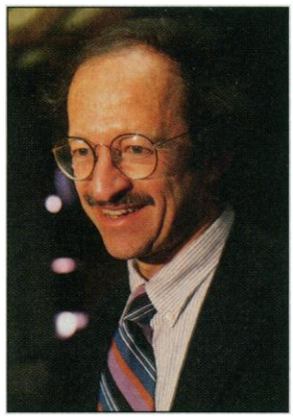
Varmus Puts His Stamp on NIH

After 2 years at the head of the world's largest biomedical research establishment, Harold Varmus has pulled off a quiet revolution, but he will face a tough test as the budget squeeze tightens

Take a middle-aged biologist who enjoys bike riding and dabbling in public policy but who has never run a clinic or a college department, put him in charge of the biggest biomedical center in the world, blast him with a stream of political crises and scandals to sort out, threaten to slice an unprecedented chunk out of his agency's $11.3 billion budget, and watch what happens. The result of this experiment, you might guess, would be chaos and internecine warfare.

Just such an experiment has been going on at the National Institutes of Health (NIH), where Nobel prize–winning virologist Harold Varmus was appointed director 2 years ago this week. But it has not yielded the results many feared. As Claude Lenfant, director of the National Heart, Lung, and Blood Institute, says: "When Dr. Varmus came on board, everybody was saying, 'We got the best scientist but probably the worst administrator.' In fact, he has turned out to be pretty darned good."



RICK KOZAK

Novice manager. Varmus's management has proven sharp.

Rather than increasing discord among NIH's 24 quasi-independent institutes and divisions, the arrival of this novice director seems to have calmed rivalries and created a down-to-business mood on NIH's campus in Bethesda, Maryland. People from widely different backgrounds said in interviews with *Science* that, although hit by spending limits and facing the prospect of even tighter budgets in the years ahead, NIH seems to be doing well under its new leadership. Says Massachusetts Institute of Technology geneticist Eric Lander: Varmus is "doing a spectacular job for science."

Varmus and his staff, many say, have boosted morale in an agency that had been dogged by internal bickering and sour relations between Varmus's predecessor, Bernadine Healy, and her bosses at the Department of Health and Human Services (HHS). Varmus has recruited several well-known scientists to top jobs, stirring fresh breezes in the intramural program. And he and his deputies have launched projects to reduce paperwork, streamline peer review, open labs to outsiders, toughen review of internal programs, and recruit talent.

Beyond the tangible achievements, Varmus has convinced researchers on NIH's campus that he cares about scientific quality. Many say they are reassured by his consensus-building style. Varmus tackles issues cautiously, soliciting opinions from a network of committees before settling on a final course. "Decisions are made on the basis of what are the scientific facts," says Francis Collins, appointed in Healy's term to be director of the National Center for Human Genome Research. And it is "gratifying," Collins says, "that issues are decided on science and not on politics."

The results have not pleased everyone, however, and there have been some disappointments: Clinical researchers grumble that Varmus has been slow to deal with what they say has been years of neglect by NIH, he has not been able to break a 15-year political moratorium on some types of embryo research, some say he got off to a rocky start with Republican chiefs on Capitol Hill, and he's been unable to fill the directorship of the National Institute of Mental Health (NIMH) for 18 months.

Varmus's academic style may also have a downside in NIH's external relations. Some congressional aides and lobbyists note that Varmus doesn't go in for back-slapping friendships among the high and mighty in Washington. Some find him aloof, even arrogant. And a few NIH staffers wonder if the agency might benefit from a more dramatic chief, one who could make legislators feel warm and cozy about spending billions of dollars on biomedicine. "We're basically in limbo" and at risk of being lost in the battle between the White House and Congress, says one NIH extramural program director, speaking on condition of anonymity. Another, an immunologist, says: "Varmus has become the invisible administrator. ... He's effective behind the scenes. But I wish he were doing more ... that his visibility were greater."

New blood

If there's one accomplishment Varmus claims as his own, it is staff recruitment—on which he rates himself "very successful." Varmus says that the "legacy you leave in a position like this—a job I don't plan to be in for an extremely long time—is the people you've hired." There's no longer talk of a hemorrhage of talent, as there was before and during Healy's tenure. Indeed, Varmus says he's proud of having lured bench scientists to administrative jobs, including several institute directorships.

In an early coup, Varmus persuaded Zach Hall, a neuroscientist and department head at the University of California, San Francisco, to take a salary cut (from $150,000 to $120,000) and move to Bethesda to take charge of the National Institute of Neurological Disorders and Stroke (NINDS). Like others recruited to the Varmus circle, Hall brought his lab with him (see box).

