



Chapter One

The Architectonics of Laboratory Animal Science

Nathan R. Brewer, DVM, PhD

Background History

With the development of civilization, trade acted to separate a wealthy class of individuals from others—a class of individuals who had time to think (1). By 500 B.C. in Greece, a major trading center, members of this class known as philosophers (lovers of knowledge) liberated themselves from the bonds of religion and magic and instituted a “systematic method of argument” based on observations. One of these men, Aristotle (384–322 B.C.), received many animals from his pupil Alexander the Great, who also had animal collections with his armies. Aristotle described 540 species of animals in his *Historia Animalium* (2). The seeds of an endeavor to classify animals were planted in that work.

Another of these philosophers, Erasistratus (304–258 B.C.), carried out studies on animal structures (3). He was the first to show that the mitral and tricuspid valves permitted only one way blood flow.

After Erasistratus a period of wars, pestilence, and famine sapped vitality and creativity. Not until the time of Galen (131–201 A.D.) were the works of the Greek philosophers revived and investigative activities continued. Galen introduced a new dimension of study—vivisection (4). He studied many species and justified experimentation as a path to the truth, although he made many teleological explanations from his studies on dead animals. His influence on biology was profound for 13

centuries.

With the death of Galen, there was a rise in antisecularism that ushered in the dark ages. An occasional free spirit like Roger Bacon (1214–1294), imprisoned because of his secular ideas, was repressed (5). Michael Servetus (1511–1553), the first to describe the circulation of the lungs, studied several animal species, but much of his recorded work was burned with him by religious fanatics (6).

Most of the studies up to the time of William Harvey (1578–1626) lacked precision. Harvey, influenced by Galileo Galilei (1564–1642) who developed the quantitative method to a high degree—gave irrefutable evidence for the circulation of the blood, probably the greatest discovery in the history of physiology (7). He studied many live animals.

Over the next century, Claude Bernard (1813–1878), probably the greatest physiologist of all time, used many animals in his investigations. He was a man of incredible industry. He wrote 18 volumes of lectures. The brilliance of his contributions magnify the importance of his output. He was the first to emphasize the concept that the comparative approach in physiology—the use of various animal species—is the most fruitful: “...the solution of a physiologic or pathologic problem often depends solely on the appropriate choice of the animal...” (8).

With the development of anesthesia in the middle of the 19th century and the increased toleration of the thirst for knowledge, an increase in the use of animals in biomedical research evolved. The increase in the use of animals in the laboratory gave rise to a new vocation, workers who took care of laboratory animals—in Germany they were called *dieners*. Some *dieners* knew more about the animals and their required care than did the researchers for whom they worked. Fortunate was the researcher who had a good *diener* work with him. Paul Ehrlich (1854–1915) had several of these valuable *dieners* at the royal Prussian Institute for Experimental Therapy, where they maintained closed colonies of rodents that were free from disease, or at least in balance with their zoonotic organisms. By 1915 they had developed “pure” strains of mice and guinea pigs (9).

Before 1945 the care of animals in most institutions was the responsibility of those using the animals for their investigations, with an attitude of toleration by administrations. Some investigators, like Benedict Stilling (1810–1879), kept animals and did research in their own homes at their own expense (10). Leo Loeb, chairman of the Department of Physiology at the University of Chicago at the turn of the century also kept animals and did research at his own home at his own expense (11). I visited the home of one investigator who had kept mice in her home since the turn of the century. The home was inhabited by the investigator, a technician, and thousands of mice. From this residence came the first strains of cancer resistant and cancer susceptible mice. It was common to have students raise and care for animals at their residences, often to have months of work nullified by some epizootic, or by an unsympathetic landlord.

The first universities to have laboratory animal colonies in this country (ca. 1880) were Harvard and Johns Hopkins (12). The first institution to have a veterinarian manage laboratory animal facilities in this country was the Mayo Clinic in Rochester, Minn. The first veterinarian to manage a laboratory animal facility was Simon D. Brimhall, VMD, employed by the Mayo Clinic in 1915. Dr. Brimhall retired in 1922, and was succeeded by J. G. Hardenbergh, VMD (1892–1963), who became a clinical investigator, as well as an animal facility manager (13). In 1927

Left page: Four of the five “founding fathers” of AALAS (from left) Dr. Nathan R. Brewer, Dr. Elihu Bond, Dr. Robert J. Flynn, and Dr. Bennett J. Cohen. Not pictured: Dr. Robert J. Schroeder.

