms react. The signal peaks at certain frequencies, indicating particular atoms. It's a bit like finding out the FM frequency of the molecule."

The frequencies are like signatures when viewed individually. When compared with the pattern of a standard, however, each signal represents a shift that has structural significance. The standard is like sea level, explains Winn, and each shift indicates a different altitude. The standards are not just an interpretive device, however. NMR spectrometers must actually be calibrated to the standard each time a new element is scanned. "You put the standard sample in and set 'sea level' to its spike," Winn explains. There is a different NMR standard for each element. The NMR standard for mercury compounds is dimethylmercury.

"Dimethylmercury happens to have all the characteristics that make it a great standard," Kent Sugden says. "It is a liquid, so it can be used in pure form. There are no shifts in the calibration signal due to problems associated with solutions, such as changes in the concentration or pH. The line is consistent every time. This is by definition what a standard should be."   "Dimethylmercury is a wonderful little compound, if not for its toxicity," says Winn.

For years, dimethylmercury's value appeared to outweigh its dangers. "Dimethylmercury didn't seem to have a history associated with it," says Russell Hughes, who has used the compound as a reagent. "People have been dealing with it for more than a hundred years." The only two previous recorded accidents with dimethylmercury had happened under very different circumstances from Wetterhahn's tiny spill. In 1865 the two English chemists who first synthesized the compound ended up dying from unprotected exposure to the fumes. ("You can generate something that's very toxic without knowing that it is," Sugden explains.) In the early 1970s a Czech chemist died while synthesizing a large amount of dimethylmercury. But the hundred or so labs worldwide that use dimethylmercury have done so without incident. "Many chemists outside Dartmouth have said to me, 'I had no idea dimethylmercury was that toxic. It can't be. Surely there would have been more cases,'" says Hughes. The general consensus seemed to be that the compound required care but was manageable. "Dimethylmercury is a commercial product," notes Hughes.

Karen Wetterhahn had only recently become interested in mercury. While on sabbatical, she began a collaboration with MIT graduate student Jonathan Wilker and her own former doctoral advisor Stephen Lippard. They were using NMR to study the active sites of proteins—the part of a protein where, as John Bushweller describes it, "the chemistry goes on." When the sabbatical was over Wetterhahn continued the research at Dartmouth. She and Wilker were planning to run their experiments on the NMR spectrometers in Burke Laboratory. The first step was to prepare a standard. Wetterhahn wanted to have it ready by the time Wilker came up from Cambridge. Kent Sugden offered to help.

But neither Sugden nor Wetterhahn was eager to work with dimethylmercury. They discussed the toxicity warnings on the material safety data sheets: dimethylmercury produced toxic fumes, it was readily absorbable through the skin, and even small doses could be lethal. "We agreed it wasn't a good thing to use," Sugden says. They opted for a safer, alternative standard—a solution made of mercury chloride salts. Like all forms of mercury, mercury chloride is toxic. But it is less volatile than dimethylmercury and doesn't absorb so readily through skin. Avoiding mercury chloride's main danger is relatively easy. "Don't eat it," Sugden says. Getting the mercury chloride standard to match dimethylmercury's accuracy would be tricky, however, since solutions necessarily involve extra factors—the pH of the solution, the amount of mercury chloride. But Wetterhahn and Sugden chose safety over risk.

They ran the mercury chloride NMR, found the peak, and calibrated the NMR spectrometer to the standard. They tested the first sample, a protein with mercury bound to it, then various other mercury compounds. The results troubled Wetterhahn. "She mentioned to me that the measurements weren't what she thought they would be," Sugden recalls. There were two possible explanations. Either the mercury had not bound to the protein in quite the way Wetterhahn thought it would, or the mercury chloride standard was inaccurate. Wetterhahn's next step, says Sugden, was to check the standard. "She decided to use dimethylmercury."
The dimethylmercury arrived in a cardboard box packed with vermiculite. Inside an airtight metal canister also filled with vermiculite was a bubble-wrapped bag. Inside of that was the sealed glass vial. Sugden placed the entire package in a fume hood. **The material safety data sheets stuck in his mind. Dimethylmercury's low lethal-dose levels made him nervous.** He bowed out. "Karen wouldn't make you do anything you're uncomfortable with," he says.

