

training nine rookie teachers.

Math instruction at Pacific, like at every Sacramento elementary school, is based on material from Saxon Publishers Inc. of Oklahoma. It emphasizes repetition and strict adherence to the text as the best way to develop computational skills. If Packard decides to support elementary school math reform, observers speculate, he's likely to back a similar approach.

But Saxon's curriculum is controversial: A recent AAAS ranking of middle school math texts omitted Saxon because "its philosophy, organization, and format ... were not well suited to a benchmarks-based evaluation." Saxon's president, Frank Wang, acknowledges that "we don't emphasize higher order thinking and open-ended problem solving." Wang says the company, which also offers home-schooling materials aimed at a Christian

audience, deliberately avoided the controversial Department of Education review "because we knew we'd get low ratings [based] on the criteria they were using."

If his reading track record is any guide, Packard is also likely to immerse himself in math reform. "He does everything himself, and he is in total control," says Betty Flannery, coordinator for Packard's Reading Lions program, which is pumping \$15 million a year into 27 California school districts that use Open Court. "David walks around with binders on every school. He analyzes the data, and he's not afraid to call school officials and ask what's going on in a particular classroom that isn't performing."

"A micromanager? I guess you could say that," laughs Marion Joseph, a California State Board of Education member and leader of the phonics movement who is widely credited with introducing Packard to

the reading debate. "But David is classically trained in literature and music, and [Open Court] appealed to his understanding of how we learn language and its structure." Adds Jim Sweeney, Sacramento city schools superintendent, "He pushes very hard for full implementation of what he is supporting. But before he gets involved, he researches it thoroughly."

Packard has not said how long he will support Pacific, although Sweeney, Kingsbury, and others have warned him that lasting gains don't happen overnight. But whatever he decides to do next, those who have worked with him say he'll want to see results. "I can tell you that David Packard has made one heck of a difference in our schools," says Sweeney. That ability to get his way is exactly what worries Bass and other math educators on the opposite side of the reform movement. —JEFFREY MERVIS

AIDS RESEARCH

Vaccine Studies Stymied By Shortage of Animals

NIH doesn't know how many Indian rhesus macaques its researchers need, nor how many are available. And that's a big problem

Paul Johnson's lab at the New England Regional Primate Research Center is one of the best equipped in the world to study the immunology of SIV, the simian AIDS virus. Johnson also enjoys generous funding from the National Institutes of Health (NIH). So why does he have to wait 2 to 6 months to start an experiment? The answer is simple: The demand for rhesus macaques, the animal of choice for Johnson and a growing number of AIDS researchers, far outstrips the supply. But the reasons for that shortage are complex, encompassing everything from international trade to internal NIH politics. And AIDS researchers are worried that, if the shortage persists, it could hinder progress in the field. "It's a huge problem," says Norman Letvin, a leading AIDS vaccine researcher based at Harvard's Beth Israel Deaconess Medical Center in Boston. "And it's going to get much worse."

For many years, AIDS researchers bemoaned the lack of a good animal model for testing vaccines, measuring the toxicity of various drugs, and exploring the disease's progression. But the Indian rhesus macaque was found to develop a disease that closely mimics human AIDS when infected by SIV and has steadily gained in popularity. NIH has stimulated the demand for these monkeys by doubling its budget in the past 5 years for AIDS vaccine research. To make matters worse, researchers in reproductive biology,

malaria, and other fields also have begun to rely more heavily on rhesus macaques.

But supplies are limited. India, once the main source, has banned exports of the species since 1978, and NIH is phasing out a domestic program to breed "clean" macaques that was begun after many imported monkeys were found to harbor pathogens. The resulting imbalance between supply and demand has caused delays of up to a year or more for animals with certain genetic features and has driven up the price of the animals to a level that is straining many researchers' budgets.

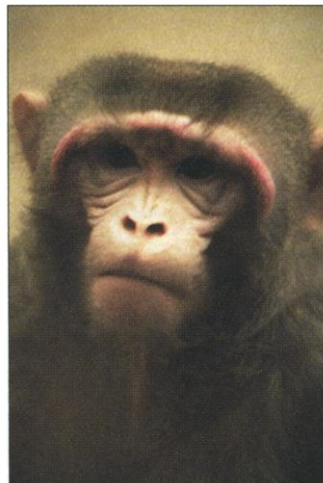
Six months ago NIH's Office of AIDS Research (OAR) sponsored a meeting at which researchers concluded that there was a "severe shortage" of rhesus macaques and urged NIH to act quickly. But NIH officials say it's not clear what should be done, or which component of the \$18 billion agency should take the lead. "There is a problem, but I'm not able at present to identify its dimensions," says OAR director Neal Nathanson. The issue, he says, falls in the

lap of another NIH branch, the National Center for Research Resources (NCRR), which in addition to funding the New England facility and seven other primate facilities specifically bankrolls breeding programs with both nonprofit and commercial suppliers. "I've conveyed my sense of the [problem] to NCRR," Nathanson says.

Some outside researchers wonder, however, if NCRR has the ability or desire to improve the situation. "It's a very isolated institute, and it doesn't collaborate well with other institutes," says Alan Schultz, a former head of AIDS vaccine research at the National Institute of Allergy and Infectious Diseases who now works with the International AIDS Vaccine Initiative. Jerry Robinson, who oversees the regional primate centers for NCRR, agrees that there is a "real crisis." But Robinson has had difficulty assessing the number of primates available for research, and no one at NCRR has tallied the number of animals required by NIH-funded researchers.

