This allowed the granulosa cells time to multiply and stick to each other in layers rather than to the dish. Then they doused the cells with growth factors and stimulatory hormones. The results—14 days later—were mature eggs.

Then the duo tried test-tube fertilization. "We were just immensely excited when we discovered that about 40% of the oocytes matured in this way after growth in vitro were actually able to undergo fertilization and cleavage" to the two-cell embryo stage, says Eppig.

Only one of 190 such two-cell embryos transferred to the oviducts of surrogate mothers grew into a live-born pup. (The pup is now 7 months old.) Finding out why the success rate was so low should give researchers a sharper picture of how oocytes grow into viable eggs, says Schultz. By changing the chemical environment to which the cultured oocytes are exposed to improve the success rate, he explains, Eppig and other researchers "may be able to get a molecular understanding of what is involved in acquiring embryonic competence. ... Eppig has laid the groundwork for some potentially really neat science."

And also for some potentially revolutionary wildlife conservation procedures and human medical treatments. In endangered, hard-to-breed species such as pandas, slices of ovary could be removed from females and their many oocytes grown and fertilized in the lab for implantation into surrogate females of related species. With infertile human couples, oocytes could be extracted and developed in preparation for test-tube fertilization. That would eliminate the need to treat prospective mothers with large doses of hormones called gonadotropins, which prompt them to ovulate the multiple eggs needed for the hit-and-miss process of conventional IVF—but whose long-term health effects are uncertain.

While significant hurdles will have to be overcome before Eppig's procedure can be attempted in humans and other species—for example, human oocytes develop very slowly, so the material would have to be kept alive in culture for a long period—researchers such as reproductive biologist Robert Clarke, laboratory director of the Center for Assisted Reproduction at Boston's Brigham and Women's Hospital (BWH), say Eppig's advance has helped clear the way for the next technological leap. BWH, in fact, plans to offer an oocyte-storage service to women at risk of becoming infertile from cancer chemotherapy. "The technology for culturing primordial human oocytes isn't there yet," Clarke says. "[But] I think the concept is probably one of the most important advances that will come through in this field in the next several years."

–Wade Roush

ASTRONOMY

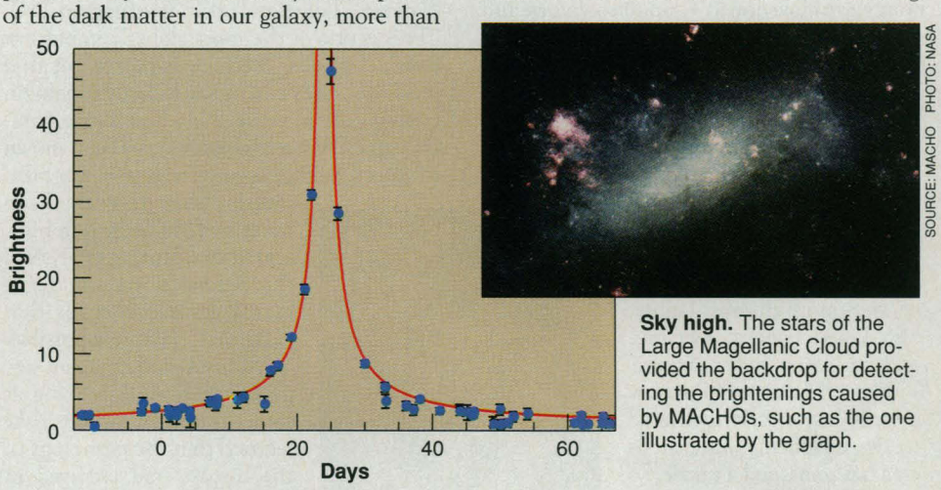
Is the Dark Matter Mystery Solved?

SAN ANTONIO—To judge from the headlines, astronomers have solved one of their field's greatest mysteries: the identity of the long-sought "dark matter." A widely reported press conference at a meeting of the American Astronomical Society held here last month left the impression that the hitherto undetectable mass whose gravity keeps our own Milky Way and other spiral galaxies from flying apart as they spin on their axes has now been found. But astronomers—including the dark-matter hunters themselves—say reports of the mystery's solution may have been premature.