Wetterhahn continued. She made time on August 14 to transfer the dimethylmercury to the NMR tube. She never mentioned to her colleagues that she had spilled a minuscule amount. Over the next few days she and Wilker ran the dimethylmercury standard and tested their research compounds.

The dimethylmercury standard assured Wetterhahn of reliable results. It also revealed that the alternative standard had been accurate. "This is the irony," says Sugden. "The mercury chloride turned out to be dead on—or close enough that it didn't matter. But we didn't know that until she ran the real standard."

Karen Wetterhahn seemed born to be a scientist. The daughter of a chemist, she gravitated early to math and science, earned degrees in chemistry and math at St. Lawrence University, and completed her doctorate in inorganic chemistry and physical biochemistry at Columbia University in 1975. The following year she became the first woman professor in Dartmouth's chemistry department. Her innovative ideas in the new field of chromium carcinogenesis quickly established her as a key player both at Dartmouth and beyond. "Only ten to 20 people internationally would have her chromium credentials," John Bushweller says. According to Sugden, "Karen was one of the best—if not the best—in metal toxicology. She was the best in chromium."


Post-accident tests showed that pairing SilverShield and neoprene gloves is the only guard against dimethylmercury.

"Karen established one of the major paradigms in chromium toxicology," explains Brooke Martin, a doctoral student who moved from Australia to study with her. Wetterhahn established that the process by which chromium damages DNA—possibly inducing cancer—has two stages rather than one: entry into the cell and reduction inside the cell. Cells readily take up chromium in its "+6" oxidation state. Once the chromium gets into the cell, the cell reduces the metal to lower—and toxic—oxidation states. Wetterhahn's work suggested that DNA damage occurs during this reduction of chromium in the cell. "She was one of the first people to appreciate the importance of the oxidation state in the metabolism and toxicity of chromium," Martin says. "Her early role is somewhat analogous to that of Watson and Crick in their 'discovery' of DNA's double helix structure. All the work was already there to see but no one had really put it all together in a way that seemed to fit. The simplicity and utility of some models makes them an enduring reference point for further research." Wetterhahn's ideas became known as the uptake-reduction model.

Wetterhahn seemed delighted that the model identified the science rather than the scientist. "Karen didn't push herself forward," Martin says. "She took it as a compliment when a later generation of her model was taken directly from one of her papers and used as the illustration on a book cover without acknowledgment or copyright considerations. She brought it in to show us all as soon as she got it. Most people would have been affronted, but Karen was laughing. She thought it was very funny."

By all accounts, Wetterhahn always focused on furthering science rather than her ego. In a field where egos loom notoriously large, that in itself was remarkable, say her colleagues. Even more remarkable was what her lack of ego allowed her to accomplish. She used herself as a catalyst to bring researchers together. She built collaborations the same way she built research models—by assembling pieces of the same puzzle. "Karen's real gift was being open to a lot of different ways of looking at the same problem. She was able to use all resources available to her," says Martin.

Wetterhahn's chromium group grew to 15 researchers ranging, as group member Sugden puts it, "from the very biological to the very chemical." Wetterhahn instituted weekly meetings so members of the group could report on their projects. "She was trying to train us to present our work," Martin says. "She would critique the presentation. But toward the end we'd talk about the science—the ideas and the experiments. Karen would correlate the different findings. 'This is so neat!' she would say. Then she would tell us how that finding fit in with someone else's work."

