

Spring 1986

A Matter of Concern: [Dr. Dennis Stark]

Fulvio Bardossi

Judith N. Schwartz

Follow this and additional works at: http://digitalcommons.rockefeller.edu/research_profiles

 Part of the [Life Sciences Commons](#)

Recommended Citation

Bardossi, Fulvio and Schwartz, Judith N., "A Matter of Concern: [Dr. Dennis Stark]" (1986). *Rockefeller University Research Profiles*. Book 22.

http://digitalcommons.rockefeller.edu/research_profiles/22

This Article is brought to you for free and open access by the Campus Publications at Digital Commons @ RU. It has been accepted for inclusion in Rockefeller University Research Profiles by an authorized administrator of Digital Commons @ RU. For more information, please contact mcsweej@mail.rockefeller.edu.



THE ROCKEFELLER UNIVERSITY RESEARCH PROFILES

SPRING 1986

A Matter of Concern

In his teens, Dennis Stark wanted to be a high school teacher, but he was discouraged by the economics of such a career. "So," he says, "I went to the encyclopedia, turned to the section on vocations, and kept going down the list until, pretty close to the end, I found something else I thought I would enjoy. It happened to be veterinary medicine." Today, Dr. Stark may be the only veterinarian on the Upper East Side of Manhattan whose working day is punctuated by the crowing of a rooster. But then, there aren't many veterinarians on the Upper East Side of Manhattan in charge of ten thousand animals. Dr. Stark directs The Rockefeller University's Laboratory Animal Research Center, a modern facility on the University's campus that houses the animals used by Rockefeller scientists in their research.

Laboratory animals are indispensable to biomedical research. They are primary models for studying basic biological mechanisms and for testing new drugs and medical procedures. Without them, medical science would effectively grind to a halt. Without them, we would not have the vaccines, miracle drugs, and surgical and diagnostic techniques that have given us a quality and span of life unprecedented in human history.

At the LARC, as the center is called, there are animal rooms for species ranging from mice, rats, hamsters, guinea pigs, rabbits, chickens, turkeys, goats, and sheep, to more exotic guests like African clawed frogs (*Xenopus*), raised for research

In the entryway to the Laboratory Animal Research Center, Dennis Stark, right, and Anthony Cerami, current chairman of the Institutional Animal Care and Use Committee, a group of senior scientists that includes Rockefeller faculty members and a non-Rockefeller representative. Dr. Cerami is R. Gwin Follis-Chevron Professor and head of the University's laboratory of medical biochemistry, a group developing drugs for the treatment of metabolic and parasitic diseases.



Margaret Harbison, the LARC's veterinary pathologist and director of the diagnostic laboratory, far right, with members of the veterinary and animal research staff. From left, Darlene Dixon, who holds a degree in veterinary medicine and a Ph.D. in pathology and environmental toxicology; Stephen Morse, a Ph.D. in microbiology; Maria Noel Jure, a visiting veterinary scientist from Uruguay; Byoung Lee Yi, a resident in veterinary pathology in a program jointly sponsored by The Rockefeller University and the Animal Medical Center; and Pamela Moore, a Ph.D. who conducts animal cardiology research. Drs. Dixon and Yi are postdoctoral fellows training in laboratory animal medicine and pathology.

on the regulation of gene expression. The handsome and vocal rooster is used in studies of viruses that cause cancer.

In a typical day, Dr. Stark might be found consulting with the LARC's pathologist about a sick animal, advising a researcher on the appropriate species for a prospective study, conducting his own research, or examining a research protocol with the University's Institutional Animal Care and Use Committee. (The University has had a review process for all ongoing research with animals since 1978. Comparable review requirements were not incorporated into the federal government's guidelines regarding laboratory animals until this year.) Not infrequently, members of the public concerned about animal welfare are invited to the LARC, where Dr. Stark provides them with the opportunity to observe the University's laboratory animal policies and procedures and to learn about the research programs he has initiated that are helping to reduce the number of animals used in experiments. Beyond the University's walls, Dr. Stark serves on the scientific board of the International Foundation for Ethical Research and is president-elect of the American Association for Laboratory Animal Science.

CHICKENS, BUDGIES, AND A WORM FARM

Dennis Stark's experience with animals began at an early age. "At home in Baltimore, my family always had pets," he says. "We had chickens, budgies, cats. Everything. Including a worm farm. As a sideline, we raised German shepherds. By the time I was in college, at the University of Maryland, I realized that there was a level of teaching—a type I really wanted to do, that also involved research—that I could pursue as a veterinarian. After graduating from the University of Georgia Veterinary School, I went to Cornell for a Ph.D. in immunochemistry."