Dr. Hardenbergh retired and was replaced by Carl F. Schlotthauer, DVM (1893–1959).

The first to demonstrate physiological principles to students by the use of animals in this country was John Call Dalton (1825–1889). [Not to be confused with John Dalton (1766–1844) of molecular weight fame.] Dr. Dalton had studied for a year in Paris under Claude Bernard, and taught at the College of Physicians and Surgeons in New York City (14).

Influential Individuals

"It is not given to any one man, however endowed, to rise spontaneously into intellectual splendor without the parentage of antecedent thought." John Tyndall

Dr. Karl Friedrich Meyer, DVM, PhD (1889–1974) had seven honorary degrees including three honorary MD degrees (15). He was a member of the National Academy of Sciences; the American Academy of Arts and Letters; and other biomedical societies in microbiology, pathology, and public health. He authored hundreds of articles—including the first article in English on all of the known diseases of laboratory animals (16). He received many awards, including the coveted Griffin Award from the American Association for Laboratory Animal Science (AALAS). He developed an excellent facility for the housing and care of laboratory animals at the Hooper Foundation for Medical Research at the University of California at San Francisco, where he was a professor in tropical medicine. I was privileged to be shown through his animal facilities in the early 1940s, while I was in practice in California.



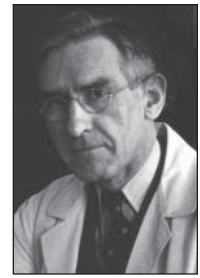
W. T. S. Thorp

Dr. William Taylor Steele Thorp (1914–1984) received his DVM degree in 1935 and Masters degree in pathology in 1937, both from Michigan State University (15). In 1938 he went to Pennsylvania State University where he became a professor in pathology. At the University, he developed a research facility to carry on his work. In 1947 he accepted the position of Chief of the Section of Comparative Pathology and Chief of the Research Services at the National Institutes of Health, where he developed the Laboratory Aids Branch (now the Veterinary Resources Branch) of NIH—the forerunner of improved animal facilities in institutions throughout the USA.

In 1960 Dr. Thorp received the Distinguished Alumni Award from Michigan State University's, College of Veterinary Medicine and the Pfizer Award. In 1965 he received the Griffin Award from AALAS. In 1967 he was the recipient of the Distinguished Service Award of the Minnesota Veterinary Medical Association and the Gold Cane Award of the Conference of Public Health Veterinarians. In 1973 the Public Service Award was presented to him by the AVMA.

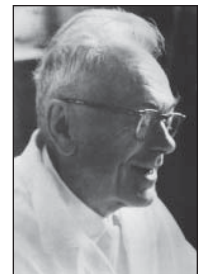
Dr. Thorp and I were at Michigan State at the same time, and he knew of my bout with brucellosis, and of my interest in laboratory animals. Dr. Thorp was one of those researchers who appreciated the exhibits I presented at AVMA meetings, and suggested to officials at the AVMA that I succeed him as chairman of the AVMA Committee on Laboratory Animals. Whenever he came to Chicago to participate in AVMA activities, the local laboratory animal veterinarians would meet with him to discuss problems inherent in the management of laboratory animal facilities.

Dr. Charles A. Griffin, DVM (1889–1955), was a bacteriologist at the New York State Board of Health Laboratories in Albany from 1919 to 1954. He was a pioneer in the concept of a disease-free animal colony before gnotobiotechnology had evolved (15). In the 1940s he utilized progeny testing to establish a rabbit colony free of pasteurellosis. Showing that *Salmonella* spp. was being transmitted from meat meal (17), he was instrumental in getting feed manufacturers to guard against contamination of feed during processing activities. The AALAS' Charles A. Griffin Award was established in his honor, and he was the first recipient of this prestigious award, which was awarded posthumously in 1955. His visits at AVMA exhibits beginning in 1946, were instructive and encouraging.



Charles A. Griffin

Dr. D. Blair Meyer (1905–) earned his DVM in 1927 and his MS in 1933, both from Michigan State. His graduate work was with *Brucella abortus* infection in cattle. He knew of my bout with brucellosis. I had been working on the pharmacodynamic action of fractions of *B. melitensis* when the "bug" hit me in 1936. While working at Michigan's Department of Public Health, Dr. Meyer developed premier regulations to insure the proper care of laboratory animals under Michigan Public Act 241. He was a member of the Animal Care Panel's first committee on standards of laboratory animal care chaired by Dr. Robert J. Flynn.



