SPACE MEDICINE

Euro-Russian Accord Begins With 30 Days of Solitude

Less money need not always mean less science. In November 1992, when the European Space Agency (ESA) held its 5-year budget meeting, European governments were in the depths of recession and were in no mood to spend vast sums on space exploration. As a result, ESA's program to build its own retrievable space plane, called Hermes, was put on ice, and the rest of ESA's program to put human beings in space was told to cut costs, principally by collaborating with Russia. This week, if all goes according to plan, should see the first fruits of this austerity measure: the start of the longest space voyage for a Western astronaut since 1974 and a potential bonanza for researchers on the health effects of microgravity.

On 3 October, ESA astronaut Ulf Merbold and two Russian cosmonauts were launched aboard a Soyuz spacecraft for a month-long stay on Mir, Russia's space station. This first joint ESA-Russian mission should give Western scientists a long-awaited chance to resume studies on the long-term effects of microgravity all but abandoned when the last crew left the National Aeronautics and Space Administration's (NASA's) Skylab space station in 1974. Experiments are carried out on the shuttle orbiter, but just as astronauts' bodies are starting to adapt to weightlessness they have to head for home. A longer mission "promises to give us more realistic science," says vestibular researcher Andrew Clarke of the Free University of Berlin. "It's an exciting venture," adds neurologist Charles Markham of the University of California, Los Angeles, who has an experiment flying with the mission.


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Medicine in a tin can. ESA astronauts Ulf Merbold *(left)* and Pedro Duque practice an experiment in a mock-up of Mir.

European astronauts are no strangers to Mir. France, Germany, and Austria have each sent one of their nationals to Russia to take part in shorter Mir missions. But Merbold's trip, dubbed Euromir-94, is the start of a much closer collaboration between the West and Russia on microgravity projects. A follow-on mission, Euromir-95, is set to keep a European in space for 135 days, while NASA is expected to dock the shuttle onto Mir next May, the prelude to closer cooperation that will lead to stays for NASA astronauts of up to 100 days by 1996.

With this string of planned missions, Western scientists can now restart lines of research begun in 1973 and 1974 during extended missions—up to 84 days in length—aboard Skylab. It was during those flights that scientists first observed the profound changes in the body caused by weightlessness, such as muscle and bone wastage, unexplained dizziness, and space motion sickness. Although Soviet cosmonauts had surpassed NASA's endurance record in their Salyut station by 1978, Western scientists say that the Soviets gathered physiological data largely to find ways to help cosmonauts cope with the changes in their bodies rather than to answer basic scientific questions. "There's a cultural difference in their scientific method. They look after their cosmonauts, but their methods are not well documented," says Clarke. That's why ESA is keen to carry out its own set of experiments. "You like to do things yourself. You can trust your own data," says Heinz Oser, ESA's chief life scientist.

A major focus of this mission will be the functioning of the vestibular system, the collection of position and motion sensors in the inner ear that helps control balance and keep the eyes fixed on an object while the head is moving. When astronauts first enter microgravity and the brain suddenly receives no gravity signals from the sensors, "eye con-

Testing the Psychology of Would-Be Astronauts

Spare a thought for the lonely astronaut: cooped up for months on end with the same few people in a glorified tin can, only a very poor communications link to the outside world, and no opportunity even to go for a walk around the block. As the European Space Agency (ESA) sends off its first astronaut for an extended stay on Russia's Mir space station and plans a 135-day follow-up mission next year, it is sparing more than a thought for astronaut psychology. Last month ESA commissioned the Institute of Biomedical Problems (IBP) in Moscow to lock three Russian volunteers in a chamber for 135 days to see how they get along together.

The experiment, which began on 1 September, aims to simulate life on Mir as closely as possible by mimicking the daily routine of cosmonauts, the lack of water and washing facilities on the station, the exercise regimens to mitigate the effects of weightlessness, and even the poor communication with the ground. "The main aim is to study the psychological effect of confinement," says Jens Schiemann of ESA's research and technology center ESTEC at Noordwijk in the Netherlands.

ESA has carried out two similar experiments before, although for shorter periods of time: 28 days in 1990 and 60 days in 1992. In these studies, Schiemann says, a definite us-and-them mentality developed between the volunteers and the controllers outside. "They were not enemies, but there was a strong group feeling inside, and they were very curious about what was going on outside." Ultimately, the project aims to identify personality criteria for choosing astronauts for extended missions and find ways to ease tensions between astronauts and ground controllers.

The IBP was chosen because of its experience and its facilities for flight simulations: Since 1963 the institute has coordinated the medical and life support for all Soviet and Russian space missions. Institute Director Anatoly Grigoryev is watching ESA's $370,000 project with envy, mixed with gratitude that it is bringing in some cash. Since the collapse in Russian research funding, the institute cannot afford long-term research of its own and has lost 30% of its staff.

–Andrey Allakhverdov and Daniel Clery

Andrey Allakhverdov is a science writer in Moscow.

trol goes out of whack for a while," says Markham. He plans to study how Merbold's eye control changes as he adapts to weightlessness, and he hopes the information will help in screening astronauts for their susceptibility to space motion sickness.

For his experiment, Markham will use an instrumented helmet brought up for the 1992 German mission to Mir. The device records eye movements on video while sensors record the actual movements of the astronaut's head. Clarke in Berlin will use the helmet for a more fundamental study of the vestibular system: Motion sensors in the inner ear are influenced by gravity, so once it is removed, it will be possible to see directly how a simple movement of the head, say tilting it to one side, is detected by the sensor and so directs eye movement. The long duration of the flight "takes the pressure off the experiment," he says.

