and will put up a fight. Funding for the bulk of science and technology efforts at those agencies would fall $400 million in 1998 to $16.2 billion, and continue dropping until it reached $15.6 billion in 2002.

The account that includes the National Institutes of Health would also decline from $24.9 billion to $24.4 billion. But biomedical research has numerous and powerful supporters in Congress who will seek to turn those numbers around. Last week, the Senate unanimously approved a nonbinding resolution drawn up by Senator Connie Mack (R–FL) that the "federal commitment to biomedical research should be doubled over the next 5 years." It also calls for an immediate down payment of an additional $2 billion for 1998. However, 2 days later, the same body voted 63–37 to kill an amendment to the budget bill that would have increased NIH funding by $1.1 billion in 1998 by taxing the administrative budgets of other agencies. That sets the stage for an intense battle over health funding later this year. "We are disappointed" by the budget bill, says John Suttie, president of the Federation of American Societies for Experimental Biology, which hopes that legislators will deliver on earlier promises for a bigger increase.

Civilian DOE spending, including nonphysics work sponsored by DOE at labs and in academia, also suffers a decrease in the plan, falling from $3.1 billion in 1998 to $2.8 billion in 2002. Funding for natural resources and environmental research would rise from $22.2 billion in 1998 to a peak of nearly $24 billion before returning to $22.2 billion by 2002.

R&D advocates generally put on a brave face last week, saying they will fight to prevent the cuts outlined in the resolution from becoming a reality. "Science will not become the type O [universal] blood donor," says the science chair, who recently took his case to House Speaker Newt Gingrich (R–GA). On the Senate side, Senator Phil Gramm will "forge ahead with" his plan to double the amount of civilian government research over 10 years, from $32.5 billion to $65 billion in 2007, says his press secretary, Larry Neal. But the resolution "will make our job more difficult," he admitted.

For all its sobering news, the budget resolution hasn't created panic in the R&D community because it is unlikely to be followed to the letter. "There's a fair amount of flexibility" in how Congress ultimately allocates taxpayer dollars, says Teich. And the vagueness of the plan makes it hard to tease out its possible effects on individual programs. But one thing is clear: R&D will face an increasingly hard struggle to hold onto its share of the federal spending pie over the next 5 years.

–Andrew Lawler

With additional reporting by Eliot Marshall.

CONSERVATION BIOLOGY

Can Cloning Help Save Beleaguered Species?

When Kurt Benirschke launched a program at the San Diego Zoo in 1975 to freeze cells from endangered species, he assumed that his colleagues would use the collection to unravel complex issues such as the genetic similarities among animals. Never did he imagine that scientists might one day pluck cells from the "frozen zoo" to grow new animals from scratch. But since February, when researchers in Scotland reported they had cloned a lamb named Dolly from the cells of an adult sheep, the notion of cloning a Przewalski's horse, Sumatran rhinoceros, or one of the other rare species whose cells are banked at the San Diego Zoo's Center for Reproduction of Endangered Species (CRES) has suddenly left the realm of science fiction.

"The possibilities for zoos are enormous," says Benirschke, a reproductive biologist who now is vice president of the zoo. Like other zoologists, he recognizes that many scientific hurdles stand between a fibroblast—a tissue-repairing cell that makes up the bulk of the frozen zoo's collection—and, say, a healthy infant rhino (see sidebar). But he thinks the field has seen so many remarkable advances in recent years that the obstacles, for some species at least, are likely to fall. Says CRES geneticist Oliver Ryder, "I think [cloning] is going to produce a paradigm shift. It offers the potential for a better safety net than we thought we had." Adds Benirschke, who began working with colleagues in China after Dolly's creation to save cells from the endangered Yangtze River dolphin, "I would love to excite the international community to save as many cells as they can from as many animals as possible."