Hall, who says being an institute director is "not something I had really ever thought of"—and definitely "not in the career path of most scientists"—believes that having a working scientist at NIH's helm has had a "trickle-down effect," luring others to Bethesda. Hall announced his own recruiting triumph in September when Story Landis—a developmental biologist and chair of the department of neurosciences at Case Western Reserve University School of Medicine in Cleveland—signed on as NINDS's scientific director. She's now planning to remake the intramural research program.

Changes like this are popping up throughout the NIH structure as appointments are made, some through the promotion of staff. A significant example is the choice of Richard Klausner to head the National Cancer Institute (NCI). Officially, the president made this nomination, but Varmus shaped the list of names that went to the president, and, according to one insider, settled on Klausner—chief of a cell biology lab at the National Institute of Child Health and Human Development—as the first choice after it became clear that Varmus's old friend and co-winner of the Nobel prize, virologist Michael Bishop of the University of California, San Francisco, wouldn't take the job. Klausner, a longtime advocate of intramural reform, is now in a position to put his views into effect. Starting on 1 October, the largest institute (with 19% of NIH's funds) began a revolution (*Science*, 18 August, p. 912).

Not every part of NIH has made a quick transition to the new era, however. NIMH has been without a permanent director for 18 months, as one top candidate died, another pulled out, and Varmus decided to restart the

Double Duty at NIH

One of the lures Harold Varmus employs in recruiting top scientists to administrative jobs at the National Institutes of Health (NIH) is to offer them a lab of their own. Varmus knows the seduction well: He couldn't bring himself to give up research when he took the top NIH job 2 years ago, so he negotiated a deal that allows him to spend a few hours a week running a small lab on the NIH campus. Varmus concedes that official duties don't leave much room for research, and much of his lab time comes in short bursts at off hours and on weekends. "My own lab now has less than 10 people," he says, and he has entirely dropped one area—retrovirus research. The lab is now concentrating on tumor suppressor genes, breast and brain cancer, signaling pathways in the cell, and the development of "knockout" mice.

Some observers, however, question whether it's wise for busy administrators like Varmus to remain directly involved in research at all. They note that it's hard for institute chiefs to give full attention to lab work, threatening the quality of the research. And they argue that government decisionmakers who set aside resources for their own work may be seen as competing unfairly with extramural scientists. "It's a real conflict of interest," claims one NIH program administrator, speaking on background. "No other part of the government allows it," this administrator says. "I don't see why we think we can get away with this." A congressional aide also says he finds it "outrageous" that scientists recruited to top positions are allowed to relocate their labs to the NIH campus, circumventing local recruitment policies.

Varmus and other NIH leaders defend the double-duty policy. Not only are lab resources—not a high salary—often a trump card in job negotiations, they say, but it's "a positive value" to have active scientists working as administrators, adds Zach Hall, director of the National Institute of Neurological Disorders and Stroke. "It's important from an intramural point of view," says Hall, that the chief "find out firsthand what the problems are" and solve them.

Varmus notes that labs run by institute directors are small and have been placed at arm's length—at his insistence—in other institutes. Two exceptions are labs run by Anthony Fauci and Francis Collins, who direct the National Institute of Allergy and Infectious Diseases and the National Center for Human Genome Research, respectively. These arrangements, made before Varmus became director, have been "grandfathered" into the system, he says.

Varmus adds that the chiefs' labs will be subjected to reviews just like any others on campus. But does the NIH director really expect his own lab to get a tough vetting? "Yes," replies Varmus, adding that it will happen soon, "and we're already getting a little nervous."

–E.M.

CHIEFS AND THEIR LABS

Investigator	Director of	Lab Location	Research Area
H. Varmus	NIH	Cancer	Oncogenes
F. Collins	Genome Center	Genome Center	Clinical genetics
A. Fauci	NIAID	NIAID	Clinical HIV, AIDS
Z. Hall	Neurology Inst.	Mental Health	Synapse development
R. Hodes	Aging Inst.	Cancer	T cell regulation
S. Katz	Arthritis Inst	Cancer	Immunology of skin
R. Klausner	Cancer Inst.	Child Health	Cell metabolism
H. Slavkin	Dental Inst.	Arthritis	Craniofacial genetics

prolonged search from scratch. Varmus has been holding out for a first-rate appointment, but didn't help the situation, observers say, when he appeared before the NIMH advisory council—composed of leading mental health professionals—and announced that the finalist might be someone the council had never heard of. This is an example, says a colleague, of how Varmus's unguarded comments can cause grief.

