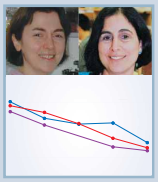
p110 Public health in peril: War has decimated Iraq's research and health systems



p114 A woman's place: Female scientists are still struggling to find a foothold

p116 Fat chance: Luck and leptin have brought fame and fortune to Jeff Friedman

US pressures publishers to honor trade embargoes

A US government agency better known for seizing the assets of dope smugglers has become an arbiter of scientific publishing. Bowing to pressure from the Office of Foreign Assets Control (OFAC), a branch of the US Treasury Department, the American Society for Microbiology (ASM) on 12 January stopped accepting papers submitted to its 11 journals from Sudan, Libya, Iran and Cuba.

The OFAC monitors and enforces the US trade embargo against the countries. The federal regulations that define the terms of the embargo specifically exempt journal articles and other forms of communication, but only if they are finished works.

According to R. Richard Newcomb, director of the OFAC, reviewing and editing are considered "services," which are prohibited if an author, editor or reviewer is affiliated with an embargoed country. A manuscript submitted in camera-ready form is legal, but if edited by the recipient—even if the changes go no further than copy-editing—it is not. Scientific manuscripts are typically passed back and forth between author, editor and reviewer, with changes occurring at each transit, until a final version is hammered out.

The OFAC provides a licensing mechanism allowing editors to apply for permission to publish, but the process is cumbersome and time consuming. In one case, it took 10 months for the agency to respond to a license request for a paper from Iran.

Following a letter from the OFAC in September 2003, the Institute of Electrical and Electronics Engineers has chosen to reject all but camera-ready manuscripts from the embargoed countries. The American Chemical Society also no longer accepts submissions from those countries.

Sam Kaplan, chair of the publications board of the ASM, says his society will apply for OFAC licenses, and will try to initiate legislation to exempt scientific exchange entirely. For the time being, however, the ASM reluctantly refuses submissions from the four countries.

"We are deeply distressed to take this action, but we cannot place our staff or volunteers in a position of jeopardy," Kaplan says. "We sincerely hope that knowledgeable people will appreciate the harm that this does to the scientific enterprise."

Other editors are also unhappy with the policy. "It's open discrimination not only against research but against people from certain countries," says Keith Yamamoto, editor of *Molecular Biology of the Cell*. "First Amendment issues aside, it smacks of ethnicism and doesn't have anything to do with science *per se*. I find it wildly inappropriate and embarrassing."

Yamamoto, who is a member of the Joint Steering Committee for Public Policy, a consortium of five learned societies that interfaces with members of Congress, says he will urge the group to oppose the OFAC licensing scheme. "For our government to be taking a stand against open scientific communication is very troubling," he says.

Potter Wickware, San Francisco

Animal research stance spells knight-mare for Blakemore

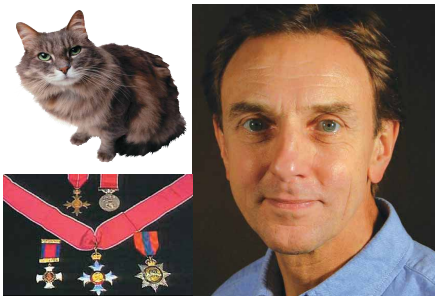
A fight has erupted in the UK over a leaked Cabinet Office document that suggests Colin Blakemore, the new chief executive of the Medical Research Council (MRC), was not recommended for knighthood because of his public support for animal research.

Heads of the MRC are typically granted knighthood. However, the document, leaked on 14 December, revealed that Blakemore had been rejected because of his "controversial work on vivisection." The document said Blakemore, an eminent neuroscientist who took on the new post in October, could be reconsidered if his reputation improved after his move to the MRC.

Blakemore has threatened to resign from his post, and says he has consistently spoken out in favor of animal research at considerable risk to himself and his family. Two letter bombs have been sent to Blakemore's home and, until recently, he had to travel with a police escort.

"My protest about the content of the leaked minutes has nothing to do with whether I deserve an honor," Blakemore says. "My expressions of concern have to do with the apparent inconsistency of government attitude to the use of animals in medical research."

Blakemore says he had planned new mechanisms to reward MRC-funded scientists for contributions to public communication. But the leak presents him with a dilemma, he says. "How can I write to MRC scientists to ask them to engage in public dialogue on animal experimentation in view of this evidence that, in secret, their reputations will be damaged by doing so?" Blakemore says the government's stance on animal research is due to the substantial donations the Labour Party has received from animal liberation groups.



Colin Blakemore's support of animal research may have cost him knighthood.

Not surprisingly, those groups are delighted that Blakemore was denied knighthood. Blakemore "had what can only can be described as a tantrum over the knighthood issue," says Andrew Tyler, director of Animal Aid. "Blakemore should either adjust his thinking or resign his position."

But several scientists and organizations are rallying around Blakemore. The new council of the Biosciences Federation, which has more than 60,000 members, has written to Prime Minister Tony Blair to ask him for a statement.

Calls for the honors system to be changed have also skyrocketed. The government has promised a review, and the system is also to be examined by the Commons Public Administration Committee.

Xavier Bosch, Barcelona

Iraq's public health infrastructure a casualty of war

Attempts to resurrect Iraq's health-care system remain hindered by a medley of factors, experts say, including the absence of national security, the scarcity of utilities like water and electricity, and a dearth of financial resources.