But even if the technical hurdles do fall, many conservation biologists argue that efforts to clone endangered species would be so expensive that they could derail other conservation efforts. "In the end, the very finite resources that conservation has are better directed elsewhere," contends Michael Bruford, a molecular geneticist at the Zoological Society of London's Institute of Zoology. Adds David Wildt, head of reproductive physiology at the U.S. National Zoo's Conservation and Research Center in Front Royal, Virginia, cloning should be viewed only as a "last, desperate attempt to try to preserve a given species."

Ryder argues, however, that cloning may offer benefits that are not immediately obvious. When people think of cloning, they often imagine legions of genetically identical individuals. But Ryder contends that the technology actually could be used to increase the genetic diversity of a dwindling species—a proposition that has taken some of his colleagues by surprise. Population geneticist Robert Lacy of the Brookfield Zoo in Illinois, for instance, says he was skeptical that cloning could enhance genetic variability, which, he notes, is "the primary thing we're trying to do with endangered species." But he was persuaded, he says, after reading Ryder's ideas on a private Internet chat group for population biologists.

R. GARRISON/ZOOLOGICAL SOCIETY OF SAN DIEGO

Cold comfort. Some scientists say cells banked at the San Diego Zoo's Center for Reproduction of Endangered Species *(above)* and other "frozen zoos" can be used to preserve rare animals.

Ryder reasons that for species that are down to just a few surviving individuals, clones grown from frozen fibroblasts could provide an invaluable source of "lost" genes. Suppose scientists could clone Asian wild horses, South China tigers, or Spanish ibex from cells in the CRES collection that were gathered from long-deceased animals, says Ryder. The clones theoretically would then be able to breed, reintroducing the lost genes back into the population. "It might allow you to go back and recover the genetic diversity," he says.

Ryder also argues that cloning could be an especially useful tool for biologists trying to save species that don't breed well in captivity, such as giant pandas. The more offspring an animal has, says Ryder, the more of its genome it will pass on. If a giant panda in a zoo has only one offspring, one half of the panda's genes are lost. But if biologists could clone the panda 10 times and each one produced an offspring, in effect, the original panda would have produced 10 offspring, and fully 95% of its genetic

Would-Be Cloners Face Daunting Hurdles

It took Ian Wilmut and his colleagues at Scotland's Roslin Institute 277 attempts to clone one lamb, the now-notorious Dolly, from adult mammary cells. For conservation biologists who ponder the possibility of applying this advance to endangered species (see main text), those 276 failures in sheep—a species whose reproductive biology is well understood—only underscore the technical hurdles they face. Even Wilmut, who first published his results in the 27 February issue of *Nature*, points out, "The success rate is so low that you would do better to breed naturally. You would get far more offspring!"

ROBER MAIER/ANIMALS, ANIMALS

Next in line? A Przewalski's horse.

The first challenge, says Oliver Ryder, a geneticist at the San Diego Zoo's Center for Reproduction of Endangered Species (CRES), is to see whether fibroblasts—cells made during wound healing—could be used instead of mammary cells. This question is critical because CRES's collection of cells—the world's largest—is made up of fibroblasts, stored in liquid nitrogen.

Assuming fibroblasts from adult animals could work, researchers face another challenge: harvesting eggs in a "ripened" state during ovulation. The Scottish group made Dolly by planting mammary cells from one sheep into another animal's egg that they had modified by scooping out its gene-carrying nucleus. Harvesting ripened eggs from sheep is routine because the animal's reproductive cycle is well understood. But plucking eggs from, say, a Sumatran white rhino is quite another matter, says David Wildt, head of reproductive physiology at the U.S. National Zoo's Conservation and Research Center in Front Royal, Virginia. "We know basically nothing about their reproductive physiology," says Wildt. "You'd have to have a rhino docile enough to allow ultrasound [to know when it is ovulating]." And once eggs are harvested, Wildt notes, different species usually require different nutritive media in laboratory cultures—media that scientists have yet to define for most endangered species.