Heinrick Kluver

Dr. Heinrick Kluver (1897–1979) received his PhD from Stanford in 1924. He earned many honorary degrees, including an honorary MD from Basel in 1965. He joined the staff of the University of Chicago in 1926, where he became a professor in 1938 and an emeritus Sewell L. Avery Distinguished Service Professor in psychology in 1963 (15). He won many awards and was a member of the National Academy of Sciences. He published many behavioral studies on monkeys, and he took care of his own colony of nonhuman primates on the top floor of the anatomy building. The primates would rest on his shoulders as he cleaned their cages. He probably knew more about the care and handling of primates than anyone during his lifetime. As he lived near me, we would walk to the university together and discuss matters. I did most of the listening.



Sewall Wright

Dr. Sewall Wright (1889–1988) received his ScD from Harvard in 1915. He received nine honorary degrees. He joined the University of Chicago in 1926. In 1938 he became the Ernest D. Barton Distinguished Service Professor, and in 1955 was named an emeritus professor. He won many awards, including the Elliot Medal from the National Academy of Sciences (1947). Among his society memberships were the National Academy of Sciences and the American Academy of Arts and Letters. His research involved genetics of the guinea pig and he had a large colony of guinea pigs, housed in a facility that he had designed just for his work. He was probably the outstanding scholar in the biology of the guinea pig and he supervised their care (15). As he approached retirement age, he spent his last years of active

research at the University of Wisconsin at Madison, retiring in 1960. He remained an active member of the scientific community until his death. The Sewall Wright Institute of Quantitative Biology and Evolution was developed in his honor.

Dr. Paul Alfred Weiss (1898–1989) taught zoology at the University of Chicago from 1933 to 1954, where he was involved in many new areas in embryology and neural organization. The precision and breadth of his thought and elegance of his experimental design had a major influence on the development in these fields. He was elected to the National Academy of Sciences in 1947 and to the American Academy of Arts and Sciences in 1954. In 1979 President Jimmy Carter awarded him the National Medal of Science. Dr. Weiss approached me about starting an important committee under the auspices of the National Academy of Sciences—a committee that would function to obtain information on sources of supply of laboratory animals. This committee would become the Institute of Animal Resources. The name was changed to the Institute for Laboratory Animal Research



Paul Alfred Weiss



Anton J. Carlson

(ILAR). I was on the first Board of Directors and, as chairman of the committee on diseases prepared the first publication issued from the ILAR.

Dr. Anton Julius Carlson (1875–1956) received his PhD from Stanford in 1903. He joined the staff of the University of Chicago in 1904. In 1940 he reached retirement age at the university and became the Frank R. Hixon Distinguished Service Professor Emeritus. Among his many honorary degrees was an MD from the American Medical Association. He spoke many languages and preferred to read books in their original language, including Latin, Greek, and Chinese. He authored several books and more than 200 original research reports. He was a member of many societies including the National Academy of Sciences. It was his influence that brought me to the University of Chicago in 1945.

Dr. Benjamin DeWitt Fremming (1924–) received his DVM from Colorado State University and his MPH from the Uni-



B. D. Fremming

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It was further suggested that a list of publications dealing with the management of animal quarters be circulated with this first letter. An incomplete, minimum list is enclosed, which will be expanded from time to time.

The ever present problem of countering the attacks of anti-vivisectionist groups in Chicago and elsewhere also was discussed. It was proposed that one of the first official acts of the new organization should be to join the National Society for Medical Research. The importance of fighting anti-vivisectionists actively and aggressively was stressed.

If you agree that a need for an organization of those actively engaged in animal care work exists, a response to this letter would be appreciated. Suggestions as to the form the organization should take will be welcomed. Information sent to us relative to the care and management of research animals will be published in the monthly information bulletin. For the time being, please direct all replies to:

Bennett J. Cohen, D.V.M.
Supervisor, Animal House
Northwestern University Medical School
303 E. Chicago Avenue
Chicago 11, Illinois

We trust that our proposal to establish a formal organization will meet with general approval.

Very truly yours,

Elihu Bond, D.V.M.
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Chicago 12, Illinois

N. R. Brewer, Ph. D., D.V.M.
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William F. Schroeder, D.V.M.
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Bennett J. Cohen, D.V.M.
Northwestern University

NORTHWESTERN UNIVERSITY
CHICAGO 11, ILLINOIS

May 12, 1950

THE MEDICAL SCHOOL
515 WEST MICHIGAN BUILDING
303 E. CHICAGO AVE.