Several factors complicate any attempt to make even a simple assessment of

the available population, says Robinson. Primate centers and private colonies reserve some animals for breeding or behavioral research, and disqualify others that are too young or old. In addition, both commercial breeders and primate centers have been known to play favorites. "The people involved



Breeding discontent. The supply of rhesus macaques can't keep up with demand.

in monkey procurement seem like an old boys' network of people calling their friends," says New England's Johnson. "Two people may call up and get different information about availability."

In addition, one size definitely doesn't fit all researchers. Scientists have become increasingly selective as they develop more sophisticated research tools and reagents. But the cost of many of the animals produced through NCRR-funded breeding programs now far exceeds that budgeted in the average NIH-funded grant. Add in the rising demand from outside the AIDS field and the result, Robinson says, is that "lots of NIH grants depend on macaques, and [the researchers] can't get the monkeys they need."

Most in demand are monkeys that don't have chronic infections. In the early 1980s, coincident with the start of the AIDS epidemic, primate researchers discovered that many rhesus macaques had been infected with what is now known as simian retrovirus. Although the virus has no relationship to SIV or HIV, it can kill monkeys from an AIDS-like disease. Many animals also harbored an array of other viruses that could either harm the monkeys or their handlers, including STLV, herpes B, and foamy. So 12 years ago, NCRR decided to fund select primate centers and commercial outfits to breed "specific pathogen free" (SPF) animals.

Unfortunately, the SPF breeding program has done little to alleviate the crunch, and rising demand has driven up prices. Kay Izard, a zoologist who runs the SPF program at LABS of Virginia in Yemassee, South Carolina, says the top asking price for an SPF animal has risen from \$2000 in 1987 to \$5000 today. That's nearly double the per capita price budgeted by most NIH-funded researchers, some of whom buy as many as 100 rhesus macaques a year.

Three years ago, NCRR decided to phase out funding for the SPF breeding program. It was a tacit admission that the animals had become too expensive for academic researchers and that the program was instead subsidizing commercial users. "The long-range goal of NCRR was to set these colonies up and not to subsidize them forever," says Robinson. But Izard and others have questioned that decision. "It's too bad they didn't extend the funding for it, since there is a real problem," says Izard, noting that they have had to raise prices even higher since NCRR cut its support.

On top of the shortage of SPF animals, AIDS researchers are also hard pressed to find females of breeding age, as well as a specific genetic type used for immunologic studies that help explain why vaccines fail or succeed. Specifically, researchers have developed reagents that allow them to measure killer cells—a critical component of the

immune system—only in animals that have a marker on their white blood cells known as Mamu-A*01. "The wait for Mamu-A*01 animals is not quantified in months but in years," says Johnson.

NCRR soon will solicit new proposals from monkey breeders, says Robinson, in hopes of boosting supply. But new housing for breeding colonies is also essential, says Ronald Desrosiers, who heads the New England center in Southborough, Massachusetts. "You can give me all the [breeding] money you want," he says, "but if I can't use it to build a building to put them in and the infrastructure to support it, it is impossible [to produce more animals]." Others suggest that centers in cold climates like New England should instead contract out the work to commercial firms in warmer climates, where animals can roam outside all year.

Some researchers see foreign stocks as a partial solution. Marta Marthas of the Cali-

fornia Regional Primate Research Center in Davis says researchers should look more carefully at rhesus macaques still available from China. Although studies suggest that Chinese macaques naturally control SIV infection more effectively than do monkeys of Indian origin, Marthas says many questions remain about their differences. David Watkins of the University of Wisconsin, Madison, hopes to implant embryos from Indian Mamu-A*01 animals into Chinese rhesus mothers. "[In vitro fertilization] is the way to go," he says, although he adds that the technique is now inefficient.

Whatever its cause, the shortage of rhesus macaques has highlighted the need for scientists to become more involved in breeding them. "What disturbs me the most is that this [issue] is looked at with great disdain by everyone," says Marthas. "We have to think ahead. If we don't, we'll jeopardize not only our own experiments but those of future scientists." —JON COHEN

STATISTICS

Revealing Uncertainties in Computer Models

Computer simulations give the impression of precision, but they are founded on a raft of assumptions. Making uncertainties evident is a tough challenge

As computers have become faster and smarter, scientists have used them to build models of complex phenomena—every-

thing from wildfires on rugged terrain to traffic snarls on urban streets. These simulations can yield precise answers to problems a person with a pencil and paper would need millennia to solve. But just how reliable are these virtual solutions? Although the precise numbers and realistic pictures produced by computer simulations give an illusion of accuracy, a ravening swarm of assumptions, simplifications, and outright errors lurk beneath. New tools are needed, scientists say, to quantify the uncertainties inherent in calculations and to evaluate the validity of the models. But, as several recent uncertainty workshops* attest, the quest for such tools is itself an uncertain and challenging process.

The worrisome scenario is not the old science fiction cliché of supersmart machines shucking the



A difficult road. To keep out of jams, modelers simulating complex systems such as traffic patterns must know the uncertainties involved.

* Two took place last December in Santa Fe and Los Alamos, New Mexico. A 2-day meeting on the "Evaluation of Complex Computer Models" (3 to 4 December) focused on how statisticians can address the problem, and a 3-day follow-up on "Predictability of Complex Phenomena" (6 to 8 December) looked at efforts currently under way.