Wetterhahn used her talent for mentorship and her sheer enthusiasm for science to address a growing problem in the sciences in the late 1980s. Between 1984 and 1989 at least 60 percent of the women who entered Dartmouth intending to major in science dropped out of the field. The attrition rate for men during this period was 44 percent. A 1991 National Research Council conference on how to retain women in science and engineering recommended providing early hands-on research experiences; faculty, student, and professional mentors; and financial aid packages that enable students to spend time on lab work. Latching onto these ideas, Wetterhahn joined with then-assistant dean of engineering Carol Muller '77 to establish Dartmouth's Women in Science Project (WISP). "She wanted to captivate students at their highest level of interest—during their first year—and get them into labs," recounts Mary Pavone, WISP's current director. "Some faculty were skeptical that first-year students could be involved in any significant way in research projects. Karen built her coalition on her own terms, starting with the people who knew and respected her. She was willing to believe it was worth the time, that working with first-year students at the height of their enthusiasm was an investment in the future." Wetterhahn's determination paid off. WISP caught on. Since 1991 more than 175 faculty and researchers have participated as sponsors for 514 interns. The number of women majoring in science has risen from 13 to 25 percent of each class, and WISP has become a national model.

Wetterhahn was tapped to become associate dean for the sciences and later acting dean of the faculty. Once again she built collaborations, this time reorganizing the life sciences to stress interdisciplinary connections rather than traditional boundaries. She fostered links between biology, chemistry, environmental studies, engineering, and the medical school. "The life sciences are interdisciplinary," Wetterhahn insisted. Once again she led by example. "She played the key role in bringing structural biology—which utilizes the power of chemistry to understand biologically important molecules—to Dartmouth," John Bushweller says. And she spearheaded a new major in biophysical chemistry. "She was the cornerstone of the biophysical chemistry curriculum," chemistry professor Jane Lipson says.

Wetterhahn's biggest collaborative coup came in 1995, when she secured a $7 million grant from the National Institute of Environmental Health Sciences' Superfund research and education program to study how heavy metal contaminants harm human health. The grant funded five related studies spanning toxicology, biochemistry, epidemiology, and the biology of lake ecosystems. The funding was the largest in Dartmouth history. In a world in which scientists tend to be judged by the size of their grants, project director Wetterhahn characteristically focused on the collaborations the money made possible rather than any glory the grant implied. "We have a lot of expertise here at Dartmouth in toxic metals. I got people together," is how she put it at the time. Calling the grant "a microcosm of the life-science issue," Wetterhahn said, "I like it as a model for how we can bring together people from different departments and schools. It's intellectually coherent, but faculty and students from different areas are coming together. So many of the large complex problems we face must be solved by the interdisciplinary approach." She herself was willing to become as interdisciplinary as necessary. "If I have to learn biophysical kinetics, whatever I need to understand the problem, I'll do it," she said.

Meanwhile Wetterhahn took on the position of acting dean of the faculty. There was talk that she might become dean. Her presence was growing beyond campus as well. "The Superfund grant had launched Karen into a new realm," explains Brooke Martin. **Dimethylmercury changed everything.**

A stroll through Burke Laboratory or the research buildings of Dartmouth Medical School is all it takes to see the hazards chemists and biochemists routinely face. Door after door bears signs cautioning that poisons, carcinogens, radioactive substances, and other dangers reside inside. Working in such an environment means making peace with risk.

"The only way to cope with worries is the law of probability," says Jane Lipson. "If events are very low probability, you can put them out of your mind." But Wetterhahn's accident showed the shortcomings of that strategy. "What happened to Karen was unbelievably low probability," Lipson says. "She wasn't stupid and she wasn't negligent. Most things in life are a lot more forgiving. This was so phenomenally unforgiving."
"You tend to get complacent about the hazards you work with on a daily basis," admits Kent Sugden. "An accident drives home that on a daily basis you have to be aware and take optimum precaution."

"The accident was a wake-up call," says Ed Dudek, one of the post-doctoral fellows in Wetterhahn's chromium group. "We're now extremely aware of everything we're doing. Everyone examined his own way of doing the work."

Chemistry has actually never been safer. "The risk of doing chemistry is less than the risk of driving a car on the highway," says Russell Hughes. But safety has traveled a long road. "In the early days of chemistry people had no idea of the consequences. They used to describe the odor and taste of compounds," says David Lemal. Like other senior members of the chemistry department, Lemal has seen safety consciousness change radically during his career. "When I was in grad school, we thought benzene smelled nice. We never wore gloves," Lemal says. Dean Wilcox says that as recently as the 1970s, when he and Karen Wetterhahn were trained, "people were more cavalier about safety. There was a kind of macho attitude toward lab work. Safety wasn't so much an issue."