Now, assume the transfer of fibroblasts into enucleated eggs worked and embryos developed. The next challenge would be implanting an embryo into a female that could carry it to term. Reproductive biologists say they would prefer to use females of a related, unendangered species as surrogate mothers so that females from the highly endangered population would be available for natural breeding. But it is not at all clear that the placenta carrying genes from the fibroblasts of a Rwandan mountain gorilla, for instance, would take in the uterus of a captive gorilla of a different subspecies. "I think it likely that there are sufficiently species-specific factors to limit mixing," says Wilmut.

Kurt Benirschke, a vice president of the San Diego Zoo who started the CRES collection, notes that some such transfers have worked. For instance, Douglas Antczak, a veterinarian at Cornell University in Ithaca, New York, and W. R. Allen at the Thoroughbred Breeders Association in Suffolk, England, have successfully grown a zebra embryo in a horse. Antczak suggests that others might build on these results by implanting into a horse an embryo from the endangered Przewalski's horse. "It would be a good example species," says Antczak.

Betsy Dresser, a reproductive physiologist at the Audubon Center for Research of Endangered Species in New Orleans, suggests that many of the next steps may be taken by researchers who work with domestic animals. "The domestic-animal field has tons of animals to work with, and money," she says. And Dresser says if they make headway, conservation biologists will surely take advantage of cloning. Says Dresser, "If we can use it as a tool to save an endangered species, you'd better believe we will." **–J.C.**

information would have been "captured." (The equation is $1 - 1/2n$, where n equals the number of offspring.)

Cloning might even serve a useful purpose with species that have never bred in captivity, such as the giant armadillo, by allowing biologists to asexually reproduce the creatures. This scenario, which would require implanting a cloned embryo of a giant armadillo in a more common relative, adds to the already formidable list of scientific obstacles. Still, says Ryder, "it could possibly guarantee genetic immortality."

In a commentary in press at *Zoo Biology*, Benirschke and Ryder contend that if cloning endangered species does become a reality, zoos may one day be able to breed fewer animals and retain smaller herds without losing genetic diversity. This is an important advantage, they argue, because most zoos already are short on space.

Intrigued as he is by these ideas, Brookfield's Lacy says cloning is so expensive and technically challenging that it should be used only with "a fairly narrow window" of species, those with "five, 10, or 15 animals." In most cases, he says, "with a little foresight, we'd be able to set up a breeding program that didn't cost millions."

The National Zoo's Wildt concurs, adding that lower tech, "assisted breeding" methods such as artificial insemination can often achieve the same goals as cloning. A few years ago, the black-footed ferret, for example, was down to as few as six individuals. But last year, Wildt and his colleagues successfully used artificial insemination to birth 16 kittens. He stresses, though, that even something as well understood as artificial insemination can be a big challenge in a new species. "We do a lot of work with assisted breeding," says Wildt. "What we've learned from working in this field for 20 years is it's really difficult."

Michael Soule, an emeritus population geneticist at the University of California, Santa Cruz, worries that cloning endangered species could distract people from saving habitats. "I don't want people to think that [cloning is] a solution to a major problem," says Soule. He heads the Arizona-based Wildlands Project, which aims to improve habitats in North America. "We've only got a few years before most of the biodiversity on the planet goes down the sink."

As they explain in their *Zoo Biology* commentary, Ryder and Benirschke do not want cloning "to minimize or supplant" current conservation efforts. "This discussion is not being advocated in lieu of saving species the only way they can be saved—in their habitats," says Ryder.

Conservation biologists will, for the first time, have a chance to discuss the promise and pitfalls of cloning endangered species at a Berlin meeting in August sponsored by the Minnesota-based Conservation Breeding Specialist Group. Ryder and Benirschke urge their colleagues to think seriously about cloning's potential. "The future for clonable species would clearly be better than that for animals that cannot be cloned," they conclude in their *Zoo Biology* commentary. Surely, that's a definition of "fit" that Charles Darwin never imagined.

–Jon Cohen