

BIOLOGY

Animals Without Germs

Reliable techniques, inexpensive equipment and valuable findings are encouraging more and more scientists to use germ-free animals in research projects of every kind.

By JUDITH VIORST

► BEHIND the walls of a four-foot-long cylinder stand ten glass jars, each containing a pair of little white mice. There is nothing out of the ordinary in their appearance or behavior, but to the scientist they are very special indeed.

Unlike their brothers and sisters, who go about their mouse-like affairs in open-top cages, these rodents are living an unusual life—a life without germs.

Until fairly recently, relatively few scientists took germ-free animals seriously. Since 1955, however, there has been a dramatic display of interest in these unique creatures, whose bodies contain no bacteria, yeasts, fungi, protozoa or parasites.

Today some 52 institutions in the United States work with germ-free animals. These include Government installations like Walter Reed Hospital in Washington, D. C., and the National Institutes of Health in Bethesda, Md.; several universities; private research institutes, chiefly the Germfree Life Research Center in Tampa, Fla.; and commercial animal breeders. Outside this country, germ-free research is being carried on in Sweden, France, England, Argentina and Japan.

What changed the "show me" attitude of many scientists to an enthusiastic endorsement of the value of germ-free animals in research? And what new developments in the field will make possible a far greater acceptance in the future?

Pasteur Tried Germ-Free Tests

Back in the nineteenth century a few researchers, including Louis Pasteur, tried some experiments with germ-free chickens. They attempted to deal with the tremendously difficult task of, first, obtaining a living germ-free creature, and, second, maintaining it in an environment whose air, food, bedding and other necessities were free of germs. In large measure they failed.

In the late 1920's these problems were tackled again, with Dr. James Reyniers, founder of Notre Dame's Lobund Institute, leading the way. Systems and techniques devised and tested over the years achieved a high level of development. For all practical purposes, the technical problems were solved by the end of the late 1940's.

Scientists who rejected germ-free research animals because they could not be sure that they were or would remain without germs were presented with isolators capable of maintaining sterile living conditions, and reliable methods of acquiring germ-free animals.

The typical isolator is a steel and glass cylindrical tank four feet long and 30 inches

in diameter, equipped with an air-filter and air-exhaust system. An autoclave located at one side receives, through an outer door, food, water and all other materials needed to maintain life inside the cylinder. These materials are steam-sterilized in the autoclave and then passed into the cylinder through the autoclave's inner door.

The scientist can sterilely manipulate materials and animals by placing his hands through rubber gloves leading into the cylinder. The gloves are the weakest link in this sealed system, but they are checked regularly for any worn areas that might allow the contaminated outside world to penetrate the germless world inside the cylinder.

Obtaining Germ-Free Animals

The germ-free animals, contained in jars standing within the isolator, are acquired in one of three ways: cesarean section, egg sterilization or germ-free mating.

In a cesarean delivery, an operating unit with sterile and unsterile chambers is used. The pregnant animal lies on her back inside the unsterile chamber, her abdomen pressed against a plastic window that leads into the sterile chamber. An electric cautery cuts through the plastic into the abdominal cavity, which is germ-free. The plastic seals itself to the abdomen.

Scientists, working through the rubber gloves, help deliver the baby animal into the sterile chamber. Nowhere in this procedure does the newborn come into contact with germs.

A germ-free oviparous animal is more easily obtained. The outside of the shell is sterilized and the egg is then incubated and hatched inside the isolator.

Germ-free animals can be born of germ-free parents inside a sterile unit. The best breeders are random bred (unrelated) white mice.

Easy to Maintain

Many scientists began using germ-free animals when they realized how easy it actually was to acquire and maintain them. Others, however, still balked because of the high cost of the isolator. The steel and glass model has a price tag of \$5,000.

Recently a plastic version of the isolator has been developed, and it can now be purchased for as little as \$250. There are, inevitably, certain disadvantages.

A separate autoclave is required for sterilization, because plastic cannot take the high heat. Also needed is a separate chamber, into which materials are placed for steam sterilization in the autoclave. When the materials are brought into the isolator, the pathway between isolator and autoclave receives a cold chemical sterilization to prevent contamination.

But one autoclave and one chamber can be used for several of these plastic units, which are cheap enough for even the tight-



National Institutes of Health

INSIDE THE ISOLATOR—Working with rubber gloves, a scientist injects a germ-free mouse inside a sterile isolator.

est budget. Dr. Carl E. Miller, head of a germ-free animal production group at National Institutes of Health, believes these units will prove a spur to increased use of germ-free animals.

Techniques and costs aside, scientists are growing increasingly impressed with the variety of studies in which germ-free animals can be used advantageously. Says Dr. Walter Newton, chief of the laboratory of germ-free animal research, National Institute of Allergy and Infectious Diseases, NIH:

"Whenever animals are used in research where microorganisms may be a variable, germ-free animals will be invaluable."

Such research areas include cancer, nutrition, dentistry, infectious diseases, and fundamental immunology. Important findings are coming from germ-free work in these and other fields.

Germ-free animals were used at Lobund Institute to examine certain hypotheses relating to the causes of cancer. It was found that animals without germs can develop cancers readily. One conclusion from this work is that production of a widely applicable cancer vaccine seems unlikely.

Dental Experiment

In a dental experiment a few years ago, germ-free rats fed a caries-producing diet were found to develop no caries. The control rats had holes in their teeth after eating the same food over the same period of time. The experiment indicates that bacteria are necessary to make a bad diet damaging to the teeth.

