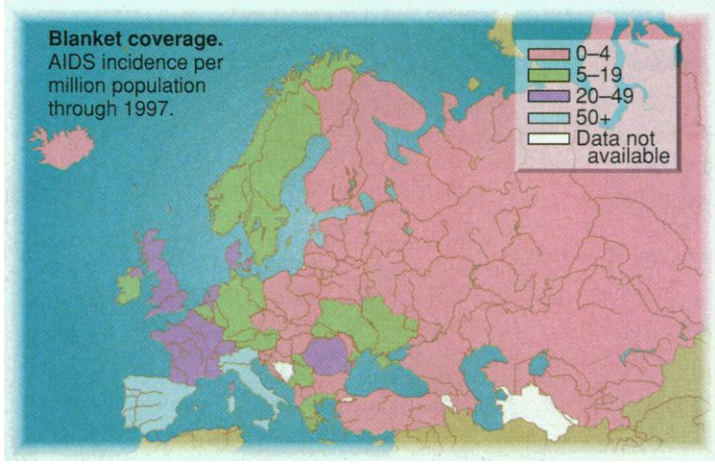
Europe: AIDS Research on a Budget

European researchers have scored some major hits in unravelling AIDS, with just a fraction of U.S. funding. Now even these modest sums are starting to slide.

PARIS—In 1978, a desperately ill Portuguese taxi driver, who had previously spent time working in Angola, was diagnosed in Paris with a rare form of pneumonia caused by the lung parasite *Pneumocystis carinii*. The three Paris-area specialists who were called in to consult on the case—infectious disease expert Willy Rozenbaum, immunologist Jacques Leibowitch, and lung specialist Charles Mayaud—were baffled. But soon a handful of other patients, many also with African connections, began showing up with similar symptoms: an inability to control normally benign infections. And when, in 1981, the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta published its first report of similar *Pneumocystis* cases in gay men in the United States, the French doctors quickly realized that they were confronting a frightening new disease of international proportions.



SOURCE: EUROPEAN CENTRE FOR THE EPIDEMIOLOGICAL MONITORING OF AIDS

In the 20 years since the first AIDS cases appeared in Europe, the epidemic has spread across the continent, leaving no country untouched. The European Centre for the Epidemiological Monitoring of AIDS, a Paris-based joint project of the World Health Organization and the European Union (EU), reported a cumulative total of more than 200,000 cases of the disease by the end of 1997. Although more than 90% of this toll is concentrated in Western Europe, the epidemic is now starting to grow in Central and Eastern Europe—Ukraine, for example, suffered a sixfold increase in AIDS incidence between 1995 and 1997.

As illustrated on the following pages of this Special News Report, European scientists have been on the front lines of the battle against AIDS from the very beginning. Rozenbaum, Leibowitch, and Mayaud soon joined forces with other researchers, including virologists at the Pasteur Institute in Paris, to form the team that first isolated HIV, the virus that causes the disease. And French scientists made a number of other early breakthroughs in HIV research, as did researchers in the United Kingdom, Sweden, and the Netherlands. More recently, Italian, Belgian, and Swiss researchers have taken their places in the front ranks, helping to unveil the mysteries of how HIV gains entry into its target cells and developing potential new therapies to block the virus.

The accomplishments of European scientists are all the more remarkable given the relatively modest sums their governments spend on AIDS research. The combined AIDS research budgets of the entire continent amount to only a fraction of the more than $1.7 billion spent annually in the United States. Even France, which has made far and away the largest and most consistent commitment, spends only about 2% of the U.S. total. Moreover, in the past few years the resources available to European AIDS researchers have begun to shrink, as one nation after another has cut its budget for AIDS research. In some countries, notably the United Kingdom, these cuts have resulted from the ending of specially earmarked funds for AIDS research; in others, such as Germany, they have exacerbated what many researchers believe is a long-standing failure to fund the scientific battle against the disease adequately (see sidebars).

Strength in numbers

These funding policies have left many European scientists feeling handicapped when it comes to competing with their American colleagues. "We do good work in Europe, but it is always 5 minutes later than the Americans," says virologist Volker Erfle, of the Center for Environmental and Health Research near Munich. "This 5 minutes we would like to catch up on." One way of keeping up with the competition, European scientists have found, is to work with it instead of against it—a strategy that has particularly profited researchers from Belgium, Switzerland, and Italy, whose collaborations with American colleagues have fueled many of the recent breakthroughs in identifying the essential "coreceptors" that HIV uses to gain entry to its target cells (*Science*, 8 May, p. 825).