His first job was at Long Island University, teaching immunology to medical technology students. "When I'd been there a while," he says, "it became pretty clear that I wasn't going to get to do much research, so I began looking around for a more research-oriented position. In the meantime, however, the federal government had passed the Animal Welfare Act, which required that any institution that maintained laboratory animals other than rats or mice had to have a licensed veterinarian on staff to assure proper care of the animals used

in research. As a result, LIU asked me to run their animal facility, and I agreed. While in college, I had worked not only in a zoo and in research laboratories during the summers, but also in the laboratory animal facilities at the National Institutes of Health."

This background later brought a call from the associate dean of the New York University Medical Center, which had received a grant contingent on the hiring of a full-time veterinarian to run its animal care program. Dr. Stark remembers thinking, "Lab animal experience is in my resume, yes, but that's not what I want to do. I'm an immunologist. I want to teach and do research.' But I went and talked to the dean and accepted the offer. At that point, their facility was in need of some good housekeeping, and I did enjoy the management aspects. I enjoyed the tinkering and making sure that things were working properly. Research would have been a nice plum but time constraints fast become obvious when you are the only professional on staff."

The call from The Rockefeller University came one evening in 1976. "Luckily I happened to be working late that night," Dr. Stark says. "I was told that The Rockefeller had a new animal research center and was asked if I would be interested in becoming its director and an associate professor at the University. I was pretty certain that at Rockefeller I wasn't going to be restricted to housekeeping."

FIRST OF ALL, GOOD CARE

Proper care and housing of research animals requires routines as rigorous as those of a hospital. The University's program is one of only four hundred, among two thousand such programs in the country, accredited by the American Association for Accreditation of Laboratory Animal Care. Proper care and housing also involves a good deal of specialized equipment and a fair sprinkling of ingenuity. For example, the aquatic *Xenopus* needs dechlorinated water kept at a constant temperature. Dr. Stark and LARC Manager H. Osborn Baggett studied the frog's biology and ecology and inspected aquatic environments at other facilities before designing what they think is the best such construction for the species.

Environmental concern is important both for the comfort of animals and consistency of research data. The entire LARC

building is ventilated by a central system that changes the air completely twelve to fifteen times an hour. Lighting is regulated to simulate an equal cycle of daylight and darkness, important for animals living indoors. "There is no daylight savings time here," Mr. Bagg notes.

To provide a barrier against infection or contamination, the building is divided into color-coded "clean" and "soiled" areas. Only the technicians who look after the animals have access to the clean areas, designated by blue floors and blue stripes on the walls and doors and on the stairways and elevators leading to the animal rooms. The areas through which soiled material and wastes are removed and treated are color-coded in gold. Because wax can harbor germs, the floors are covered with seamless urethane, which doesn't require polishing.

In his office, Ozzie Bagg has an impressive file of forms that are checked off and initialed daily by staff members assigned to various duties. "We have set schedules," he says, "for cleaning and changing cages, for food checks, water checks, sick animal checks, for changing room filters.... Everything is on a scheduled protocol."

Perhaps the most vital check occurs first thing in the morning before anything else is done. Every animal in the building is inspected and if the animal husbandry crew spots any animal that seems to have something wrong, they place a tag in its area. This alerts the veterinary services staff, who begin their rounds about nine, very similar to the rounds in a hospital. Health or environmental problems are corrected after discussions with the investigator or a resident veterinarian, or both.

Most members of the LARC's technical staff come from training programs in the New York area, but they must also go through extensive on-the-job training. "What we look for in prospective employees, Mr. Bagg says, "are people who have feeling and concern for animals. They may be changing cages all day, but they've got to have their minds and senses alert to pick up signs of trouble, like a piano tuner picking up notes that are off."

About a third of the LARC staff are certified as laboratory technicians by the American Association for Laboratory Animal Science. At this point, about half of them have at least an associate degree in veterinary technology or a bachelor's degree in laboratory animal science. The veterinary pathologist, Dr. Margaret Harbison, not only assists Dr. Stark and conducts

her own research program, but also acts as a consultant to faculty members on medical problems encountered with their research animals. Dr. Stark's staff provides such support involving laboratory animals as anesthesia, immunizations, specimen collection, breeding, and metabolic studies, services that are not available at most animal research facilities.

"The standards we maintain are in constant flux because laboratory animal science, like every other science, is growing," says Dr. Stark. "New information is added every day. The regulations we are governed by are also in flux. Just this year, the National Institutes of Health issued a new policy and new guidelines. Although this may seem like simply a creation of a bureaucracy or a response to public pressure, which to some extent it is, these constraints are by and large beneficial to research as well as to research animals. The vast majority of people believe that animal experimentation is necessary for medical progress, but they want it done humanely and not unnecessarily. I couldn't agree with them more."

ANIMALS FOR RESEARCH AND RESEARCH FOR ANIMALS

Enthusiastic as he is about the progress he and his staff have made in the environment they have provided for the animals at the LARC, Dr. Stark is quick to point out that the LARC is more than a service facility. Since he became director, he has launched and won support for research programs of his own—one of his major incentives for coming to The Rockefeller.