Dear Sir:-

The many common problems facing the supervisors of research animal quarters in some of the medical schools and research institutions in the Chicago area have prompted the individuals concerned to form an organization whose purpose is directed toward the solution of those problems. The purpose of this letter is to sound out opinion in other parts of the country concerning the feasibility of placing the organization on a national footing.

Until this association develops a more formal structure, it was considered expedient not to plan meetings on a national scale. Rather, it would seem more appropriate to have local groups meet, exchange ideas, and circulate those ideas to individuals throughout the country who have indicated they would like to receive such information. Inter-group meetings might be held at such times as to coincide with the meetings of the Federated Societies for Experimental Biology in the Spring, the meetings of the American Veterinary Medical Association in the Summer or with other comparable groups. Temporarily at least, no dues would be levied.

At the April meeting of the Chicago group, the following suggestions were made:

1. Membership in the organization should be open to all individuals interested in animal care work on an institutional scale.
2. A free exchange of ideas and criticisms should be encouraged among individuals directly and indirectly concerned with the management of animal quarters.
3. An attempt should be made to review and appraise published work affecting the management of animal quarters.
4. The name of the organization should be decided on at some time in the future when more individuals concerned will have had an opportunity to make suggestions.

There was considerable discussion about cage equipment for animals, especially monkey cages. Blueprints are available for several types of cages now in use in the Chicago area.

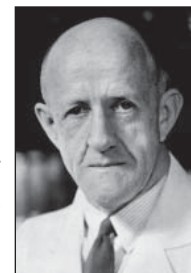
Panleucopenia in cats, and the distemper complex of diseases in dogs also were discussed. It seems that no two laboratories represented manage the diseases in the same way.

Letter sent in May 1950 to all persons in the United States and Canada know to have professional interest in care of laboratory animals.

that earned him an award from the Central Association of Obstetrics and Gynecologists.

Laboratory Animal Care in 1945

In most institutions before 1945, the quality of care given the animals varied widely. At one time, there were 42 different colonies of laboratory animals at the University of Chicago. Some, like the colony of mice run by the Department of Pediatrics originally managed by a student in the university, George Collins, were under excellent care. Dr. Huggins, a Nobel Prize recipient, had an excellently run colony of dogs and rats,



Dwight Ingle

versity of California in 1952. He became a diplomate of the American Board of Public Health in 1954, of American College of Laboratory Animal Medicine (ACLAM) in 1957, and of the American College of Veterinary Pharmacology and Therapeutics in 1978. From 1954 to 1958 he was executive board member and chairman of the Committee on Nonhuman Primates of the ILAR. He was president of ACLAM in 1960, 1961, and 1962. He was the author and co-author of a number of original scientific papers including one in 1972

taken care of by an animal care man who he trained to be a very fine worker that the animals “loved.” Dr. Sewall Wright’s guinea pig colony was exemplary. There was a colony of wolves that were so well-treated they were like puppies with the men who handled them. Dr. Dwight Ingle, who may have known more about rats than anyone in his lifetime, was responsible for his well-kept colony of rats. Although there were many fine colonies of laboratory animals in all of the institutions, there were also many problems.

Problems existed in animal procurement. There were dealers who arranged for children to raise rabbits or guinea pigs in their basements or garages, thus underbidding legitimate breeders. This method exposed animals to cross-contamination and disease. The lack of consistency in the quality of animals required an increase in the numbers of animals used to answer a specific question. This problem ceased by convincing purchasing departments that only approved dealers should be considered as legitimate sources.

Problems existed in the feed provided for the animals. Surplus food from kitchens was often given, and its quality was poorly regulated. Commercial feed for animals was often contaminated with *Salmonella*. We owe credit to Dr. Griffin of the New York State Board of Health Laboratories for his activity in getting most commercial feed manufacturers to guard against gross contamination of feed prepared for animals.

Problems in transportation also existed. The overheating of animals in airplanes and trucks was not uncommon. As I was the only biologist on the Transportation Committee of the American Humane Association (AHA), I drafted the first regulation promoted by the AHA on the transport of animals.

Space for animal housing was relegated to basements, former horse barns, or other spaces unfit for offices or laboratories. Some of the home-built cages of wood or wire were difficult to sanitize and not always escape-proof. Temperature control was a serious problem. Colonies of rodents were often decimated by overheating. The use of unsanitized bedding, usually sawdust, was common. Cockroach infestation was so common that it was considered by some as a condition to be tolerated. Air ducts were often plugged with animal hair, and thermostats were frequently inoperative.