In their presentation at the meeting, a multi-institutional team of astronomers announced that MACHOs—for massive compact halo objects—most likely make up 50% of the dark matter in our galaxy, more than doubling the team's earlier estimate, which they published less than a year ago in *Physical Review Letters* (*Science*, 5 May 1995, p. 642). Because MACHOs consist of ordinary matter, such as the burnt-out normal stars known as white dwarfs, the revision—if it holds up—could mean that all the galaxy's missing mass consists of ordinary matter rather than the exotic particles some theorists favor. The rest of the mass, some astrophysicists suggested, could be in objects larger than the team has searched for yet, or too far away to detect. "My sentiment is that if half of it is ordinary stuff, then the rest of it is ordinary stuff, too," said astrophysicist John Bahcall of the Institute for Advanced Study in Princeton, New Jersey, who is not a MACHO team member, at the press conference.

And that could pose problems for current astrophysical theories, including some predictions of the big-bang scenario for the origin of the universe and its later evolution. Many theorists believe that during the big bang, a cosmos of purely "ordinary stuff" would have had trouble cooking up observed elemental abundances unless the matter's overall density was extremely low. And later, the primordial soup might not have collapsed into galaxies and the large galaxy clusters known to exist. Some theorists argue, too, that the universe as a whole should have enough mass to slow its expansion toward a standstill. That would require far more mass than could be supplied by ordinary matter and has led some cosmologists to favor swarms of massive neutrinos or other, more exotic particles as candidates for the dark matter, both within galaxies and in the vast reaches in between.

For these reasons, says the University of Chicago's Michael Turner, "if indeed [the MACHO group] has solved the dark-matter problem, they would have started a revolution." But Turner and others, including MACHO team members, note that the data so far are too sketchy to really settle the dark matter issue. "We still only have less than two handfuls of events," concedes team member Kem Cook of Lawrence Livermore National Laboratory.



SOURCE: MACHO PHOTO: NASA

Sky high. The stars of the Large Magellanic Cloud provided the backdrop for detecting the brightenings caused by MACHOs, such as the one illustrated by the graph.

Even if they're plentiful, after all, MACHOs are hard to find. By definition, these clumps of dark matter can't be seen directly. To detect them, the team, including astronomers from Livermore, the Center for Particle Astrophysics at the University of California, Berkeley, and the Mount Stromlo Observatory in Australia, instead takes advantage of the fact that a MACHO's gravity bends rays of light. When it passes between Earth and a distant star, the MACHO acts as a lens, temporarily increasing the star's apparent brightness.

The group scanned for the objects in the Milky Way's spheroidal halo, where theory says the dark matter should be, using the Large Magellanic Cloud (LMC), a nearby galaxy, as a starry backdrop. The researchers monitored 9 million LMC stars each night for any that showed such transient brightness

increases. After 2 years, the team announced, it has picked up seven MACHOs. From the duration of the brightenings, it estimates that their average mass is between 0.1 and 1 solar mass—a size suggesting that they are old, dim, cold white dwarfs.

Extrapolated to the whole halo, the results imply that half its mass consists of MACHOs, double what the group found in their first year's scan. In light of the new results, "it's certainly viable that all the dark matter in our galaxy is made of [ordinary matter]," says team member David Bennett of Livermore.

But uncertainties in the data also open the way to more mundane conclusions. The team already threw out two "really ratty" events in the original first-year data set of three MACHOs, says Bennett, before coming up with the new total of seven over 2 years. And if, as the team now suspects, one of the new lenses is actually in the LMC and not in our galaxy's halo, the most probable fraction dips to 40%. Finally, the unfolding of an object's mass, speed, and relative distance from a single number—the duration of the brightening—depends strongly on the halo model chosen, such as the flatness of the spheroid and whether it rotates or not. Given the doubts, "you could go down to 20% and not be outrageous," says team member Charles Alcock, also at Livermore.

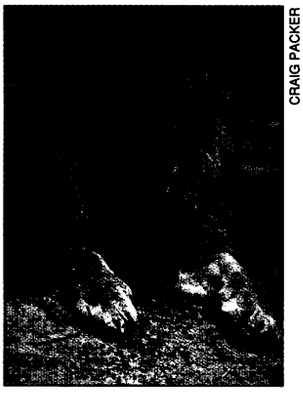
The resolution of the dark matter puzzle will probably have to wait until more MACHOs have been detected, most researchers say. "We are dealing with small-number statistics," says Bohdan Paczyński of Princeton University, whose own team will begin searching the halo for dark matter in 9 months. "I would rather wait 2 or 3 years and see how things look at that time."

