lattice. Researchers speculate that even if a room-temperature superconductor is discovered, it will be unable to carry any current without resistance.

There is one hope for the high-temperature superconductors. If some way can be found to pin the flux lattice so that it does not move easily, it may still prove possible to run large amounts of current through them with negligible resistance. Several researchers believe they have found hints of a way to do this.

Matthew Fisher, a theorist at IBM, suggests that if there are enough pinning defects in the material, the superconductors may arrange themselves into a "vortex glass state" in which the flux lines (also called vortices) do not move. "The flux doesn't creep in this state, at least not at a rate proportional to the current," he says, which results in a material that is a perfect conductor, just as if it were in a zero magnetic field. Experiments by Worthington and Roger Koch, also at IBM, give some evidence for the existence of such a state, he says.

At Bell Communications Research, Steve Gregory and Charles Rogers have done very sensitive "vibrating reed" experiments, in which a thin film of superconductor is mechanically vibrated in a magnetic field and observed as the oscillations die out. These experiments, they say, strongly imply that the superconducting films were in a vortex glass state. They interpret the state as arising from an entanglement of the flux lattice lines. If the lines are flexible enough, they may twist around each other like a tangled pile of spaghetti. This tangling may then allow the entire flux lattice to be pinned with many fewer defects than would be necessary if the lines were free of each other.

If the vortex glass state is real, then developing useful superconductors may become a job of learning how to introduce the right number and type of defects into the superconducting materials. Right now, no one understands exactly what types of defects cause pinning, so that opens up a whole new line of research. Another line will be to find the right balance of defects, since too many defects damage the superconductivity of a material, but too few may allow the flux lattice to move around too much.

Even if the flux lattice problems can be overcome—by means that researchers cannot yet predict—at the very least they create one more obstacle to application. If it were not clear before, it certainly is now that molding high-temperature superconductors into commercially useful forms will be a long, slow process. "I would never want to go on record as saying it can't be done," Bishop says. "But it certainly will make the job harder." ■ ROBERT POOL

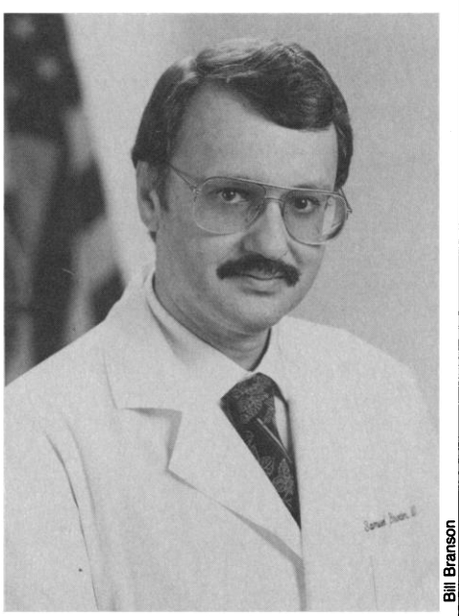
The Trials of Conducting AIDS Drugs Trials

Five years ago there were virtually no promising AIDS drugs. Now there are so many that the clinical testing system is rapidly becoming overloaded

AIDS RESEARCHERS HAVE RECENTLY encountered an unexpected dilemma: as they find more potential AIDS drugs, they are beginning to overwhelm the system they depend on to evaluate new therapies. "There is a bottleneck now in our ability to test all the drugs identified as having potential," says Mathilde Krim of the American Foundation for AIDS Research in New York City.

"It's an ironic situation that most people did not predict in '84 or '85," says Samuel Broder, the director of the National Cancer Institute and a prime mover in the clinical development of AZT, or Zidovudine, the only drug currently approved by the Food and Drug Administration (FDA) for combating AIDS virus infections. Five years ago there were few attractive candidates for testing. Now, some 60 new drugs are in or near clinical testing in AIDS patients, according to the Pharmaceutical Manufacturers Association, and more are on the way (*Science*, 21 April, p. 287).

As the drugs roll out of the laboratory, however, the AIDS Clinical Trials Group (ACTG) of the National Institute of Allergy and Infectious Diseases, the largest single source of funds for clinical AIDS drug testing in the United States, is hitting its maximum level of operation. "We have reached a level where we don't think the system can absorb much more," says the group's director, Daniel Hoth.