Over the last decade, OSHA, the federal Occupational Safety and Health Administration, has made laboratory safety very much an issue. OSHA required labs to develop chemical hygiene plans, safety instruction manuals and sessions, and place safety monitors in labs. It has fined companies and institutions for safety violations. But scientists—from OSHA and from labs worldwide—are still writing the safety book. "There is no general body of knowledge about what scientists are taught about safety," says Dartmouth's Michael Blayney, who has been upgrading safety campus-wide since arriving in 1995 from the National Institutes of Health. Yet even as greater knowledge reduces risk, safety literally remains in the hands of each researcher. "The ultimate locus of control is the individual. The ultimate responsibility for safety comes down to the individual," says Blayney.

Even the main source of chemical information—material safety data sheets—has flaws. As Wetterhahn tragically discovered, sometimes data sheets reflect the limits, rather than the extent, of knowledge. Many contain inaccuracies or deficiencies, says Blayney, author of a recent assessment of data sheets. There is a problem with balance as well. "The MSDS are all starting to sound scary," Dean Wilcox says. "Even sodium chloride—table salt—sounds dire. True hazards like dimethylmercury should jump off the page and shout for attention." The lack of balance is prompting a potentially dangerous backlash in which scientists downplay warnings—or discount them altogether. "The material safety data sheets sound hyperbolic. If you took everything literally you'd be frozen. You wouldn't get anything done," says Jane Lipson. "You have to find the balance between being confident and wary—without crippling yourself."

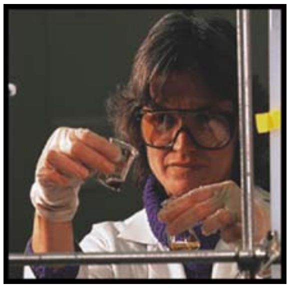
Scientists do not always find the same point of balance. People have their own levels of comfort. "If you're terrified of a substance, you're going to make mistakes," says John Bushweller. Although he routinely works with oncoproteins, the substances that cause cells to carcinogenically divide, he draws the line at working with the heavy metals that were Karen Wetterhahn's focus. "To work with heavy metals, you have to be careful all the time," he says. "I don't think I have the discipline to be safe all the time." Russell Hughes says he has refused to work with some highly toxic and highly volatile chemicals. Jane Lipson knows where she draws the line: "I would never work with dimethylmercury or let anyone work with it."

Wherever they draw the line, chemists rely on prudent lab practice. "If we have a choice, we try to work with things that are safer. Sometimes we have to use the more dangerous. We take precautions but still do it," says David Lemal. Precautions, however, involve interpretation. Dean Wilcox suggests that Wetterhahn's busy schedule may have influenced her approach to the dimethylmercury transfers. "She handled it in the most efficient way, but not the safest," he says. He suggests that a special piece of equipment called a vacuum line might have reduced the risk involved—although he acknowledges that it would not have reduced the risk of exposure inherent in merely opening the sealed vial, a risk Wetterhahn thought she had covered by wearing latex gloves. According to John Winn, specialized equipment tends to be tied to the frequency of a procedure. "If you are using a toxic substance a lot, you build a container to do it in," he explains. "If you don't use it everyday, you do it with prudent practice, not specialized equipment."

But given the scope of chemistry, neither equipment nor prudent practice provides a complete guarantee. "When you use a thousand different chemicals in a year, you're never going to have complete protection," says Kent Sugden. "You would never do any science if you spend all your time working out what your protective gear should be." "In research you're always making new compounds," says Lemal. "You have to assume that new things are dangerous. Treat everything as if it is dangerous. Don't breathe it, don't get it on you. Nearly all the time that works." **"Once in a while," says Michael Blayney, "you get to the trembling edge of science and something bad happens."**