War has shattered Iraq's primary health and disease control and prevention services, and has decimated the country's research infrastructure (*Nature* **423**, 468; 2003). Nurses and primary health-care workers are in chronic short supply. Public health laboratories, clinics and several hospitals also lie in ruins.

The most likely diseases to arise after conflict are communicable diseases such as typhoid, vector-borne diseases such as malaria, and vaccine-preventable diseases such as measles, says Kawa Maruf, a World Health Organization (WHO) medical officer in Dahuk, Iraq. In central and southern Iraq, fluctuating electricity and poor sanitation have led to spikes in water-related diseases such as cholera and dysentery. In the summer of 2003, several Iraqi hospitals also reported cases of diarrhea that were up to four times higher than the seasonal average.

Stunted vaccination programs threaten the health of Iraq's approximately 4 million children under the age of five. Vaccine supplies were destroyed last April, when looters broke into the Vaccine and Serum Institute of Baghdad and destroyed large repositories of vaccines for hepatitis B, meningitis, measles, polio, tetanus and yellow fever. The United Nations Children's Fund reported that 270,000 Iraqi babies born after the war began have not received any vaccinations. Recently, however, a fledgling national immunization initiative has been slowly taking root.

EPA Photo/EPA/Nabil Mounzer

The war in Iraq has reduced hospitals to rubble.

Experts say the recovery of Iraq's health infrastructure—once among the most advanced in the Middle East—will hinge on repairing public health programs, forming a national health policy and sustaining financial investment. Apart from regulating the flow of drugs and sending some medical staff overseas for training, however, relief organizations have not made much headway, says Jafar Hayder, a WHO medical officer in Sulaimania, Iraq.

Other recovery efforts under way include a $7 million children's vaccination program by the US Agency for International Development, as well as a new scientific academy that aims to revitalize Iraq's research climate by luring expatriate doctors back home (*Nature* **426**, 484; 2003). But a lot more resources are needed to restore Iraq's health system to its level in 1990—Iraq's health ministry estimates that it will require an additional $1.6 billion each year.

Despite Iraq's steep path to good health, however, experts say the nation has better prospects of recovery than other war-torn countries such as Afghanistan and Liberia, which had inadequate health systems to begin with.

"In Iraq, sophisticated office buildings and hospitals were bombed into rubble. In Afghanistan, rubble was bombed into rubble," says Ronald Waldman, professor of clinical population and family health at Columbia University. The media spotlight on Iraq overshadows reconstruction efforts in other post-conflict nations, adds Waldman, who advised Afghanistan's health ministry. "When the spotlight of news is off, the donors disappear."

Relief funds are plentiful immediately after an emergency, but decline as the world shifts its attention elsewhere—a phenomenon widely known as donor fatigue. "There is far too much money initially when there is little capacity to absorb it," says Jan Kolaczinski, a conflict and health expert at the London School of Hygiene and Tropical Medicine. "That's why you get lots of stupid implementations by emergency [non-governmental organizations] that just try and blow their budgets as quickly as possible." Pointing to experiences in both East Timor and Afghanistan, Kolaczinski adds, only time will tell whether Iraq will go down the road of other postwar has-beens—"a cycle that happens over and over again."

Paroma Basu, Kolkata

Soldiers battle 'Baghdad boil'

More than 300 US soldiers in Iraq have been diagnosed with the parasitic skin disease leishmaniasis, which is expected to infect nearly 1,000 soldiers by the end of 2004. "This is probably the largest outbreak of leishmaniasis that the US military has ever seen," says Lt. Col. Peter Weina, director of *Leishmania* diagnostics at Walter Reed Army Medical Center.

Known in Iraq as the 'Baghdad boil', the cutaneous form of the disease is transmitted by the bite of sandflies carrying various species of the protozoan *Leishmania*, and causes craterlike skin lesions. Leishmaniasis is the "major medical issue" facing troops in Iraq, says Lt. Col. Russell Coleman, assistant chief of entomology at Walter Reed.

Most soldiers were infected during the sandfly season that began in April 2003, but did not show symptoms until recently because of the disease's long incubation period. There have been no cases reported thus far of the more serious visceral form of leishmaniasis, which affects the liver and spleen and can be fatal.

The standard treatment for the skin disease, GlaxoSmithKline's Pentostam, has not been approved by the US Food and Drug Administration, but is available to soldiers and civilians through an Investigational New Drug protocol. Soldiers are sent to Walter Reed for treatment because potentially severe side effects require that the drug be administered under strict controls.

More than a million new cases of cutaneous leishmaniasis are reported worldwide each year, with current large outbreaks in Sudan and Afghanistan. As a result, the availability of Pentostam is limited and the Army is investigating alternative treatments for the disease.

Although vaccines for leishmaniasis are in early development, an effective one is "a long way off," says Lt. Col. Weina.

To prepare for the return of the sandfly season in April, the Army has deployed medical units in Iraq to control insects and animals that may act as reservoirs for the disease, and to educate soldiers about preventive measures. "Living conditions certainly play a large role in this because there is no drug you can take to prevent the disease," says Lt. Col. Coleman. "All you can do is keep that infected sandfly from biting the soldier."

Deirdre Lockwood, New York

World agencies try to stem flood of fake drugs

Procrit, a drug to treat anemia, is replaced with bacteria-contaminated tap water. Nearly 200,000 bottles of Lipitor, an anti-cholesterol pill, are recalled after patients complain of a bitter taste. Vials of Neupogen, a medication given to cancer patients, are found to contain saline.