Bill Branson

Samuel Broder: *The abundance of potential AIDS drugs "is an ironic situation that most people did not predict in '84 or '85."*

The ACTG, which has a total budget of $94 million for fiscal year 1989, now has 57 trials, on 27 drugs or drug combinations, in progress. As studies end, others can take their place, but, Hoth says, 50 to 70 trials are about all the clinical trials group can sponsor at one time. The number of studies is limited not just by the funding available but also by the ability of the academic medical centers, which traditionally conduct clinical trials, to handle the workload.

But AIDS activists and some clinicians think that there is another problem as well. "Lack of access is the problem. The system is getting overloaded because it is too restrictive," says Jerome Groopman, a physician and AIDS researcher at New England Deaconess Hospital in Boston.

He notes that for entry into many trials, a patient's count of CD4 cells, a type of immune cell wiped out by the AIDS virus, has to be very low, below 200. Yet patients may also be barred from participation if they have had a history of several types of infection or are taking other drugs, including those used to combat the pneumonia and virus-induced blindness that often afflict AIDS patients.

Whether or not there is blame to be apportioned, AIDS researchers are now facing some hard choices about which drugs to test first. "We may have to say no to things we would like to do," Hoth remarks.

At this stage there is little agreement on how to set the priorities for which drugs to test first. "If you asked ten people, you could get 11 opinions," Broder says. The NCI director himself would favor drugs that have novel structures or attack the AIDS virus at different points in its life cycle to increase the likelihood of finding combinations that could control the AIDS virus. AIDS researchers generally think that multidrug reg-

imens will be needed to control the disease.

AIDS activists, meanwhile, want to see more research on drugs that control opportunistic infections. "There's been far too much emphasis on anti-virals," says Mark Harrington of the AIDS Coalition to Unleash Power. He maintains that drugs to prevent the pneumonia caused by *Pneumocystis carinii* have been slow to reach AIDS patients, even though prophylaxis against the infection has been standard care since the mid-1970s for organ transplant recipients, who take immunosuppressive drugs to prevent graft rejection.

In May, however, an FDA advisory committee recommended that the agency approve aerosolized pentamidine for preventing *Pneumocystis* pneumonia in AIDS patients as a result of a clinical trial conducted by a consortium of community physicians based in the San Francisco Bay area. There is a growing trend toward such community-based trials as a way of broadening patient access to experimental drugs and speeding data acquisition. (Also, see box on this page.)

Ironically, the advances that clinicians have made in treating AIDS, although limited, have helped to make clinical trials of newer drugs more difficult to perform. Early on, Broder points out, there was little that could be done for AIDS patients, who had a relentlessly downhill course. That made it easier to see that AZT was having a beneficial effect.

Now, with AZT and aerosolized pentamidine, patients may have temporary remissions and live longer. "We really have made a difference in the life span of people with AIDS," Groopman says.

The improvements, however, make placebo-controlled trials ethically untenable, except when testing drugs to control certain of the opportunistic infections that afflict AIDS patients and for which there are currently no therapies at all. Patients do not want to participate in a study that would prevent them from having prophylaxis for *Pneumocystis* infections, as has been the case in the past, Harrington says. In any event, both Broder and Anthony Fauci, the director of the National Institute of Allergy and Infectious Diseases, are on record as opposing placebo controls in future AIDS drug studies.

Improved AIDS therapy also means that more time will be required to determine whether an experimental drug is effective, especially if increased survival is used as the criterion. "We don't want all our trials to depend on saying whether a drug improves survival. We would have to wait 2 to 3 years," Hoth says. "If a drug is a wonder drug, it won't take that long to find out. But most drugs aren't home runs. They are

Grass-Roots Drug Testing

Once greeted with skepticism, community-based trials for AIDS drugs are now proving their mettle as workable alternatives to the more traditional type of clinical trial conducted at academic research centers. What distinguishes the AIDS community trials is their grass-roots origin. They sprang up originally in New York and San Francisco as AIDS patients and their physicians became dissatisfied with what they saw as the slow pace and restrictiveness of medical center trials.

Taking matters into their own hands, they began designing drug studies that could be performed by community physicians in the hospitals where they ordinarily practice. Although not without disadvantages—record-keeping is the principal problem—the approach is beginning to pay off in improved patient care. On 1 May, for example, an advisory committee of the U.S. Food and Drug Administration recommended that the agency approve the use of aerosolized pentamidine to prevent *Pneumocystis* pneumonia, which affects some 80% of all AIDS patients, on the basis of a community-based trial conducted in the San Francisco Bay area.

