Military AIDS Testing Offers Research Bonus

But a $40-million appropriation to conduct AIDS research in the Army is on hold, and the reliability of data on transmission of the disease in the armed forces may be open to question

LATE last year, Congress gave an unexpected bonus to researchers in the Army medical corps: $40 million to conduct research on AIDS (acquired immune deficiency syndrome). The appropriation, which was included in a catch-all spending bill approved just before Christmas, would make the Army one of the leading sponsors of AIDS research.

The Pentagon did not ask for the funds. They were inserted in the bill largely at the initiative of Senator Ted Stevens (R–AK), who chairs a key military appropriations subcommittee. Nevertheless, Army researchers have enthusiastically supported the measure because they believe it will provide an opportunity to conduct a variety of studies in a military setting that would be difficult to do elsewhere.

Scientists outside the military have also lent their support, in part for the same reasons and in part because they view the impending entry of the Army into the AIDS-funding business as a welcome diversification of sources of support. Although much of the work would be done in-house, the Army has made known its interest in supporting outside groups and has received a flood of research proposals, including one for $12 million from a group at Harvard.

However, the program has hit a snag before it has even begun. The $40 million has been put on ice while a dispute over $6 billion worth of military appropriations is sorted out, and there is no guarantee that the frozen funds will be defrosted.

The problem is that, in its chaotic last-minute efforts to provide funding for a variety of government departments for fiscal year 1986, Congress appropriated money for several defense programs that had not been approved by the usual authorization process. The AIDS program is among them. Funds for these programs are now being held up until the necessary authorizing legislation has been passed.

If the AIDS appropriation is not shaken loose, many believe that a golden opportunity to conduct some key epidemiological studies could be lost. The opportunity arises from the fact that a wealth of data will be generated over the next year from a massive screening program in which all 2.2 million people on active military duty will be tested for antibodies to the virus that is widely believed to be the cause of AIDS.

This screening program, which is just getting under way in earnest, should be completed by next spring. "The spin-off value of the testing is potentially enormous. It is a superb opportunity to gain a better understanding of the natural history of the disease," says Donald Darrow, a research sociologist at the Centers for Disease Control in Atlanta. It could also provide some information on the extent to which the AIDS virus is being transmitted beyond what are currently recognized as the main risk groups.

Robert Redfield: *Data on heterosexual transmission "are really going to hold up when people start thinking in other than preconceived notions."*

The research value of this program stems from the sheer scope of the testing and from the ability to follow the medical course of those who test positive.

Although blood banks are testing more people, the results are less useful for epidemiological purposes because donors who test positive are not generally enrolled in any research study. In contrast, those who test positive in the armed forces will be followed through the military medical system, and this could provide a veritable bonanza of standardized information on the course of the disease.

That, at least, will be the case if the Pentagon does not discharge from military service those found to have antibodies to the AIDS virus. According to one senior researcher, the initial attitude of some military officials was to get antibody-positive people out of the services in order to prevent spread of AIDS in the armed forces. The current policy, set out in a memorandum issued last October by Secretary of Defense Caspar Weinberger, is far less drastic, however.

Those who test positive will be restricted to assignments in the United States for their own protection, the memorandum says. The rationale is that service abroad could expose them to exotic disease agents and could require inoculation with live virus vaccines, both of which would be risky for people whose immune systems have been impaired. In addition, those with antibodies to the AIDS virus will be excluded from battlefield service to ensure that they do not participate in emergency blood donation programs. Those who have AIDS itself may, however, be given a medical discharge.

The aim is to give those who test positive standardized physical examinations on a regular basis. Information from this medical follow-up for Army personnel will be stored in a database at the Walter Reed Army Institute of Research (WRAIR), and it should provide a valuable resource to study the natural history of the disease processes resulting from infection with the AIDS virus. The information could, for example, shed light on one of the big uncertainties in AIDS epidemiology: why some people experience a steady deterioration of their immune systems while others can go on for years without apparent ill effects from infection with the virus.