The sale of such counterfeit drugs has skyrocketed in recent years. In some countries, nearly 25% of drugs on the market are fraudulent, according to the World Health Organization (WHO). Counterfeit drugs make up an estimated 10% of the Southeast Asian market, and Chinese authorities say more than 50% of certain products in that nation are fake. In a WHO survey of seven African countries, 20–90% of antimalarial drugs there failed quality testing.

In the US, the Food and Drug Administration (FDA)'s investigations on counterfeit drugs have increased to more than 20 per year from an average of 5 in the late 1990s, according to an interim report filed by the agency in October 2003.

The FDA, the WHO and other public health and regulatory agencies around the world are taking initiatives to fight this growing problem. In November 2003, the WHO and the governments of Cambodia, China, Laos, Myanmar, Thailand and Vietnam announced they would work together to strengthen inspection and post-marketing surveillance of drugs. In those countries, the products imitated most often are antibiotics, and drugs used to treat tuberculosis, malaria and HIV/AIDS.

The WHO is also conducting workshops in many African countries to help drug manufacturers upgrade their standards and assist officials in improving drug screening and testing practices. "It takes a lot to battle the problem," says WHO spokesperson Daniella Bagozzi.

Pharmaceutical companies are taking their own steps to fight the problem. In December 2003, Johnson & Johnson and Pfizer—which manufactures Lipitor—told their wholesalers that they could only buy medicines directly from the company.

In the US, New York State congressman Steve Israel introduced legislation in October 2003 that would give the FDA the ability to recall counterfeit drugs and increase criminal penalties for counterfeiters.

Some nations are taking more extreme measures. In December 2003, the Indian government approved an amendment to its Drugs and Cosmetics Act, allowing lawmakers to seek the death penalty for people who manufacture or sell counterfeit drugs.

The FDA plans to take a multipronged approach to combat the problem. In its interim report, the agency recommends using authentication and track-and-trace technologies, implementing rapid-alert and -response systems, and increasing the awareness and education of health-care workers and consumers. Because the FDA does not regulate products bought from foreign countries through the Internet, the agency also suggests developing global standards for packaging, and international collaboration in law-enforcement efforts.

The FDA is also testing technologies such as radio-frequency chips, near-infrared spectroscopy and organic vapors to identify products. "The FDA is evaluating all available technologies," says agency spokesperson Jason Brodsky. "There is no single 'magic bullet' solution to stay ahead of the counterfeiters."

Aparna Surendran, New York

For HIV vaccine trials, size does matter

When California-based VaxGen announced in February 2003 that its HIV vaccine selectively protects blacks from infection, experts questioned the statistical significance of the results. Out of the resulting controversy has emerged a real push to change the way minorities are recruited and retained in HIV vaccine trials.

"We have learned some important lessons from the AIDSVAX trial," says Peggy Johnston, director of AIDS vaccine research at the US National Institute of Allergy and Infectious Diseases. "We have to ... apply it to the future so we don't end up in this situation again."

In response to VaxGen's announcement, a US National Institutes of Health (NIH) working group reanalyzed the data and concluded that the protective effect observed in certain subgroups was a fluke. The group said the minority population in the trial was too small to detect any differences.

"The study population should mirror the people who are at the highest risk, and in the VaxGen trial, this simply was not the case," says Mark Feinberg, a professor of medicine at the Emory University School of Medicine. What's more, Feinberg says, VaxGen's claims actually make recruiting minorities for clinical trials more difficult.

"People from diverse racial and ethnic backgrounds are already skeptical of scientific researchers," he says. "The publicity generated by the AIDSVAX trial makes a complicated situation even worse."

Although the NIH set guidelines on minority participation in clinical trials in 1994, the numbers of women and people of diverse ethnic backgrounds in trials remain low. "This means that broad and deep community support will be needed, rather than a narrow focus on recruitment for a particular trial," says Steve Wakefield of the HIV Vaccine Trials Network (HVTN).

At a conference in September 2003, researchers renewed their commitment to making trials more representative of populations at risk. In October, the US sponsored a symposium on recruiting and retaining racial and ethnic minority participants in clinical trials.

As a result, the HVTN and the NIH are working closely with community leaders to engage local organizations, develop community education plans and build trust among minority populations.

"The challenge," says Wakefield, "is to turn all of this into realistic activity which addresses the legacies of mistrust in communities of color."

Amy K Erickson, Washington, DC

In world of epidemics, WHO's in control

Last year's outbreak of severe acute respiratory syndrome (SARS) provided the World Health Organization (WHO) an opportunity to show the world its teeth. Newly installed director-general Jong-Wook Lee intends to use them to take a bite out of the world's costliest diseases.

In recent months, Lee has sounded a clarion call for the WHO to lead a scale-up of AIDS treatment and other targets spanning a wide spectrum—from eradicating polio to curbing tobacco use, combating cardiovascular disease, and significantly reducing childhood mortality.

But the WHO's new stances on SARS and HIV/AIDS have by far received the most attention. The organization has updated guidelines for AIDS treatment and redoubled its commitment to providing antiretroviral therapy to 3 million people (of the 6 million who need it) worldwide by 2005—a $5.5 billion initiative.

The rapid emergence and spread of SARS stirred something of a crisis mentality. Through its Global Outbreak Alert and Response Network, the WHO—under former director-general Gro Harlem Brundtland—responded by deploying epidemiologists and other experts throughout the world. The experts pieced together their findings in Geneva during daily teleconferences, resulting in the eventual identification of the mysterious coronavirus.