With the growing respectability has come some much-needed funding from the traditional granting agencies. Last November, the AIDS Clinical Trials group of the National Institute of Allergy and Infectious Diseases announced that it would award $6 million—out of a total budget of $94 million—for community trials in fiscal year 1989. "Our view is that some community trials will make a difference," says the clinical trials group director Daniel Hoth, citing the pentamidine trial. The American Foundation for AIDS Research in New York City is also earmarking $1 million for community-based clinical trials.

Three or four years ago, it was a different story, says Donald Abrams of San Francisco General Hospital, who was instrumental in organizing the County Community Consortium of Bay Area HIV Health Care Providers, as the San Francisco group is officially known. Back then, a traditional funding agency turned down the consortium's grant application as being "too novel." Abrams notes, however, that even then the community approach was not completely unprecedented. The National Cancer Institute already had in place a community program for testing therapies for relatively rare cancers.

The major advantage of community trials is that they allow more patients to be enrolled more rapidly than trials conducted at medical centers, primarily because community physicians see most AIDS patients. This means that faster answers can be obtained about whether a therapy is working.

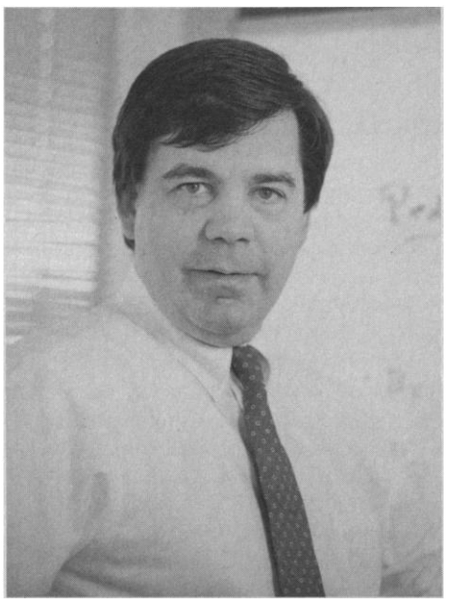
Community trials also reach a broader scope of patients, attracting those who might not want to leave their primary physicians for a research center. In addition, patients can have more to say about how a trial is conducted. They may also be more likely to tell physicians they already know and trust if they are taking drugs on their own that could compromise the outcome of a clinical trial. AIDS patients frequently do take other drugs of various kinds.

On the downside, it is more difficult to collect data in community trials in a way that will withstand scrutiny by the FDA, which Bruce Montgomery, a principal investigator in the San Francisco pentamidine trial, likens to an IRS audit. Community physicians are trained to take care of patients, not to collect data, says Thomas Mitchell, project director for the San Francisco study. Consequently, the community groups need a central staff with expertise in conducting clinical trials to keep a close eye on the data as they come in.

Another problem is that community physicians frequently have to be educated about the rigors of adhering to the treatment protocols in a clinical trial. They are accustomed to making their own decisions about what therapies to use and whether to alter them.

Nor are all drugs suitable for community testing. Agents that have not yet gone through Phase I–testing, which requires that patients be closely monitored for toxic effects, would generally be excluded from consideration.

The San Francisco County Consortium and the Community Research Initiative, a group based in New York, are now conducting several additional drug studies. And newer groups across the country are also beginning community-based trials of their own. They should help to extend experimental therapies to AIDS patients who are, for whatever reason, beyond the reach of more traditional clinical trials. ■ **J.L.M.**



Daniel Hoth: *"If it is a wonder drug, it won't take that long to find out. But most drugs aren't home runs. They are singles."*

singles."

Instead, researchers are trying to identify "surrogate end points" that can give them faster information than survival does about whether a drug is working. In fact, selection of surrogate end points will be the first issue tackled by a new panel of government, academic, and industrial drug experts recently established by the Institute of Medicine. Panel members, including Food and Drug Commissioner Frank Young, agreed unanimously to make this their first priority.

Two end points under consideration are the patient's CD4-lymphocyte count and his blood concentration of the p24 antigen of the AIDS virus. The CD4 lymphocyte is one of the major cell types infected by the AIDS virus; a decline in the number of these cells reflects a failing immune system. The p24 antigen concentration is an indicator of AIDS virus reproduction.