Yet in other appointments, Varmus has shown himself to be politically savvy. His most important early decision may have been to name as his deputy Ruth Kirschstein, former director of the National Institute of General Medical Sciences. She and her husband Alan Rabson, deputy director of NCI since October, are longtime civil servants and experts in the foibles of government. Kirschstein serves as a troubleshooter as well as manager, trying to shield the agency from major embarrassments. This, NIH's power couple, has helped maintain continuity and avoid political reefs, as novices like Varmus learned the ropes.

Pulling down barricades

Less visible than the leadership changes, but just as critical in the long run, are efforts by Varmus and his chosen deputies Wendy Baldwin (extramural research) and Michael Gottesman (intramural) to change the way NIH works. Varmus's style in making many of these changes has been to bring in panels of outside experts to conduct sweeping reviews of programs or areas of research and then act quickly to put their recommendations into effect. Top-level panels have already reported on NIH's $1 billion intramural research program, the operations of NCI, and the grant review system. Others are currently looking into NIH's support for gene therapy, clinical studies, AIDS research, and NIMH. Among the new thrusts:

Tenure reform. An idea conceived before Varmus's time and reinforced by Varmus's intramural research panel has now been carried out—opening intramural jobs to outside competitors and giving junior employees a clearer sense of career prospects. As Hall of NINDS sums it up, NIH has switched from a "person-based" selection system to one in which candidates are evaluated according to set criteria. In the past, few junior positions were advertised. Now all are, and Varmus says: "We are competing now with Harvard and Rockefeller; we get from 300 to 600 applicants for these jobs." Procedural changes have also made tenure review more critical and independent. According to Gottesman's report on the first 14 months of the new system, the tenure approval rate has dropped from 95% to 75%.

Flexibility. Nowhere is the push for administrative change more visible than at NCI, where Klausner, the new director, has shaken up the central office. Under a new manager, Mary Ann Guerra, NCI is planning to reduce overhead and assign a smaller number of administrative staffers to work in teams directly with labs. Performance will be rated in part by the scientific staff.

At a higher level, Varmus has negotiated a plan for reduced oversight of NIH at HHS. As of 1 October, the NIH director no longer reports to an assistant but directly to the HHS secretary, eliminating layers of approval and paperwork. Varmus has also won greater independence to make personnel decisions. In addition, he now has clearance from the White House to make sparing use of two pay provisions to support candidates' preexisting pension programs and award salaries above the civil service line—up to $200,000 for some clinical specialists.

NIH as university. Varmus has tried to tear down walls between institutes and make NIH more like an academy. He has instituted a monthly seminar to highlight the work of junior staffers and a Wednesday series—with refreshments—to bring outside scientists to the campus and create "a place where the community gathers every week." Says Varmus: "The place needs to be more congenial."

Clinical research. One area where Varmus has come in for criticism is his perceived bias toward molecular biology rather than clinical research. His tried-and-true response has been to create a panel to look into clinical researchers' needs, but this community wonders, as one lobbyist says, whether the effort is merely "cosmetic." In the words of one panel member—Herbert Pardes, dean of Columbia University's College of Physicians and Surgeons—Varmus is "approaching it the right way," but "the committee hasn't done anything yet."

Embryo research. Although Varmus has been quick to implement proposals from outside committees, one exception is research on human embryos. Just over a year ago, a blue-ribbon panel recommended guidelines under which NIH should fund embryo research, but President Clinton intervened in the face of a mounting conservative protest. He ruled that no embryos would be created in the lab for research, and the committee's other recommendations have been tabled for now. Varmus failed to anticipate the backlash this review would ignite and now views it as "one of the things I regret." He thinks it might have helped if he'd called it a review of fertilization (not embryo) research.

Money troubles

While Varmus has been praised for making changes in NIH's intramural program, extramural researchers worry about the big cloud hanging over their future: How will they afford to keep pace with the increasing cost of research? The NIH staff, of course, doesn't control congressional appropriations, and NIH is being forced to cut costs, like most federal agencies. But this is a new experience for NIH, and it is not clear how Varmus and his top staff intend to allocate the pain over the long term. So far, NIH has been trimming on many fronts and allowing administrative and intramural staff to shrink. A bolder plan may be needed soon, but none has yet been discussed.

Earlier this year, Varmus warned in a major lecture that biomedical research could be trapped in a "steady-state" economy for some time. That forecast is being borne out. The president's 1996 budget request for NIH aimed to increase funding at the biomedical inflationary rate of 4.2%, with little growth in the future. Republican budget committees in Congress went the other way, proposing to cut NIH and other agencies by 10%. This caused panic.