Another strategy is to work together across Europe, rather than across the Atlantic. In the past few years, the EU has funded several programs designed to strengthen ties and foster collaborations among European AIDS researchers. "A new culture of European collaboration has been born," says Jean-Louis Virelizier, a viral immunologist at the Pasteur Institute in Paris. Virelizier, who coordinates a network of French, British, and Spanish scientists investigating how the replication of HIV is regulated, adds that not long ago, "European scientists [would] ignore their immediate neighbors and were almost exclusively occupied by transatlantic collaborations."

Despite the boost from these Europe-wide programs, the level of EU funding for AIDS research, at about $20 million for the period 1994–98, is quite modest compared to the national AIDS research budgets of many individual European countries. Moreover, most EU money goes to support travel and meeting costs rather than laboratory research. "The EU just puts a little cream on top" of national budgets, says Erfle.

That leaves most European AIDS research at the mercy of national priorities. But the financial commitment from each European nation only loosely reflects the extent

THE BIG SPENDERS: GOVERNMENT EXPENDITURE ON AIDS RESEARCH* (in 1997)

Country	Estimated Annual spending	Cumulative AIDS cases
France	$39 million	47,407
United Kingdom	$20 million	15,081
Germany	$17 million	17,048
Italy	$14 million	40,950
United States	$1730 million	641,086

* Estimated totals for clinical and basic research

SOURCE: WHO, CDC, AND GOVERNMENT MINISTRIES AND DEPARTMENTS

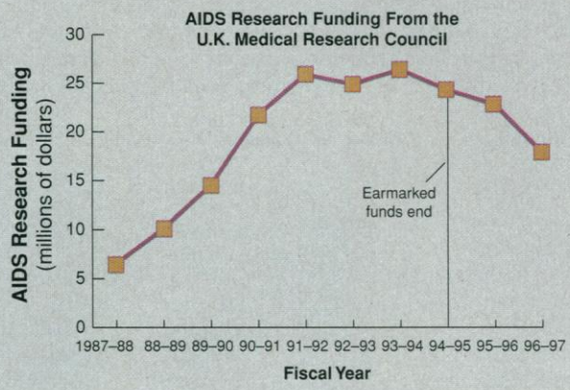
U.K. Community Finds It's a Jungle Out There

In the early days of the AIDS epidemic, British scientists were quick out of the starting gate when it came to making AIDS discoveries. In 1984, for example, Robin Weiss's group at the Institute of Cancer Research in London made the critical finding that HIV used a protein called CD4 as a receptor to enter the T lymphocyte immune cells that are its main target. This discovery (which was reported simultaneously by a French group) put British AIDS research on the map. The U.K. Medical Research Council (MRC) quickly followed up with a high-profile commitment to fighting the disease. Its AIDS Directed Programme, begun in 1987, "ring-fenced" special funds for AIDS research and attracted some of the nation's most talented scientists into the field.

This flying start was not to last, however. In 1994 the MRC terminated its special AIDS program, on the grounds that AIDS researchers no longer needed special treatment to compete for funds with scientists working on other diseases. The result, researchers told *Science*, has been a sharp decline not only in their funding but also in the morale of the AIDS research community. "There was a good esprit de corps throughout British AIDS research, and that has fallen by the wayside," says Weiss. "There is no longer the same sense of community." Moreover, at many research centers, the number of people working on AIDS has shrunk along with the funds available for research. "Three years ago we had 25 people working on HIV [with] MRC support," says Andrew Leigh Brown, an AIDS researcher at the University of Edinburgh's Centre for HIV Research. "Now there are eight funded research posts, only three of which are supported by the MRC."

MRC officials defend their decision to end the program. "By the early 1990s, we decided that we had a pretty large portfolio of AIDS research," says Tony Peatfield, manager of the MRC's physiological medicine and infections board. "Once it became evident that there was a comprehensive effort, we thought we should level the playing field" in the competition for grant funds. Peatfield adds that the MRC also had to listen to researchers in other fields. "We had people saying to us, 'Why is AIDS so special that it should get ring-fenced money, rather than asthma or malaria or transmissible spongiform encephalopathies?' "

Yet some AIDS researchers, while agreeing in principle with the idea of a level playing field, argue that the MRC has recently turned down even highly rated AIDS proposals. An example cited by many is a long-running program coordinated by Oswald Jarrett and James Neil at the University of Glasgow, which uses the cat version of the AIDS virus, FIV, as an experimental animal model to study possible vaccines against HIV. This project, which received the MRC's highest possible rating in its most recent review, nevertheless lost most of its MRC funding last year. Peatfield insists that AIDS research is not being singled out, pointing to the physiological medicine and infections board's decision not to fund another top-rated grant in another field of research.