More controversial were the advisories against travel to Toronto, Hong Kong and parts of China, providing an unprecedented illustration of the WHO's singular discretion.

"I didn't realize until later that that was the first time [travel advisories had ever been issued]," says Ray Arthur, associate director for global health at the US National Center for Infectious Diseases. "If you look at it from the perspective of what measures needed to be taken, it's not a surprise," he adds.

The WHO is now trying to draw on the clout it gained during the SARS epidemic to foster similar urgency in battles against HIV/AIDS and other long-entrenched enemies.

"We looked very hard at the SARS example and we realized that you can do this and you can survive it and have a very real impact," says Jim Yong Kim, an advisor to Lee in Geneva. Previous recommendations for AIDS treatment took years to adopt and prescribed dozens of protocols—such as CD4 counts and the measurement of viral loads—that made treatment prohibitive to a large part of the world, Kim says.

In a matter of just months, the organization developed new guidelines incorporating models such as Haiti's HIV Equity Initiative. "Up to now," Kim says, "what we have done has been much too complicated and much too slow."

Lee's tenure has been marked by such emphasis on activist, ground-level goals, but his biggest challenges, say some observers, could lie in galvanizing the member states.

"I don't think [the WHO] has the resources yet to manage that," says epidemiologist Ernest Drucker of Montefiore Medical Center in New York. The WHO remains dependent on its member states to commit material, financial and ideological backing. Channeling diverse, and occasionally competing, agendas, Drucker says, is often a tall order.

Others point to a heightened sensitivity to international health. "Any time there's a major epidemic, obviously it attracts a lot of attention from the public," says Arthur. "You perform well when you're under the spotlight, and that's recognized; you don't perform well, and there are probably some consequences."

Bruce Diamond, New York

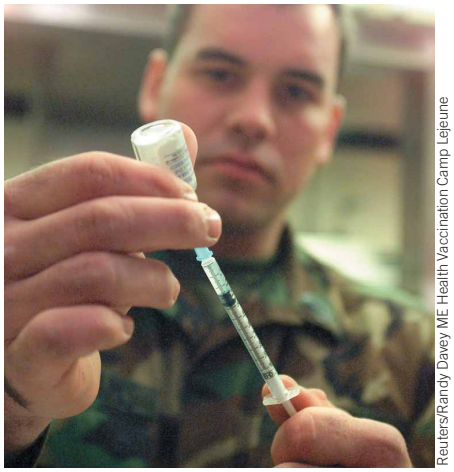
US soldiers refuse to fall in line with anthrax vaccination scheme

US soldiers are battling with the federal government over the military's anthrax vaccination scheme. After a flurry of rulings and counter-rulings over whether the vaccine can protect soldiers from inhalation anthrax, a federal court in January lifted a temporary ban on the program. But the debate over the drug's efficacy is likely to continue as the case moves through the courts.

The US has vaccinated more than a million soldiers since 1998. Opponents of the program say the vaccine causes both long- and short-term health problems, including pneumonia, joint pain and gastrointestinal disorders.

Thousands of adverse event reports have been filed with the US Food and Drug Administration (FDA). However, based on existing evidence, several scientific panels have determined that the vaccine is safe. Those who refuse the shot have been disciplined and, in some cases, court-martialed.

No one argues that the vaccine is effective against cutaneous anthrax. A 1962 study—the only placebo-controlled human trial of the anthrax vaccine—followed 1,200 workers in four textile mills. Only 1 of the 26 subsequent cases of anthrax occurred in a fully vaccinated worker, but only 5 of the 26 cases were of inhalation anthrax (*Am. J. Public Health* 52, 632–645; 1962). Based on those data, a scientific panel in 1973 concluded that inhalation anthrax "occurred too infrequently" to assess the vaccine's efficacy against it.



Reuters/Randy Davey ME Health Vaccination Camp Lejeune

US soldiers are suing the Department of Defense over forced vaccinations.

The panel's recommendations languished in regulatory limbo, however. They were finally published in 1985, but the FDA never formally adopted or rejected them. In his initial ruling, Judge Emmett Sullivan said the vaccine is an investigational drug being used for an unapproved purpose. He ruled that the US "cannot demand that members of the armed forces also serve as guinea pigs for experimental drugs."

One week later, the FDA published a belated analysis of the 1985 recommendations, disputing the panel's finding. Analyzing the two exposure routes together, it concluded the vaccine is 92.5% effective against all forms of anthrax.

Based on the FDA's new analysis, the judge lifted the temporary ban. But the new interpretation of the data is a matter of semantics, not science, argues Gene Stollerman, who chaired the 1973 panel. "I will defend our interpretation," Stollerman says. "Any other interpretation has to do with legal issues."

The existing evidence doesn't meet the FDA's usual standards, adds Mark Zaid, the Washington-based lawyer who brought the case against the US Department of Defense (DOD). "When had the FDA ever said to anyone, 'it's probably effective so we're going to give you a license'?" Zaid asks.

Confident it will prevail, the DOD has ordered a $30 million batch of the vaccine. Laywers for the soldiers, meanwhile, have asked the judge to grant the case class-action status.

Tinker Ready, Boston

US finds first case of mad cow disease

At least 36 nations banned the import of US beef after the US Department of Agriculture (USDA) reported the first case of bovine spongiform encephalopathy (BSE), or mad cow disease, in the US in December.