According to several Capitol Hill aides and biomedical lobbyists who spoke to *Science* on condition of anonymity, Varmus reached out first to Senator Edward Kennedy (MA), the once-powerful Democrat, for help. The new Republican appropriations chief in the Senate, Mark Hatfield (OR), was offended. But Republicans later came to NIH's rescue—Hatfield, by leading a surprisingly successful effort to spare NIH from the sweeping cut, and Representative John Porter (IL), by pushing a 5.7% increase for NIH through two committees and the full House.

Since then, however, Congress has been mired in partisan disputes, creating a stalemate that has actually reduced NIH spending to a rate below that of 1994. "If we had the budget that everybody seems to want to give us, namely a 4.2% increase," says Varmus, "we could do quite a few new things." But lacking it, NIH may have to postpone its most exciting new projects. Among those likely to be hit: a plan to start large-scale sequencing of the human genome.

Like other government executives, Varmus has the tricky task of campaigning for his constituency without appearing to do so. To this end, Varmus has been working more closely with NIH's Republican friends on Capitol Hill. In October, for example, NIH staffers report, he made a special effort to include Porter at an exclusive dinner and strategy meeting with NIH's institute chiefs. Recently, Varmus and other institute directors have been running a "minimed school" on the Hill, educating members of Congress.

In the end, though, Varmus's strategy for promoting NIH is quite simple: "Go back to the science," he says. When it comes to soliciting funds, the appeal "that will finally win the day" for NIH, Varmus believes, is first, "the intense desire of everybody to have better health," and second, "the excitement that's generated by biomedical discoveries." And those are the themes he will continue to stress.

–Eliot Marshall

RUSSIA

Antarctic Research Ship Narrowly Saved

MOSCOW—Russia narrowly averted losing its foremost Antarctic research ship—the *Akademik Fyodorov*—earlier this month. At the eleventh hour, Russia's finance ministry came up with $3.2 million to pay off a German shipyard that was threatening to sell the ship to pay for repairs to it and another research vessel. Although the ministry has agreed to fork over another $1.3 million to complete the repairs to the $25 million *Akademik Fyodorov*, the several weeks of delay already incurred because the shipyard impounded the vessel while it was waiting for payment may make it necessary to temporarily shut down Russia's Vostok research station.

Both ships are the property of the Arctic and Antarctic Research Institute in St. Petersburg, but the German shipyard, Motorenwerke Bremerhaven in Bremen, charged Russia's Federal Service for Hydrometeorology and Environment Monitoring for the work because it pays for the annual Antarctic cruise. Anatoly Yakovlev of the Federal Service told *Science* that the *Akademik Fyodorov* docked at the shipyard on 11 July for repairs, followed on 25 July by another of its vessels, the *Mikhail Somov*, which required maintenance.

The Federal Service did not have the money to pay the usual 50% deposit for the work because it had not yet received this year's funding from the finance ministry for its Antarctic campaigns. So Federal Service officials persuaded the shipyard to repair one ship on credit, and a month later the *Mikhail Somov* left the shipyard. The Federal Service was still unable to pay its debt, however, and Motorenwerke Bremerhaven set a deadline of 10 November, after which the *Akademik Fyodorov* would be sold at auction to cover all repairs and the shipyard's financial expenses.

On 19 October, with the finance ministry ignoring their pleas, says Petr Nikitin, head of the Federal Service's Arctic, Antarctic, and Maritime Department, service officials appealed to Prime Minister Viktor Chernomyrdin for help in saving the ship. Chernomyrdin sent an official letter to the ministry ordering it to transfer the funds, but the ministry left it until the first week of November before relenting. "I don't understand the position of the finance minister," says Nikitin. "Being a member of the Cabinet he has to obey the prime minister."

The sum paid covers only the cost of the repairs of the *Somov* and the 50% deposit for repairs to the *Fyodorov*. Although the risk of losing the ship is now gone, Nikitin says, the delay is putting the service's Antarctic research in jeopardy. The *Fyodorov* was due to depart for the Vostok station at the end of last month, says Yakovlev, but completing the repairs and sailing the ship back to St. Petersburg to load stores will take another 40 days. This may make it impossible to carry out essential work on the station before next winter. "It may be very dangerous for the research team to work in the Antarctic, and in this case we will simply have to rescue the researchers," Nikitin says.

The Vostok station is sited near the southern geomagnetic pole and specializes mostly in paleo-glaceology. Researchers there have spent the past few years extracting a core from an ice layer 3.7 kilometers thick. They had hoped to bore the last 500 meters in the coming year. Now they may have to put their plans on ice.

–Andrey Allakhverdov

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