In many other cases bacteria have been shown to have an intimate and essential relationship with disease causers.

The protozoan producing amoebic dysentery fails to evoke the full symptoms of the disease in germ-free animals. But when one species of bacteria, along with the protozoan, is injected into the animal, the disease flourishes.

The early development of certain worm parasites may also be fostered by bacteria. And scientists are studying the relationship between the increase of certain kinds of fungus infection and the use of certain antibiotics. The theory: "Good" bacteria, knocked out with the "bad," may serve to keep specific fungus growths in check.

A project recently completed by the National Institute of Arthritis and Metabolic Diseases, NIH, has provided some interesting information on the relationship between bacteria and nutrition.

It has long been suspected that rats can obtain a supply of folic acid (a B vitamin) without receiving it from the outside. The assumption has been that bacteria in the rat's intestinal tract manufacture this vitamin. However, this assumption was never tested until a few years ago.

Experiments with germ-free rats showed that the absence of bacteria resulted in the development of a folic deficiency. When the rats were infected with a specific strain of bacteria, however, the folic acid was supplied.

When sulfa drug was given to conventional rats, it suppressed the bacteria producers of folic acid. This drug, taken in

large quantities, might also cut down or destroy the vitamin B supply in human beings. Therefore, some scientists suggest, it might be found necessary to balance large intakes of sulfa with sufficient dosages of vitamin B.

In science there are endless avenues to be explored. It is expected that germ-free animals will play an ever larger role in increasing fundamental knowledge.

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GENETICS

Hereditary Disease In Three Generations

► THIRTEEN persons in three generations of one family have been found to have a rare hereditary disorder called Lindau's disease.

The disease is characterized by tumors and cysts of the eyes, brain and other organs. If diagnosed soon enough, the investigators believe it can be treated successfully.

Dr. Jack Goodman, chief resident in neurosurgery at Albany Medical Center Hospital, New York, uncovered one of the largest series of family-linked cases of Lindau's disease in medical history.

He was assisted in his genealogical research by Dr. Fremont C. Peck Jr. of Albany Medical College and Emil J. Kleinholz, a medical student at the college.

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PHYSICS

Bricks Without Mortar For Future Buildings

► SOME DAY a ray of light, a laser beam, could be used to make brick buildings stand without mortar. It would be used to fuse bricks together to form a single solid wall, Dr. Isay Balinkin, University of Cincinnati physicist and ceramics expert, suggests.

The laser, a narrow ray of light several thousand times brighter than the sun, can weld many ceramic materials considered non-fusible.

The new "lasing" method of bonding would be practical in erecting buildings of brick or stone if time is short, as in military installations. Locally available materials could be used. Mortar hardens slowly but welding with the laser ray can be done in seconds.

Dr. Balinkin suggests that ceramic surfaces can be decorated by using the laser as a knife to cut and mold the ceramic material.

The heart of a laser is a pink ruby rod of a synthetic crystal of corundum (aluminum oxide, an important ingredient of common clay) doped with chromium. An optical resonator forces the atoms to radiate in phase, resulting in a very narrow, intense beam of coherent light.

The laser can also be used to help analyze defects. A microscopically small foreign spot on a glazed ceramic tile would be vaporized by the needle-sharp laser ray and the resulting luminous vapor streak analyzed by a spectroscope to show the contaminant.

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PUBLIC SAFETY

Summer Slaughter Is On; Accidents High in July

► AS THE FOURTH OF JULY weekend showed, the "good old summertime" abounds with accidents of every kind. More persons lose their lives from accidents during the months of June, July and August than in any other season.

Traffic accidents, the all-time champion killer, get an assist from drownings, accidental falls and electrocutions during this period, and the overall accident fatality rate in the U.S. rises to 270 a day. Drownings alone account for 10 each day, while falls take another 50 or 60, the Metropolitan Life Insurance Company, New York, reports.

Lightning also strikes more often during the summer, with 100 to 200 each year being struck fatally. Deaths from man-made electricity are twice as frequent in the hot months as during the rest of the year.

With virtually every type of accident at its peak, particularly those associated with outdoor sports, summer is a good time to be extra careful in whatever you do.

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PHYSICS

Heart of Atom Chamber Seen With Endoscope

► A DEVICE to enable a viewer to peer into the heart of an atomic reactor while remaining at a safe distance has been developed.

Called an endoscope, it is used for making detailed examinations of the inaccessible and highly radioactive reactor's interior and is capable of detecting a pipeline crack as small as a thousandth of an inch at distances up to 17 feet. Other features include high maneuverability and a constant-magnification focusing system. The instrument can also be used with a Polaroid camera to obtain pictures.

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SOCIOLOGY

Population Problems Hit With New Grants

► HITTING the population problem from all sides, the Ford Foundation awarded \$7.5 million for research, training and experimental programs.

The grants have been made to organizations within the U.S., committed as a nation to giving birth control information to countries that request it; to India, where the problems of overpopulation are outstanding; and to Tunisia in an attempt to control population for the sake of economic growth.

Grants to the U.S. are mainly for research by private agencies, laboratories and universities. Scientists will be studying both the physical and social aspects of birth control and stepping up information output.

Actual family planning programs are being supported in India and Tunisia. Training abroad and home-based research programs are to add to the project work.

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