Meat from the infected Holstein cow—and 19 others slaughtered on the same day—was shipped to eight US states and to Guam. About 10,000 pounds of beef has since been recalled. US officials said the cow originated from the Canadian province of Alberta, also the site of Canada's first case of BSE last May (*Nat. Med.* **9**, 809; 2003). In January, the USDA announced plans to kill 450 quarantined calves, including the infected Holstein's offspring.

The agency also set new regulations, including banning meat from 'downer' cows—those that are too sick or old to stand or walk. Also banned are small intestines, and the head and spinal tissue from cows older than 30 months. In addition, meat will only be shipped from slaughterhouses after testing negative for BSE.

Meanwhile, there is new concern that vCJD, the human version of BSE, can be spread through blood transfusions. British health officials are investigating the death last fall of a patient who received blood from a donor who later died of vCJD. More than 150 cases of vCJD, most of them in the UK, have been reported worldwide. —*AS*

FDA bans ephedra sales

The US Food and Drug Administration (FDA) in December banned sales of dietary supplements containing ephedra, an herb widely used to aid weight loss and enhance athletic performance.

Ephedra's ability to speed up the body's metabolism has been linked to reports of heart attack, stroke, seizures and sudden death (*Nat. Med.* **9**, 634–635; 2003). After reviewing thousands of reports of adverse reactions, the FDA ruled that the drug poses an "unreasonable risk of illness or injury," and is urging consumers to stop buying and using ephedra-based supplements immediately.

Manufacturers of the supplement are expected to challenge the ban, claiming the drug is safe when used as directed. Sales of ephedra spiked after the ban was announced, as anxious consumers stocked up on their favorite products. —*PL*

News briefs written by Aparna Surendran, Pierrette Lo and Peter Vermij

Asian nations face bird flu, SARS

Chinese health officials have confirmed the return of severe acute respiratory syndrome (SARS) to the nation. As of 15 January, China reported three cases of SARS, all in the Guangdong province where the illness first surfaced in November 2002.

Chinese officials immediately ordered the culling—by boiling, drowning, electrocuting or burning—of 10,000 civet cats, which many Chinese scientists suspect as the source of SARS, as a protective measure. Chinese officials also said they would kill rats and cockroaches. However, the World Health Organization (WHO) cautioned that slaughtering civets, which are related to mongooses, could help spread infection and destroy scientific evidence. Chinese officials banned the sale of civets last year when SARS was on the rise, but lifted the ban in August.

Reuters/China Photo ASW/DL China Guangzhou

China is culling civet cats as a precaution against SARS.

There have been five suspected cases of SARS since the epidemic sickened 8,000 and killed 774 in 27 countries last year. Two other cases appeared in late 2003—one in Singapore in September and another in Taiwan in December. Both involved researchers who had accidentally become infected while working with the virus.

Meanwhile, South Korea, Vietnam and Japan reported outbreaks among poultry farms of the avian influenza virus H5N1. The WHO confirmed that the virus was responsible for three human deaths in Vietnam and is investigating several other cases. As of 15 January, however, the agency said there was no evidence of human-to-human transmission. —*AS*

EU drops cloning ban

The European Parliament backed down from a proposed ban on therapeutic human cloning after the European Council declared it unacceptable. During negotiations in December 2003, the two bodies of the European Union (EU) agreed on a compromise, saying the new rules will "not interfere with member states' decisions" on the use of specific types of cells.

Citing health concerns, the Parliament had adopted the proposal to prohibit transplantation of cells derived from human clones. But the Council insisted that individual countries such as Sweden and the UK maintain their right to allow the procedure.

The compromise cleared the way for much-awaited EU regulation on the use of all types of human tissues and cells. Those rules—which individual European countries can only tighten—regulate donation, testing, processing, storage and distribution of all human material, except whole organs and blood. Public and private users have to abide by the same quality and safety standards, which proscribe, among other things, that donors may not gain financially from their generosity.

The European biotech industry, which had lobbied hard for some form of legislation, welcomed the compromise, expressing hope that market regulation of industrial products based on human tissues and cells would soon follow. —*PV*

NIH resets conflict-of-interest limits

The US National Institutes of Health (NIH) increased the financial conflict-of-interest threshold, effective 4 February, from $5,000 to $10,000 for extramural researchers who participate in the peer-review process. The rules, which have not been updated since 1985, are necessary to reiterate that outside researchers are not accountable to the same conflict-of-interest rules as federal workers, the agency says.

Meanwhile, a US House committee and a Senate subcommittee have both asked NIH director Elias Zerhouni to produce documents on agency scientists who served as paid consultants to drug companies with NIH funding. The request came a day after the *Los Angeles Times* published a high-profile article on NIH employees' conflicts of interest.

In a December letter to the House committee, Zerhouni said he had begun a review of all nongovernmental payments made to NIH employees since 1 January 1999, and would put forward recommendations for improving the agency's ethical policies within 90 days.

The controversy comes months after a congressional committee said NIH researchers, including former National Cancer Institute director Richard Klausner, had broken federal criminal laws by taking 'lecture awards' from NIH grantees (*Nat. Med.* **9**, 984; 2003). —*AS*

A lab of her own

Why do women continue to drop out of research in record numbers? Charlotte Schubert and Gunjan Sinha plumb the 'leaky pipeline'.