Military physicians predict that as many as 2000 to 3000 service personnel will test positive. They base this estimate on early results of screening at military blood banks and on the first 3 months of testing all recruits hoping to enter the armed forces. (The screening of would-be recruits began last October; those who test positive are denied entry into the services.) Both recruits and military blood donors show a rate of infection of around 1.4 per thousand.

This is well above the rate turning up from screening at civilian blood banks, which is running at around 0.2 to 0.3 per thousand. According to Robert Redfield, a physician at Walter Reed who has headed

most of the Army's AIDS research so far, the difference may be due to the fact that the average age of those tested in the military is lower than that of civilian blood donors.

Because the military screening program is the largest effort directed toward looking for infection with the AIDS virus beyond what are currently the chief risk groups, it could in theory provide some interesting data on the extent to which the virus is spreading in the general population and the means by which it is being transmitted. The problem, however, is that the two practices known to carry a high risk of transmitting the virus—homosexual anal intercourse and intravenous drug abuse—are grounds for dismissal from the armed forces. Service personnel who test positive may thus be reluctant to admit to having engaged in either of these practices.

In an attempt to get around this problem, Weinberger's memorandum setting out the screening policy states that test results and "information concerning personal drug use or consensual sexual activity disclosed by a Service member as part of an epidemiological assessment" may not be used in legal proceedings. They can be used as the basis of an honorable discharge, however, but that would require a hearing by a board of officers and approval by the secretary of the service concerned. Peter Wyro, the Pentagon spokesman for the screening program, concedes that this does not provide solid protection but says it is "an effort to balance out the fact that we want the information with a policy that prohibits homosexuality and nonmedical drug use."

Military researchers have faced this problem before, both in studies of drug abuse during the Vietnam War and more recently in investigations of AIDS cases that have

AIDS Patent Negotiations Break Down

The Pasteur Institute has won an important round in its increasingly bitter contest with the U.S. government over profits and prestige resulting from research on AIDS. This development was quickly followed by an apparent breakdown in negotiations aimed at settling the dispute.

A ruling issued on 29 April by the U.S. Patent Office appears to favor the Pasteur Institute's application for a patent on a test for detecting antibodies to the AIDS virus, rather than a patent already awarded to the U.S. government. The ruling was part of a decision by the Patent Office that set in motion a legal process to sort out the competing claims of both sides.

Three days after the ruling, the U.S. Department of Health and Human Services notified the Pasteur Institute that it would publicly propose settling the dispute by creating an international foundation to which the disputed patent would be assigned. This arrangement, which was first put forward by the United States in settlement negotiations some time ago, would channel royalties from the patent into research. The funds would be open to any applicant. However, according to a Pasteur lawyer, the Pasteur Institute had proposed a counter offer that would share credit and royalties between the competing parties. After U.S. officials said they would announce their original proposal, Pasteur Institute president Raymond Dedonder sent out a statement on 5 May accusing the United States of breaking off settlement negotiations and indulging in a "public relations gesture." Dedonder's statement, which was distributed by a New York public relations firm, seemed designed to blunt the impact of the U.S. announcement.

The Pasteur Institute's patent application is based on work by a group headed by Luc Montagnier. Early in 1983, the French researchers isolated from a patient with lymphadenopathy a virus that later proved to be the cause of AIDS. They propagated the virus in cultures of fresh lymphocytes for several months, growing small quantities that were used for research and to develop an antibody test. The Pasteur Institute filed for a patent on the test in England in September 1983 and in the United States in December.

Meanwhile, in November 1983, a group headed by Robert C. Gallo of the U.S. National Cancer Institue achieved a key breakthrough by establishing a cell line that could be used to mass produce virus isolated from patients with AIDS and AIDS-related conditions. This enabled Gallo's group to develop reagents to characterize the virus and to produce an antibody test of their own. These developments led to the publication of a series of papers in May 1984 that convincingly showed that the virus is the cause of AIDS. The U.S. government filed for a patent on Gallo's blood test on 23 April 1984, and it was awarded on 28 May 1985.