Reduced priority. Funding has fallen since special program ended.

The end of special AIDS funds from the MRC has led some researchers to seek money elsewhere, and some have been encouraged by the recent decision of the Wellcome Trust—Britain's mammoth biomedical charity—to begin funding AIDS research. But the trust's commitment, about $2.4 million for the 1996–97 fiscal year, covers only a fraction of the more than $8 million drop in MRC AIDS funding since its high point in 1994. The shortfall, researchers say, does not bode well for the future of British AIDS research. Says Rodney Phillips, an immunologist at Oxford University: "I think the next generation of researchers is being dissuaded from going into this field." **–M.B.**

to which it is afflicted by the epidemic. France, for example, whose cumulative total of 47,000 AIDS cases makes it second only to Spain on the continent, spends $39 million on AIDS research annually, almost twice as much as any other single European country (*Science*, 16 January, p. 312). Spain, on the other hand, which lags behind much of Western Europe economically, spends about $530,000 per year on AIDS research, while the relatively wealthy Netherlands, with a third of Spain's population and less than one-tenth of its AIDS cases, has spent an average of $4 million annually—although these funds are now under serious threat (see p. 1859).

Struggling to catch up

José Alcamí, a virologist at the 12 October Hospital in Madrid, says that Spain's explosive AIDS epidemic is the result of "a lack of preventive measures over the past 10 years." To a large extent, Alcamí says, the failure to take firm action during the early days of the epidemic was due to the fact that most of those affected in Spain are in "marginalized" groups: 62% of AIDS patients in the country are intravenous drug users. And this negligent attitude, Alcamí adds, also made it very difficult for Spanish AIDS research to get off the ground: "During the 1980s, [Spanish health authorities] did not create an AIDS research agency in Spain, like the [U.K.] Medical Research Council's Directed Programme on AIDS or France's National Agency for AIDS Research." As a result, there are only about a half-dozen research groups in Spain doing basic AIDS research on a full-time basis.

The news from Spain is improving, however. Although research spending remains very low, Spain has budgeted about $13 million for AIDS prevention programs this year and is making anti-HIV therapies available free to all patients. Francisco Parras, head of Spain's National AIDS Plan, told *Science* that these measures have already resulted in a decrease in newly reported AIDS cases, down 25% between 1996 and 1997. And the widespread use of antiviral therapies, Alcamí says, is now allowing Spain's hospital-based clinicians to participate in international drug trials, which are bringing Spanish researchers into closer contact with their international colleagues: "We are finally starting to create a more coordinated [AIDS research] network."

Although lack of research funds is chronic in poorer European countries such as Spain, Portugal, and Greece, scientists from nations that have traditionally made major commitments to AIDS research have recently suffered cutbacks and funding instability. An example is Italy, which ranks fourth in Europe

German Powerhouse Gives AIDS the Cold Shoulder

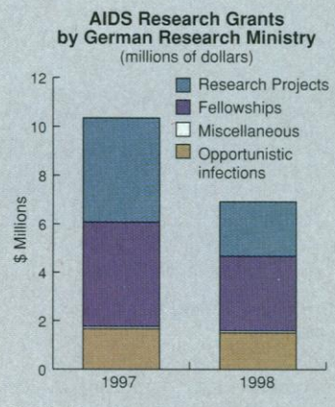
If any country in Europe is well placed to make major contributions to AIDS research, it is Germany, traditionally a biomedical research powerhouse. Indeed, in the mid-1980s, the German pathologists Paul Racz and Klara Tenner-Racz, now at the Bernhard-Nocht Institute for Tropical Medicine in Hamburg, were the first to carry out detailed studies of HIV infection of the lymph nodes of AIDS patients, pioneering work that paved the way for more recent studies on how the virus destroys these immune system organs.

Despite this promising start, German AIDS researchers and colleagues in other countries told *Science* that Germany hasn't pulled its weight in the battle against the disease. "Given their excellent tradition in biology and medicine, the German AIDS effort has been, with few exceptions, stunningly poor," says Simon Wain-Hobson, an AIDS researcher at the Pasteur Institute in Paris. And Volker Erfle, a virologist at the Center for Environmental and Health Research near Munich, agrees that "we have not played a leading role in AIDS research, neither in a European nor an international context."