One program began in 1978 when the NIH awarded The Rockefeller a grant to establish a diagnostic laboratory and laboratory animal research program within the LARC. As Dr. Stark explains, "It's essential for an investigator to know that the animal he or she is working with is free of any disease that might compromise research results. Tests for most of the many endemic diseases of laboratory animals can't be performed in a typical human-oriented lab. We've developed virological tests, for instance, that are unique for rodent diseases. Even when it comes to hematology—blood studies—different species vary enormously in the size and appearance of cell types. It's crucial that this work be done by a technician with lab animal experience.

"The diagnostic lab we've established is certainly the best in the metropolitan area. In fact, eight other institutions in New



Dr. Stark with H. Osborn Bagg, left, manager of animal care services at The Rockefeller for 17 years, in a rodent holding room.



*From left, Drs. Charles Shopsis, Harvey Babich, and Ellen Borenfreund, of the *in vitro* research group at the LARC, who are developing test tube alternatives to the use of animals for testing toxic substances.*

LARC technical staff with Mr. Bagg, seated center, and Dr. Emmanuel Acheampong, manager of veterinary technical services, seated left.



York use it as a part of their husbandry and care programs.

"We are reducing the number of animals that have to be used experimentally by providing better animals with fewer variables in their disease status. This complements the tight control of variables built into the environment of the LARC building," Dr. Stark continues. "Beyond that, we're also learning more and more about animal diseases. In recent years, a great deal of work has been done in this field, here and at other institutions. In my office, there are six shelves of books about the diseases that affect animals used in research. Most of those books didn't exist ten years ago."

A second research program at LARC was launched in 1981 and bears the somewhat formidable title of Laboratory for In Vitro Toxicological Assay Development (in vitro means in glass). Many drugs and other products intended for use by human beings are first tested on animals. This is an essential step in evaluating safety and effectiveness, but it can have drawbacks with relation to scientific accuracy, cost, and, sometimes, humane considerations. Dr. Stark and his colleagues hope to lay the groundwork for effective alternatives to the use of live animals in product testing.

As he explains: "It's not only more humane to use in vitro tests whenever possible, it's usually more efficient. Tissue cultures grown in a flask can be better standardized, since they present fewer variables than live animal colonies and they provide more precise measurements. Culture procedures are far more economical, and they can also be applied to human tissue."

The focal point of the research has been to explore the possibility of a non-animal substitute for the Draize ocular irritancy test, which at present is the only federally approved method

for determining the toxicity of a substance to the human eye. The test, which employs rabbits because their eyes are suitable models for the human eye, is applied by manufacturers of ophthalmological drugs, household products, and cosmetics.

The investigators working with Dr. Stark on this project, which received initial and continuing support from Revlon, Inc., are Drs. Ellen Borenfreund, Charles Shopsis, and Harvey Babich. They are looking into such questions as how irritants affect the movement of substances across a cell membrane and how chemicals change the structure, viability, and growth rates of certain cells. They have developed four assays that they hope can eventually be used in place of the Draize test.

The assays were initially tested with pure substances, then on complex mixtures such as shampoos, cleaners, and drugs. In a process that will probably take another year or two, their in vitro data are being compared with data supplied by four other collaborators who have tested the same substances by the Draize method.

A MAN FOR ALL SPECIES

The debate over the use of live animals in research has reached a new peak in recent years with some extremist groups demanding a prohibition of all such experimentation. In a recent report, the Office of Technology Assessment, which advises Congress on scientific matters, stated that such a ban would "effectively arrest most basic biomedical and behavioral research and toxicological testing," with "dangerous" consequences for the nation's health. The report stressed the continuing importance to basic medical research of live animals for observing complex interactions of cells, tissues, and organs. But the rising costs of laboratory animals and the heightened public concern for their welfare are stimulating scientists to explore ways to reduce the numbers of animals used in experimentation.

"The trend nationally is toward fewer animals in research," Dr. Stark says. "At the LARC, we've reduced the number by forty-nine percent in recent years. But the likelihood of being able to eliminate animal experimentation completely is very slim. My job, and the responsibility of all of us using animals, is to be sure they're used sparingly and appropriately. Their health and well being is a matter of humanitarian concern and of good science." □

RESEARCH PROFILES is published four times a year by The Rockefeller University. It is written and edited by Fulvio Bardossi and Judith N. Schwartz. This is issue Number 24, Spring 1986. Inquiries should be addressed to the University's Public Information Office, 1230 York Avenue, New York 10021, or phone (212) 570-8967. Photographs, Ingbet Grüttner. Design by Angelica Design Group, Ltd. © The Rockefeller University. Printed in the United States of America.