Pasteur officials have long maintained that the French work has not been accorded due scientific and financial credit, and they sought in negotiations last fall to share in the U.S. patent. When these talks broke down, the Pasteur Institute initiated proceedings with the Patent Office that culminated in the 29 April ruling. The ruling recognizes the claim in the French patent application, which normally would be prelude to issuance of a patent. However, because the U.S. patent had already been awarded, the Patent Office declared an "interference," which sets up a formal process that could take 2 years to determine who is the true inventor of the blood test.

In a key determination that favors the French application, the ruling declared the Pasteur Institute the "senior party" in the interference. This means, says Charles Lipsey, the attorney handling the Pasteur's case, that "the burden of proof has been placed on the [U.S.] government and Dr. Gallo," rather than on the Pasteur Institute.

U.S. officials have maintained all along that the French patent is useless without a means of growing the virus in bulk, because the test could not be mass produced without large quantities of virus. To support this contention, they note that tests based on the U.S. work were developed and marketed many months before those based on the Pasteur Institute's work.

However, the Patent Office ruling removes from the interference proceedings a claim in the U.S. patent relating to growing the virus in the cell line, called H9, established by Gallo's laboratory. This would also seem to favor the French application by narrowing the case to a determination of which group has precedence in patenting the detection technology alone. (The U.S. government has a separate patent application pending that covers growing the virus in the H9 cell line, which is used in preparing most of the test kits currently on the U.S. market.)

One immediate effect of the ruling is that a test kit manufactured by Genetic Systems of Seattle under license to the Pasteur Institute can be marketed in the United States without fear of running foul of the U.S. patent. The test was recently approved by the Food and Drug Administration. ■ **COLIN NORMAN**

shown up so far in the armed forces. They believe they can get reliable data. Last year, for example, a team headed by Redfield looked at the likely source of infection in 41 AIDS patients at Walter Reed and concluded that heterosexual sexual contact was implicated in 15 cases.

When the findings were published in the 18 October *Journal of the American Medical Association*, they were viewed with a great deal of skepticism because national figures reported by the Centers for Disease Control show very low rates of documented or suspected transmission by heterosexual contact. Redfield dismisses the criticism. "The data are really going to hold up when people start thinking in terms other than preconceived notions," he says. The spread of AIDS, he argues, will eventually follow a pattern similar to that of other venereal diseases.

If so, then the armed forces may have reason for concern. "The military has always had a problem with venereal disease, and [AIDS] is a venereal disease," says Colonel Edmund Tramont, chief of the Division of Bacterial Diseases at WRAIR. There is already one indication of the potential problem: since last October the Army has been testing for AIDS antibodies at venereal disease clinics and is finding an infection rate of about 1%—some seven times the rate anticipated in the general military population.

Epidemiology is not the only area that could benefit from the $40-million appropriation, if it finally comes through. WRAIR researchers are eyeing the possibility of moving into drug testing and vaccine work. Again, they point to the screening program as a golden opportunity.

At present, drug testing is mostly confined to patients already displaying symptoms of AIDS, but the general expectation is that eventually medication to block the life cycle of the virus will have to be taken as early as possible in the disease process. The military screening program will identify many people shortly after infection, and their medical progress will be closely monitored. Military physicians therefore argue that they are ideally placed to conduct controlled clinical trials.

As for vaccine development, WRAIR researchers point to a large number of vaccines that have been developed and tested in the military, including most recently a vaccine against the malaria parasite. In the control of infectious diseases "we are a national resource," says Tramont. The chief problem preventing the resource from being developed, Army physicians say, is the hold put on the $40-million appropriation they did not seek but now are eager to use. ■

COLIN NORMAN

NAS Elects New Members

The National Academy of Sciences has elected 59 new members and 15 foreign associates. This brings the membership total to 1477 and the foreign associates total to 238.

Gerald D. Aurbach, National Institute of Arthritis, Diabetes, Digestive, and Kidney Diseases; **Robert Axelrod,** University of Michigan, Ann Arbor; **Peter J. Bickel,** University of California, Berkeley; **Emilio Bizzi,** Massachusetts Institute of Technology; **Walter L. Brown,** AT&T Bell Laboratories; **John Carbon,** University of California, Santa Barbara; **Michael J. Chamberlin,** University of California, Berkeley; **Michael D. Coe,** Yale University; **Samuel Danishefsky,** Yale University; **William H. Daughaday,** Washington University, St. Louis; **Gerard H. deVaucouleurs,** University of Texas, Austin; **Peter B. Dervan,** California Institute of Technology; **Peter H. Duesberg,** University of California, Berkeley; **Bradley Efron,** Stanford University; **Gert Ehrlich,** University of Illinois, Urbana.