Germany's lackluster performance was clearly revealed in June 1997, when an international review board convened by the Ministry of Education, Science, Research, and Technology (BMBF)—the biggest single source of AIDS research funds—concluded that more than a third of BMBF-supported AIDS research projects no longer deserved to be funded. The BMBF duly slashed its HIV research budget for 1998. And although researchers are not happy with these spending cuts, some say they are nevertheless pleased to see German AIDS research subjected to international review. "In the past, many groups applied for grants when it was trendy to have an AIDS project running in the lab," says virologist Andreas Meyerhans at the University of the Saarland in Homburg. "Scientifically, the research was often unfocused and of limited value."

Researchers cite a number of possible reasons for Germany's disappointing contribution, including the fact that the nation spends relatively modest sums for AIDS research (see table on p. 1856). But Peter Lange, director of BMBF's health research unit, says that the ministry sometimes found it difficult to convince scientists to go into the field: "I often heard researchers say that if they went into AIDS research they would have no future, because AIDS is not a very socially accepted disease." And Erfle comments that public support for AIDS research has never been very high in Germany. "When the projected figures [for AIDS incidence] did not come up to the worst case scenario, the interest from the public and the press went down considerably."

For the moment, research officials are hoping that their trimmed-down AIDS effort—like a tree that has undergone a badly needed pruning—will now begin to bear fruit. Says Lange: "There is now some modest indication that the quality of research is improving." **–M.B.**



Critical review. Grant spending plummeted after harsh appraisal.

in AIDS research spending. Italian scientists—whose roster has recently been boosted by several talented researchers returning after doing postdocs in the United States—have made key contributions to AIDS research, including important insights into how the body's immune system responds to HIV infection (*Science*, 7 July 1995, p. 24). "Italy's contribution has been overwhelmingly impressive," says immunologist Jean Claude Gluckman of the Pitié-Salpêtrière Hospital in Paris.

Despite this impressive performance, 2 years ago Italian health officials threw the nation's AIDS research program into disarray by suspending its funding as part of a major shake-up of biomedical spending (*Science*, 11 April 1997, p. 191). When the funds were finally restored late last year, AIDS research had suffered a cut of almost 20%. Although this meant considerable hardship for many research teams, some researchers say the effect of the shake-up was not all bad. "I do not think the cuts in AIDS research will affect the best research groups," says Mario Clerici, an immunologist at the University of Milan. "On the other hand, there are dark clouds on the horizon for those researchers who are not doing cutting-edge science or who have used AIDS money as an excuse to finance other research projects."

More of a threat, say some Italian researchers, is the instability created by health ministry policies that require all AIDS grants to be renewed annually. "This creates a substantial waste of time and energy in rewriting grant applications," says immunovirologist Guido Poli at the San Raffaele Scientific Institute in Milan. Italian AIDS researchers have been lobbying Italy's national health institute, the ISS, to change this policy. But microbiologist Antonio Cassone, head of the ISS's bacteriology and medical mycology department, says that these efforts will meet tough resistance from health authorities "as long as the institute follows the typical rules and bureaucracy of an Italian governmental institution."

Pulling together

Given these ups and downs in national funding policies, a number of AIDS researchers told *Science* they would like the EU to step in and fund a greater proportion of direct research costs. "At this stage the EU should support more basic research, not just provide funds for traveling" to meetings, says Kai Krohn, director of the Institute of Medical Technology at Finland's University of Tampere. And Arsène Burny, a molecular biologist at the Free University of Brussels, says that meetings are useless unless scientists have new research to report: "It's fine to get people together, but you have to have something to say to each other." Although most EU-funded AIDS programs do not directly support laboratory work, researchers involved in the handful of so-called "shared cost" programs, which do provide research funds, say these projects have helped boost collaborations that might have been too expensive to receive funding at the national level.

"In general, our program has worked very well," says Paolo Lusso, a virologist at San Raffaele and coordinator of an EU project studying the possible role of viruses other than HIV—particularly human herpesviruses—as cofactors in the progression of AIDS. The project, which began in 1996 and received a 3-year grant of nearly $1 million—a large amount for the EU—has brought together scientists from Italy, Sweden, Austria, Belgium, and Finland.

At the moment, however, it is unclear how AIDS research will fare when the 5th Framework Program—the multibillion-dollar umbrella for the EU's spending on science and technology—is finalized later this year. But as national AIDS budgets continue to shrink, international collaborations—both within Europe and around the world—may be key to keeping European scientists on the front lines. Says Krohn: "The economic policy of the EU is to beat the Japanese and the Americans, but as AIDS researchers, we must think globally."

–Michael Balter