Risk can never be completely eliminated, either from research or the chemistry classroom. As Lipson puts it, "If you have no uncertainty in what you're doing you're not doing research." In chemistry classrooms the goal is to reduce risk to the level that students can handle. "If students follow the precautions they'll be fine," Lipson says. Before they start lab work students are required to read and sign safety information in their lab manuals. Safety information is also included in each week's lab lectures. Sally Hair, senior lecturer and coordinator for the general and organic instructional laboratories, puts students through a safety scavenger hunt to make them aware of where equipment is located. The foundation of all chemistry laboratories, however, is a well-thought-out plan for what students can do safely. "I have to put myself in the student position and try to figure out everything that can go wrong," Hair says. "Anything that's of pedagogical value has to also be OK in terms of safety. I try to avoid things that are really dangerous or toxic. And I emphasize safety." Students learn the basic rules: no eating in the lab; don't store food or drink in the lab refrigerator; do not eat ice from the lab ice machines; always wear eye-safety goggles; if gloves get holes, take them off right away; do not wear sandals; clothing must cover the knees; wash hands before leaving the lab. According to Hair, a handful of accidents—cuts from broken glass or minor burns from acids or hot plates—happen most terms. Visits to general chemistry labs and organic labs revealed that students appeared relaxed but intent on what they were doing. Only one sign—gloves— indicated that Wetterhahn's accident was on anyone's mind. "Most students wear gloves most of the time now, even when they don't need to," reports Hair. "We're spending a lot on gloves. We're going through hundreds of pairs per week."

After Wetterhahn's diagnosis, Michael Blayney and John Winn alerted OSHA about the accident, triggering a standard OSHA investigation. OSHA cited the College for not providing training on the limitations of protective gloves in the laboratory and the College's chemical hygiene plan for not being explicit about the uses of the gloves. Given the state of knowledge at the time of the accident, not even those preventive measures would have saved Wetterhahn. No one, including OSHA, knew of dimethylmercury's ability to instantly penetrate latex gloves until Dartmouth had the testing done. "OSHA admitted to me that she didn't do anything wrong," Kent Sugden says. Nevertheless, OSHA fined the College $9,000 and required Dartmouth to hire a chemical hygiene officer and increase its safety instructions, especially on gloves. "OSHA recommended measures we were already in the process of taking," says Blayney. Now posters warning about the limitations of each kind of lab glove hang in every lab. Safety classes have taken on an edge of determination. The search for a chemical hygiene officer has just been completed.



After years of adeptly handling the known risks of heavy metals, Karen Wetterhan chanced upon the unknown.

Jon Gilbert Fox; all other photos by Joe Mehling '69

Heeding Karen Wetterhahn's last directive, Blayney, Winn, and Nierenberg are continuing to spread the word about the dangers of dimethylmercury and the necessity of wearing SilverShield gloves when handling it. They would like to see dimethylmercury become a thing of the past. They are trying to convince chemical suppliers to stop selling it altogether—or to regulate it more stringently at the very least. And in the NMR community, Northwestern's Thomas O'Halloran, a key proponent of the dimethylmercury standard, is leading efforts to place a safer standard into widespread use.

In the months since the accident Wetterhahn's colleagues, like her husband Leon Webb, 15-year-old son Leon Jr., and 13-year-old daughter Charlotte, have faced both emptiness and regret. Kent Sugden, who backed away from using dimethylmercury, talks of survivor guilt. "Perhaps if I'd done it in the beginning this wouldn't have happened. I might have been able to get away with it," he says, even while acknowledging, " that's what it would have been—getting away with it." "I wish I had given my standard talk on permeation," says Blayney, even though he knows that dimethylmercury would not have entered the discussion.

"I wish she had talked to me," says John Bushweller. "I would have shown her a computational trick used by the biological NMR community to calculate the chemical shifts pretty closely." This, even though he knows that "pretty closely" might not have been close enough for Wetterhahn.

"I wish she had told us what she was planning to do," says Ed Dudek. "We might have tried to talk her out of it. Or if we had known she was doing the work we might have asked how it went. She might have said, 'I had a little spill.' We would have said, 'You should talk to someone.'"

Karen Wetterhahn died June 8, 1997. At her funeral people spoke of irony, of how the dangers of heavy metals first claimed her interest and then claimed her life. Kent Sugden, who continues to work with heavy metals, sees the loss in a starker light. "There's no irony in it," he says. "Only lion tamers get eaten by lions. It's the people who work with toxins who get exposed."

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