Ellis Englesberg, University of California, Santa Barbara; **Charles O. Frake,** Stanford University; **Martin F. Gellert,** National Institute of Arthritis, Diabetes, Digestive, and Kidney Diseases; **Arthur S. Goldberger,** University of Wisconsin, Madison; **Major M. Goodman,** North Carolina State University, Raleigh; **David J. Gross,** Princeton University; **Robert W. Hellwarth,** University of Southern California; **Ira Herskowitz,** University of California, San Francisco; **Bertil Hille,** University of Washington, Seattle; **Marion L. Jackson,** University of Wisconsin, Madison; **Yuet Wai Kan,** University of California, San Francisco; **Seymour Kaufman,** National Institute of Mental Health; **Susan W. Kieffer,** U.S. Geological Survey, Flagstaff, AZ; **Daniel Kleppner,** Massachusetts Institute of Technology; **Ernst Knobil,** University of Texas, Houston.

Leonard S. Lerman, Genetics Institute, Cambridge, MA; **Robert L. Letsinger,** Northwestern University; **Rodolfo Llinas,** New York University; **Philip W. Majerus,** Washington University; **Brian W. Matthews,** University of Oregon, Eugene; **Frank B. McDonald,** NASA Headquarters, Washington, DC; **Josef Michl,** University of Utah, Salt Lake City; **John L. Moll,** Hewlett-Packard Co., Palo Alto; **C. Bradley Moore,** University of California, Berkeley; **Richard A. Musgrave,** University of California, Santa Cruz, **William L. Ogren,** University of Illinois, Urbana; **Robert T. Paine,** University of Washington, Seattle; **Sheldon Penman,** Massachusetts Institute of Technology.

Robert C. Richardson, Cornell University; **Liane B. Russell,** Oak Ridge National Laboratory; **Clarence A. Ryan, Jr.,** Washington State University, Pullman; **David N. Schramm,** University of Chicago; **H. Bolton Seed,** University of California, Berkeley; **Charles G. Sibley,** Yale University; **Joseph V. Smith,** University of Chicago; **Robert M. Solovay,** University of California, Berkeley; **Shlomo Z. Sternberg,** Harvard University; **George J. Todaro,** Oncogen, Seattle; **Donald L. Turcotte,** Cornell University; **Karen K. Uhlenbeck,** University of Chicago; **Roger H. Unger,** University of Texas, Dallas; **Hans Wallach,** emeritus, Swarthmore College; **James C. Wang,** Harvard University; **Harold M. Weintraub,** Fred Hutchinson Cancer Research Center, Seattle.

The new foreign associates are:

Georges Charpak (France), CERN, Geneva, Switzerland; **J. Desmond Clark** (United Kingdom), University of California, Berkeley; **T. P. Feng,** Academia Sinica, Shanghai, Peoples Republic of China; **Walter J. Gehring,** Biozentrum, University of Basel, Switzerland; **Friedrich Hirzenbruch,** University of Bonn, Federal Republic of Germany; **Kenneth Jinghua Hsu,** Swiss Federal Institute of Technology, Zurich; **John H. Humphrey,** Royal Postgraduate Medical School, London, United Kingdom; **Leslie L. Iverson,** Merck Sharp and Dohme Research Laboratories, Essex, United Kingdom; **Hans L. Kornberg,** University of Cambridge, United Kingdom; **Viktor Mutt,** Karolinska Institute, Stockholm, Sweden; **Karl R. Popper, Sr.,** Royal Society, London, United Kingdom; **Osvaldo A. Reig,** University of Buenos Aires, Argentina; **Michael J. Seaton,** University College, London, United Kingdom; **Susumu Tonegawa** (Japan), Massachusetts Institute of Technology; **Marc C. E. Van Montagu,** State University of Gent, Belgium.