As an undergraduate, Elodie Pastural attended Paris' École Polytechnique, the most prestigious science and engineering school in France. Pastural was one of only 8% of women at the military academy, where she won a coveted scientific prize. She later served a year in the armed services. After receiving her Ph.D. in human genetics from the Université Pierre et Marie Curie, Pastural seemed well on her way to a promising career. But she decided instead to take time off to rear two young children.

The decision was not easy—but neither were the circumstances. She could not find child care in Paris, and her husband, a businessman, was offered a lucrative position in the French countryside—far from any science hubs. The family relocated.

After four years away from the bench, Pastural was ready to return to science. But much to her chagrin, she found that she was not competitive for most postdoctoral fellowships, and many others were closed to her, with requirements that she be a recent graduate or of a certain age.

Fortunately, she found a lifeline. She applied for and received a 'restart' grant from the European Molecular Biology Organization (EMBO), which supports scientists who take time off to rear a family. "The EMBO fellowship was the only one adapted to me," Pastural says. This January, she plans to begin studying cell signaling at the Institut de Biologie et Chimie des Protéines in Lyon.

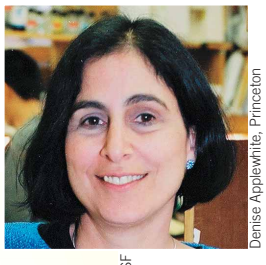
Lodged on the lower rungs

The EMBO restart grants are just one of a handful of fellowships in Europe and the US intended to kick-start a scientific career after a break. Others include the UK's Dorothy Hodgkin Fellowships, the Swiss National Science Foundation's Marie Heim-Vögtlin grants, and ADVANCE fellowships from the US National Science Foundation. Most are open to men as well as women, although few men apply. Out of a total of 50 applicants for the EMBO restart program in the last two years, only one was male.

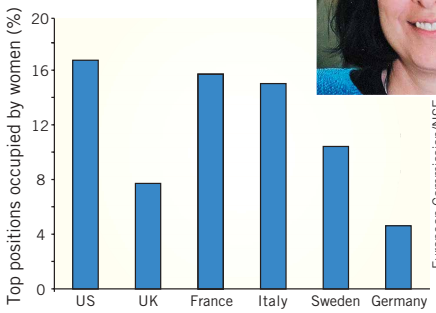
The fellowships aim to patch what's been called the 'leaky pipeline' for women in science. According to a European Commission report in 2000, nearly half of graduate students in the life sciences are women, but few make it to the top. Women occupy fewer than 10% of top positions—equivalent to a full professorship—in the medical and natural sciences. Another comprehensive European report, "She Figures 2003," and similar analyses in the US show the same process of attrition. The studies debunk one popular explanation for such attrition—they found that the gender gap in the top echelons is not just a result of fewer women entering the field.

Countries spend enormous resources training scientists, notes Nicole Dewandre, head of the European Commission's women and science unit. When women drop out, it is a "tremendous waste" of those resources, Dewandre says. "It's not fair if women train as scientists and then cannot get up the ladder." At the current pace, European women are not expected to reach parity with men in academic science positions until 2050, adds Gerlind Wallon, program manager for the EMBO restart grants.

Grants like those from EMBO are crucial in retaining women in science, but most experts say they barely make a dent in the widespread institutional and cultural barriers that strand women on the lower rungs, or cause them to abandon scientific careers altogether. "It would be preposterous to say that our restart fellowships are going to change things in a big way," says Wallon.



Denise Applewhite, Princeton



European Commission/NSF

Unlike Virginia Zakian (inset), few women scientists occupy top positions at universities.

Family first—and other myths

Women scientists are thought to drop out of science for two main reasons. First, many women, like Pastural, choose family over career when they find it difficult to juggle both. The second is the proverbial glass ceiling—an institutional matter that raises the thorny issue of discrimination.

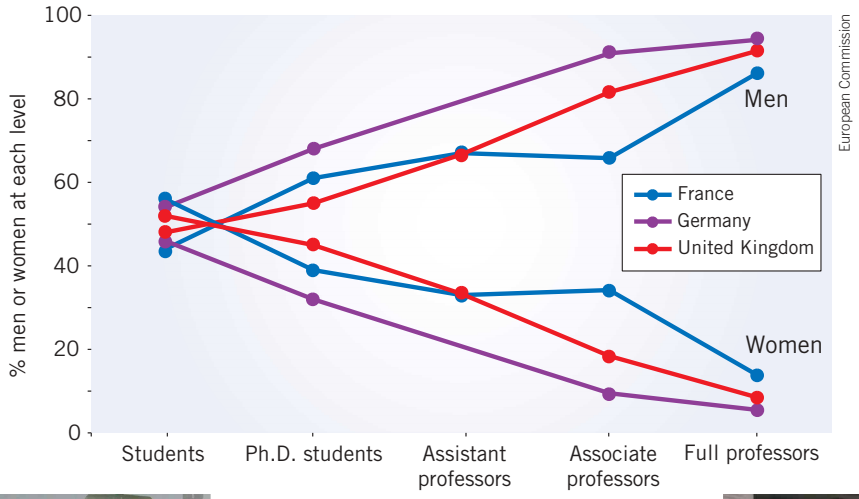
Science can be notoriously unfriendly to families. The swift pace of scientific progress discourages absences, the rush to tenure overlaps with child-rearing years, and moving from a country or institution—sometimes necessary to boost a career—can break up a family. In many European countries, such as Germany and Austria, child care is expensive and difficult to find. Both men and women can find themselves beleaguered.