Experiments like Clarke's are designed to shed light not only on the problems caused by prolonged weightlessness but also on how the human body functions on Earth. "We are using space as a tool. It is no different from ground-based research," says Oser. The distribution of blood and other fluids throughout the body, for example, is dominated by hydrostatic pressure caused by gravity. By removing gravity, scientists can see how volume shifts are regulated. "Space unmasks the mechanism," says Oser.

In one such study of the control systems of bodily fluids, devised by Peter Bie of the University of Copenhagen, Denmark, Merbold will draw some of his own blood with the help of a Russian colleague, mix it with salt solution, and reinfuse it. By comparing blood samples taken during the flight as well as just before and after it, Bie hopes to learn how salt defuses through the body. Other experiments into bone and muscle loss will be limited to examinations of Merbold shortly before and after the flight because of the lack of suitable instruments onboard.

If all goes according to plan, ESA will have another astronaut on Mir in a year's time, and some of these experiments will be repeated then. The extra time until Euromir-95 will allow ESA to complete development of a bone densitometer that will use ultrasound to monitor wasting of the astronaut's heel bone during the mission. ESA also hopes to send up equipment to analyze respiration and urine during the flight, lessening the need to bring samples back to Earth. By the time the international space station is up and running around the year 2000, the Europeans and Russians will already have amassed substantial data on space physiology—and at a bargain price.

–Daniel Clery

cDNA SEQUENCES

HGS Opens Its Databanks—For a Price

The biologist-entrepreneurs who run the world's largest commercial human gene sequencing project are announcing a plan this week to share their data with academic researchers—at a price. Human Genome Sciences (HGS) and its nonprofit research partner, the Institute of Genomic Research (TIGR) of Rockville, Maryland, say they're ready to share detailed information they've collected on 35,000 complementary DNAs representing genes of unknown function that are expressed in human tissue. But those who use HGS's proprietary data would first have to agree to give HGS the option of licensing derivative products at a reasonable royalty rate. And they would have to provide 30 to 60 days' prior notice of publication.

William Haseltine, president of HGS, says his company will soon give researchers broad access to genetic data on these terms—after HGS and TIGR have published a paper this fall describing the cDNAs they've analyzed. As *Science* went to press, Haseltine was preparing to discuss the plan at a meeting of the international Human Genome Organization in Washington, D.C., attended by the major players in the human genome effort. One of the players, Maxwell Cowan, chief scientific officer of the Howard Hughes Medical Institute, said he thought the group would find the terms "acceptable."

Even if Cowan's prediction is correct, however, HGS may soon may face some new competition from a venture planning to make similar information available with no strings attached. Last week, Merck & Co., the pharmaceutical giant, announced that it will bankroll a new effort based at Washington University in St. Louis to sequence human cDNAs. Unlike HGS, Merck plans to put sequence data into a public database as soon as they become available. According to a Merck executive, the company hopes to encourage basic research that will go beyond sequencing genes and begin to explain their function. Merck officials say they want to speed up the discovery of new drugs.

The first big cDNA drive began in 1992, when HGS and TIGR launched an effort to clone and patent human cDNA using robotic methods developed by J. Craig Venter, a scientist who left the National Institutes of Health (NIH) in 1992 to take charge of TIGR. In 1993, Haseltine and Venter signed an agreement with SmithKline Beecham (SB) to develop medical products, and since then, their sequencing project has received $85 million from SB and a promise of roughly $40 million more. So far, according to Haseltine, the partnership has generated 120 million expressed nucleotides, identified more than 80,000 unique sequences, validated the process by independently confirming the existence of 202 of the 248 human genes already named in reports, and filed for patents on 70 full-length cDNAs.

The companies are now ready to share this "magnificent achievement," Haseltine says. In the past, Haseltine notes, the HGS-TIGR partnership has shared data in tailored agreements on a "one-off basis" with individual scientists. For example, a collaboration with Bert Vogelstein of Johns Hopkins University led to the discovery of a colon cancer gene. But in recent months, HGS, TIGR, and SB have drafted a new "material transfer agreement" to make it easier for scientists to tap into their data.

The goal of the new arrangement, says Haseltine, is to speed up the process of genetic research. The gesture may also give HGS and TIGR a public relations boost. In recent months they've been criticized for trying to hold valuable scientific information too close to the chest. Some researchers have balked at restrictions HGS has placed on commercial use of the data in the past. For example, *Science* has learned that the Baylor College of Medicine, the Howard Hughes Medical Institute, and NIH objected to the conditions of an HGS data-sharing agreement proposed earlier this year.

And that's one reason why Merck jumped into the sequencing business. Merck feels that "this should be public information," says Alan Williamson, Merck's vice president for global research strategy. The real "value added," as Williamson sees it, is in the basic biology that must still be done to determine the function of the DNA sequences. Some HGS and TIGR officials, however, regard Merck's move as a "spoiler strategy" designed to "throw a wrench in the machinery."

Details of Merck's project are still being negotiated. But Williamson and Robert Waterston, director of Washington University's genetic sequencing laboratory, say the initial Merck grant will amount to several million dollars and last for 18 months—or, as Williamson says, long enough to get the job done. Waterston says he expects the new project will be up and running before the end of the year. He adds that he's delighted by the recognition of the lab's accomplishments, especially Richard Wilson's effort to sequence DNA from a model organism, the nematode *Caenorhabditis elegans*. While the "public sometimes has trouble understanding why NIH would spend money on sequencing a nematode," Waterston says, "Merck didn't have any trouble."

–Eliot Marshall