–James Glanz

EMERGING DISEASES

New Virus Variant Killed Serengeti Cats

"If you were a dog, I'd say you had canine distemper," veterinarian Melody Roelke-Parker remembers thinking in February 1994 as she watched a male lion in Tanzania convulse and twitch. "But you're a cat, and cats don't get canine distemper." Yet by June of that year, Roelke-Parker—who works at Tanzania's Serengeti Wildlife Research Institute—had her suspicions confirmed: Researchers had identified canine distemper virus (CDV) as the culprit in an epidemic that wiped out more than a third of the Serengeti's lion population. The pathogen, a member of the morbillivirus family, also killed hyenas, leopards, and bat-eared foxes (*Science*, 17 June 1994, p. 1664). But how a virus historically restricted to dogs suddenly jumped to cats has remained a puzzle.



CRAIG PACKER

Face of disease. Adult lion's facial twitching is caused by canine distemper virus.

Now, thanks to a new genetic analysis, an answer is beginning to appear: The Serengeti organism seems to be a new variant, or biotype. In this week's issue of *Nature*, Linda Munson, a veterinary pathologist at the University of Tennessee's College of Veterinary Medicine, and her colleagues report that the Serengeti strain is genetically different from normal CDV. While the researchers have not yet been able to show how the genetic shift caused the new infection pattern, they have been able to trace environmental changes that apparently prompted the mutation: growing human settlements along the Serengeti National Park's western border, with large populations of CDV-infected domestic dogs. "When you have a wildlife population in close proximity to domestic animals like this, you're going to see an exchange of diseases—and you're going to encourage the emergence of successful mutations," Munson says.

This, to other researchers, is convincing evidence. "These findings fit with the overall pattern of emerging viruses" such as that of the hantavirus, says Richard J. Montali, head of pathology at the Smithsonian Institution's National Zoological Park in Washington, D.C. "This is one of the most globally important cases," he adds, "because it points out that morbilliviruses have made incredible gains in evolving to increase their host range." Although CDV itself has previously been shown to infect black-footed ferrets, new morbilliviruses have recently been identified in seals, dolphins, and horses. Further analysis of the Serengeti variant might reveal genetic changes that make such expansion possible.

Munson and her team suspected they were looking at something new when they learned that the pathology of the disease had changed in the jump to the cats. "It infects the lions' hippocampus, whereas the other strain primarily causes inflammation of the brain stem in dogs," explains Munson. And while both strains cause pneumonia, they do so in different ways: Normally CDV affects dogs' bronchial tubes, but the Serengeti variant attacks the alveoli, air sacs in the lungs. These changes could simply be the result of new opportunities in a new host, Munson says. "But when you see a virus that not only has a broader species range but affects different tissues, you suspect you're looking at an emerging biotype," she adds.

To confirm these suspicions, her team compared virus samples from the lions to the best known strain, Onderstepoort, which was isolated from a domestic dog in South Africa. Margaret Carpenter, a molecular biologist at the U.S. National Cancer Institute's research center in Frederick, Maryland, who did the genetic analysis, explains that the group focused on a well-studied gene, coding for a phosphoprotein that helps transcribe the viral genome as it prepares to replicate. In her analysis of a 389-base-pair fragment, Carpenter found 18 nucleotide substitutions, suggesting that the two viral strains were "significantly different."

Changes in genome replication could underlie the virus's ability to jump into a new host, says Carpenter. Then again, she says, "we really don't know which parts of the virus's genome need to be changed in order for it to switch hosts." Carpenter is now sequencing part of the viral hemagglutinin gene, which is thought to affect the host's immune response. Again, mutations in this gene might enable the virus to take up a new residence.

Although the team has not been able to pinpoint the genetic mechanism for the jump, they have been able to point a finger at the jumping point. Between 1993 and 1994, a CDV epidemic swept through villages to the west of the Serengeti, killing thousands of domestic dogs. Monoclonal antibody tests show similarities between this strain and the one that infected the lions. The researchers propose that the virus then entered the park, perhaps via jackals and spotted hyenas, which frequently scavenge near humans. Because CDV is shed in mucus, these animals, in turn, probably infected lions at kill sites, where there is often a lot of biting and snarling between species.

Then, between February and October 1994, at least 1000 of the park's 3000 lions are thought to have died of the disease; the survivors probably developed immunity. Like all morbilliviruses, CDV requires a susceptible population to sustain itself, and no new cases have been seen in the last year.

The lion population is now on its way to recovery, reports Craig Packer, director of the Serengeti Lion Project and one of the study's authors. Veterinarians have also launched a program to vaccinate the local domestic dogs against CDV and other diseases—a step that they hope will stop the virus before it jumps again.

–Virginia Morell