Barbara Belletti, an Italian scientist, found herself temporarily overwhelmed after the birth of her second child while she was a postdoctoral fellow at the Kimmel Cancer Institute in Philadelphia. Belletti says she wanted to spend time with her new baby, but was also determined to stay in science. "I'm quite stubborn and I like my work," she says.

After eight months at home, Belletti won an EMBO restart fellowship to work at Italy's National Cancer Institute in Aviano, where her husband has a permanent scientific position. Luckily, she found daycare, a precious commodity in Italy.

One solution often touted as key to keeping more women in the workforce is establishing family-friendly policies. At the Kimmel Institute, for instance, parents can walk down the hall to visit their children at the day-care facility. But good child-care options don't necessarily translate into greater success for women.

"In the Scandinavian countries and the Netherlands, where there is very good child care, you still have similar patterns of women not getting into high-level positions," says Judith Glover, professor of employment studies at the University of Surrey, Roehampton. In fact, argues Glover, countries allowing women to take up to three years off for each child might hinder the jump back into science.



European Commission

EMBO

Elodie Pastural (L) and Barbara Belletti (R) returned to research after taking time off, but most women never find their way back.

EMBO

Studies suggest that, like Belletti, as many as 50% of women scientists marry other scientists. When the pair's careers are at odds, the husband's career often comes first, surveys report (http://www.haverford.edu/econ/faculty/preston_research.html).

Belletti says that in her family, she does most of the household and child-care work because her husband is trying to gain a foothold as a new professor. She's not alone: several surveys show that like their counterparts in other professions, women scientists often shoulder more of the burden of child-care and household work.

Despite that, numerous studies show that female scientists with children are just as productive—whether in publishing papers, gaining grants or other criteria—as their childless female peers (*N. Engl. J. Med.* **335**, 1282–1290; 1996 and *Ann. Intern. Med.* **129**, 532–538; 1998). Still, if men shouldered more domestic tasks, Belletti says, "women would have more time for their science."

The glass ceiling

Virginia Zakian is a professor at Princeton University and an expert in telomere biology. She has encountered "blatant discrimination" in her rise to the top, Zakian says. "But I think many women scientists have experienced this."

In 1995, Zakian left the Fred Hutchinson Cancer Research Center—and a Howard Hughes appointment—to begin a new life at Princeton. Zakian declines to discuss her time at Hutchinson, but says conditions for women scientists at the center have improved since her days there.

Zakian is now trying to improve the institutional climate for women scientists at Princeton. No one has yet systematically studied the myriad reasons women fail to move up the ranks of science, Zakian says. But there have been a few small steps in that direction.

In 1999, the Massachusetts Institute of Technology (MIT) released a report that threw the issue of institutional barriers to advancement into sharp focus. The study found differences in salary, space allocation, awards and resources between male and female faculty at MIT with equivalent professional accomplishments. It also found that the percentage of women faculty at MIT had remained constant for at least 10 years.

"I believe that in no case was this discrimination conscious or deliberate. Indeed, it was usually totally unconscious and unknowing," Robert J. Birgeneau, then dean of science at MIT, wrote in the report. "Nevertheless, the effects were and are real."

The report galvanized change at MIT and sent ripples throughout the scientific community. At a meeting in 2001, nine US institutions, including Princeton and the University of California at Berkeley, agreed to perform similar assessments; Princeton released its report in September 2003. Although less damning, the Princeton report identified areas of weakness, such as few women as department chairs—positions that, Zakian says, can pivotally influence the climates of individual departments. Only 2 of 13 departments at Princeton had ever had a woman chair.

Both the MIT and Princeton reports suggested placing more women in top positions, increasing hiring of women, and changing policies for resource allocation. They also called for more family-friendly policies, such as automatic tenure extension for all faculty members who have children.

Studies in Europe also document systematic and invisible barriers to women's advancement. For example, in 1997, Christine Wennerås and Agnes Wold, researchers at Göteborg University, created a furor with a study of peer-review scores at the Swedish Medical Research Council (*Nature* **387**, 341–343; 1997). They found that a woman applying for a post-doctoral fellowship had to be two-and-a-half times more productive than a man to rate the same scientific competence score—a situation that Wennerås says has since been rectified.

Institutional response to the gender gap is long overdue, experts say. "Most of the research and most of the campaigning has focused on women scientists," says the University of Surrey's Glover. Most existing programs encourage girls to study science and help women stay in the system, Glover says, but the focus needs to shift to the institutions.

"Of course, that would require the scientists on the inside agreeing that there might be something bad with the way that they conduct themselves," she says. "It's been more convenient for them to put the focus on women rather than on themselves."

In 2001, the US National Science Foundation's ADVANCE program began offering grants of up to $4 million to institutions that address barriers to women's advancement. No such program exists in Europe, Wallon says.

Even the future of the EMBO program is uncertain. The fledging initiative, only two years old, may not continue if EMBO pulls funding for the program in January. Although prospective grant seekers will have to wait and see, last year's winners are already planning their long-term careers. Pastural, who hopes to have an academic teaching career in Lyon, says her family is prepared to move if they have to. "I feel I am a valuable scientist," she says. "I would like to prove it now."

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Jeff Friedman

When Jeff Friedman began his career as a doctor, there was slim chance he would wind up a world-renowned researcher at Rockefeller University. But his discovery of leptin turned this 'accidental scientist' into a heavyweight among obesity researchers.