The CD4 count presumably would climb, and the p24 antigen concentration fall, in response to an effective AIDS drug. However, questions remain about what these changes might actually mean in terms of benefits for the patient. Says Hoth: "It's not absolutely certain that when the CD4 count gets better that the patient gets better, although it is clear the other way around." Broder suggests that the best approach might be to use several surrogate end points to evaluate drug activities.

With as many as 1.5 million people in the United States now infected with the AIDS virus, finding better drugs and better and faster ways of testing them will remain a high priority with AIDS researchers.

■ JEAN L. MARX

ARCO Solar Sale Raises Concerns Over Potential Technology Export

Could photovoltaics go the same way as VCRs, semiconductors, and stereos—technologies pioneered in the United States but exploited by foreign companies? The concern is being fanned by rumors that ARCO Solar, Inc., the largest U.S. manufacturer of solar cells, is on the block and Japanese and European companies are among the bidders. Whoever buys the company would immediately acquire 15% of the world market for photovoltaics and a lot of state-of-the-art technology.

ARCO Solar President Charles Gay declines to identify any of the bidders, but he says that the parent corporation "is interested in seeing the business stay healthy" and is looking for a buyer with strong financial resources. The petroleum company is reportedly talking with Showa Shell Sekiyu, K.K., of Japan, Siemens Solar GmbH of West Germany, a Swiss consortium, and several U.S. investor groups. ARCO expects to select a buyer this summer.

ARCO Solar produces two forms of photovoltaic cells, which convert sunlight into electricity to operate anything from pocket calculators to refrigerators. The company is producing crystalline cells that are used for supplying large power needs, but the electricity from these devices is costly compared to conventional power supplies in the United States. Also in production is a line of less powerful and less costly cells made with thin films of silicon applied to architectural glass. A second high-power thin-film solar cell line with copper-indium-diselenide (CIS) chemistry is nearing production.

These cells, which make electricity nearly as efficiently as single crystalline cells, one day could compete with conventional power stations if manufacturing costs can be lowered sufficiently. The company's total sales last year are estimated by industry analysts to be around $25 million. One industry analyst says ARCO Solar could go for around $30 million.

Of particular concern is the potential export of the company's expertise in CIS cells. ARCO has been a leader in this technology, thanks in part to financial help from the Department of Energy. Says Robert Annan, director of photovoltaics technology for the department: "That is an American technology. DOE has supported it all the way along." ARCO does not, however, have a monopoly on the technology. Boeing Electronics and Chronar Corporation are also pursuing CIS with DOE assistance. Should a foreign competitor acquire ARCO Solar, Annan adds, it would get access to the technology just as it is about to hit the market.

ARCO Solar is "basically several years ahead of any competition [in CIS]," says Thomas Surek, manager of the photovoltaics program at the Solar Energy Research Institute in Colorado. Europe and Japan are just starting CIS research, he says, and will likely take 4 to 5 years to develop it.

The fears about export of technology are heightened by the fact that the U.S. photovoltaics industry is already facing stiff foreign competition. Over the past 10 years, in fact, U.S. manufacturers have seen their share of the world market cut from 80% to about 40%.

These arguments have struck a chord in Congress. Representative Vic Fazio (D–CA) and Senator Tim Wirth (D–CO), have both expressed concern about the potential sale. And the Commerce and Defense departments already have been alerted to the possibility of a foreign takeover and may require the sale to be approved by the Committee for Foreign Investment in the United States. The multiagency federal review panel was created as part of last year's trade bill to look at national security issues connected with the sale of high-technology companies to overseas owners.

But Gay contends that the technology transfer issue is overblown. "It has become an emotional lightning rod for some folks," says Gay, noting much knowledge transfer already has occurred at the basic research level. "This is an international business," notes Gay. "Some of the very best science in this area is being done in Japan and Europe." Stanford Ovshinsky, president of Michigan-based Energy Conversion Devices, Inc., agrees. "There is nothing that ARCO solar has that is not available to other technology companies," argues Ovshinsky, who has been a pioneer in the use of amorphous silicon for photovoltaics and in other electronic applications.

Nevertheless, John Corsi, president of Solarex Corporation, says it is hard to conclude that a foreign purchaser will not reap some benefit in buying ARCO Solar. Adds Roger Little, president of Spire Corporation, a supplier of photovoltaic manufacturing equipment, "it would be a big mistake" to export key technology, especially when the U.S. industry is already under such pressure.

■ MARK CRAWFORD