While working for my PhD in physiology in the early 1930s, I was approached by Dr. A. J. Carlson and Dr. A. B. Luckhardt with the challenge of managing the laboratory animal facilities. The concept of a veterinarian with a grounding in the scientific method, dedicated to improving conditions under which animals were kept was recognized as a needed step-one that would improve public confidence in the care given animals in research. I recognized the opportunity as a wide open field, but some of the finest of investigators were fearful of someone telling them how to manage their animals and how to do research, so I was not hired at the University of Chicago until 1945.

Starting in 1946, when Dr. A.R. Roseberg was in charge of the facilities at Northwestern University, and Dr. Robert Litt joined the staff at the University of Illinois Medical School, we would meet about once a month to discuss various problems. We would hold special meetings when Dr. Carl Schlotthauer of the Mayo Foundation or Dr. W.T.S. Thorp of the National Institutes of Health visited the city. We also initiated a series of lectures which animal caretakers, technicians, and graduate students were encouraged to attend, the first being at the University of Illinois Medical School in 1946. Many of the attendees came from Loyola Medical School and the Chicago Medical School.

The large number of people in attendance was strong evidence that the field of laboratory animal care was open for improvement. The lectures were designed to impress those working with animals of the importance of their work—each was part of a team contributing to the health of the nation.

We developed exhibits featuring laboratory animal care and use for national meetings of biomedical societies. The first exhibit, presented at the AVMA meeting in Boston in 1946, featured problems related to the care of dogs preceding and following gastrointestinal surgery. It was so well received that Dr. Litt and I prepared an exhibit on bronchoscopy at the 1947 meeting of the AVMA in Cincinnati. The exhibits, highlighting the care of laboratory animals, continued for a number of years. Most important, were communications and relationships that developed at the exhibits with Dr. Charles Griffin of the New York State Board of Health Laboratories; Dr. Mark Morris, then a practitioner in New Jersey; Dr. W.T.S. Thorp of the National Institutes of Health; Dr. Ben Fremming, then at the University of Texas and a former pupil of Dr. K.F. Meyer of San Francisco; and Gen. Wayne Kester. The encouragement received at these exhibits proved to be a major factor in the decision of several individuals to sponsor a national meeting for participants interested in the care and use of laboratory animals.

It was recognized that there were large areas in laboratory animal management and diseases where no information was available. The information which was available was widely scattered, suggesting collocating the information. Of particular interest were the animal diseases and the morphophysiological differences among animals. The more we know about an animal and its biological differences from other species or strains, the more optimal care could be provided, and the more judicious the choice of which animal should be utilized to answer a specific question.

In 1948, Dr. Elihu Bond succeeded Dr. Litt at the University of Illinois and, in 1949, Dr. B.J. Cohen was in charge of the animal facilities at Northwestern University. Dr. R.J. Flynn was appointed at the Argonne National Laboratory, and Dr. W.F. Schroeder joined the staff at the Hektoen Institute. The great personal drive of these individuals—and their appreciation of the need for information and improvement in this field cannot be overstressed. At a meeting in April, 1950, we agreed to send a letter to potentially interested individuals in the United States and Canada to schedule a forum to be held on laboratory animal care.

Dr. B.J. Cohen, secretary of our group, mailed the letters signed by the five veterinarians, from his office on May 12, 1950. The response was encouraging and the date of the forum was set at November 28, 1950, and was held at the University of Chicago. The proceedings of the forum were assembled with the aid of Dr. Bond, typed by Myrtle Junker, my secretary, and distributed by Dr. Cohen. Details of this meeting are meticulously reported in a paper by Dr. R.J. Flynn (18).

Following the forum, we had dinner at the Quadrangle Club at the University of Chicago, where it was decided that the forum should be repeated the following year at Northwestern University. The group also decided that the name of the organization would be called the Animal Care Panel. The organization was to be open to anyone interested in the care and use of laboratory animals, to facilitate the accumulation of information, and to lead to the improvement of such care and use. The group recognized a moral obligation to grant those animals we use for our benefit every practical consideration

for their comfort and well being. I was voted chairman; Dr. Slanetz of Columbia University was vice-chairman; and Dr. B.J. Cohen as secretary. The Animal Care Panel, the progenitor of the American Association for Laboratory Animal Science (AALAS) was born. Today, AALAS is recognized as the leader in the field involving laboratory animals. AALAS has performed its *raison d'être*.

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