The year was 1980. Jeff Friedman, a resident at Albany Medical Center Hospital in New York, had tickets to the men's hockey semifinal at the Lake Placid Olympics. Friedman was a huge hockey fan, but he had been on call the night before and the US team was not expected to win. He decided to give the game a miss. In what has since been dubbed the "Miracle on Ice," the US stunned the Soviets. The game, which captured the tensions of the Cold War, was recently voted by the sports network ESPN.com as the greatest game of the twentieth century, and is the subject of a new movie.

The year was 1999. Friedman, now a full professor at Rockefeller University, had season tickets to a New York Rangers game. Too busy to attend, Friedman gave the tickets to Wolfgang Liedtke, an assistant professor in his laboratory. What Friedman didn't realize was that it was legendary player Wayne Gretzky's last game—scalpers were selling tickets at four figures—and another historic moment in hockey.

"I'm probably the only person to have tickets to the [Olympic] men's semifinal and the Gretzky game and have not seen them," Friedman says. "I have a history of missing important hockey games."

Fortunately, luck has favored Friedman in nearly every other walk of life. Although he began his career as a doctor, a series of coincidences brought him to obesity research. In 1994, after an eight-year quest, Friedman cloned the elusive *ob* gene and propelled the undeveloped field to new heights. "I wasn't sure this lab would ever find it," Friedman says. "I really tried to avoid even fantasizing what it would be like, but I had a lot invested in it at every level."

Genetically obese mice were first described decades ago, but until Friedman's team cloned the *ob* gene—quickly followed by the identification of leptin and the cloning of its receptor—progress in the field was slow. Simple as the task might now seem, in those days positional cloning was a tough job, notes Jim Darnell, Vincent Astor professor of molecular cell biology at Rockefeller, and Friedman's Ph.D. advisor. "The scientific impact of all this has made the study of weight control more a scientific matter than one that was in the dark ages before," Darnell says.

In his search for the *ob* gene, Friedman systematically mastered every emerging technique that might help him. Even after he had cloned the gene and its receptor, he continued to apply new techniques—he was among the first to use Affymetrix chips, for instance—to transform his genetics lab into one that could tackle the metabolic and neurobiological questions surrounding leptin and obesity.

"One of the things I most admire is that [Friedman] always has a big picture in mind—he never thinks small," says Markus Stoffel, Friedman's close friend at Rockefeller. "He tries to go where most people don't even think to go." Friedman pursued the *ob* gene to the exclusion of all else, Stoffel notes. If someone else had identified it first, Friedman's career would have looked very different, Stoffel adds. "Jeff took an enormous risk—he only did this one thing and nothing else. It was very, very brave."

Friedman, who describes himself as an "accidental scientist," grew up in Long Island, New York, where becoming a doctor was a foregone conclusion. After opening seven college rejection letters on the same day, he enrolled in a six-year program that allowed him to finish medical school at 22, but with little research experience. He recalls that when he tried to submit one early paper for publication, a reviewer wrote back saying, "This paper should not be published in [this journal] or anywhere else."

"That was my experience with research," Friedman says. "For that period of time and a long time after, I thought you had to be a genius to write and a publish a paper—that it was a monumental achievement that was highly likely to elude me for the rest of my career."

In his third year of residency, Friedman missed the deadline to apply for a fellowship. The department chair at the time, John Balint, suggested Friedman try research. Balint called his good friend Mary Jeanne Kreek, a researcher at Rockefeller University, who happened to have a postdoctoral position open. After just a few months in Kreek's lab, Friedman fell in love with research. He also realized he had no desire to be a doctor.

"I saw into my own future [as a doctor] and got nervous that as the learning curve flattened out more and more, I would get bored," Friedman says. "It's one thing to get bored and muddle by—it's another to get bored and muddle by in medicine, where people's lives are in the balance. I found that responsibility overwhelming."

Determined to pursue a career in research, he decided to enroll in Rockefeller's graduate program. He has stayed at the university ever since. On one wall of his spacious office hangs the northern blot that first identified leptin. He says he still remembers the feeling of elation when he developed the blot at 5 a.m. on a Sunday in 1994. There have been other great moments in his career since then, he says, "but never quite like that."

> "I wasn't sure this lab would ever find [the *ob* gene]. I really tried to avoid even fantasizing what it would be like, but I had a lot invested in it."

Margherita Maffei, a postdoctoral fellow in his laboratory, had developed a film and found that one candidate, unevocatively called 2G7, was fat-specific. It was 10 a.m. on a Saturday, so the lab was nearly empty, but Friedman was there anxiously awaiting the results, Maffei recalls.

The next day, Maffei had to attend a wedding. After frantically trying to reach her, Friedman decided to hybridize the blot himself. In those days, there was a constant sense of urgency in the lab, says Maffei, who now heads a small lab at the University of Pisa. "One thing I recall very clearly is that everything had to be done right away—in the next 48 hours," she says. "There was a lot of anxiety, but now I realize how important it was—he really wanted everything done, and he was right."

Despite his single-minded focus in the lab, people describe Friedman as an extraordinarily enthusiastic, bright, funny, friendly and generous man. "You'll never meet anyone as generous as Jeff is," says Alex Soukas, a former graduate student. "Jeff will give you a glass of his best bottle of wine without having one himself."

Friedman's interests span books, music, history, politics, wine and food, friends say. But his biggest passion is sports, including basketball, tennis and skiing. As for hockey, Friedman says he is determined not to miss any more historic games. "The moral from all that is don't jump to conclusions," he says. "I won't make that mistake again."

Apoorva Mandavilli, New York