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Preface

The Institute of Laboratory Animal Resources (ILAR) was founded in 1952 within the Division of Biology and Agriculture. It serves as a coordinating agency to disseminate information, survey existing and required resources, establish standards, promote education, hold conferences, and generally to upgrade laboratory animal resources.

In the winter and spring of 1970 the Executive Committee and Advisory Council of ILAR discussed the impact of present fiscal restraints on medical research and on the future of laboratory animal resource and research programs. This conference resulted from these discussions. The problems involved are considered from the perspective of federal and private granting agencies, institutional administrators, animal resource program directors, and animal users. Together, the papers provide a basis for critical reappraisal of priorities for this program to facilitate wise use of limited funds in the national interest.

Bennett J. Cohen

The Future of Laboratory Animal Research and Resource Programs

A. C. Upton and S. H. Weisbroth

BACKGROUND AND NEED FOR APPRAISAL

This conference comes during a period of national reappraisal, when many of our established norms are being scrutinized in the light of new priority imperatives. The changing directions imposed on science and medicine may be expected inevitably to affect the development and utilization of laboratory animal resources. Hence, it is logical at this time to consider the future of laboratory animal resource and research programs.

The sweeping reassessments now in progress throughout the country have come in response to demands and difficulties in many quarters. Groups as disparate as the Puerto Rican Young Lords and organized labor have voiced dissatisfaction with the availability and quality of medical care. The poor continue to suffer seriously from dental neglect, malnutrition, lack of assistance in family planning, and inability to secure psychological counseling, physical rehabilitation, cosmetic or elective surgery, and many other health services. Even for the middle class, financial catastrophe may be the grim consequence of prolonged illness. There is a growing consensus that this situation can no longer be tolerated in the United States.

These concerns are dramatically manifest in the attitudes of students, who are deeply troubled about the purposes and quality of our way of life. For many of them, the pursuit of knowledge can no longer be justified in the face of our recurrent failure to use technology wisely. They are deeply concerned about the deteriorating prospects for tomorrow they see reflected in our ravaged environment. They hold our priorities to be askew when we devote millions of dollars and the energies of many health workers to a single heart operation, while at the same time we allow children to become mentally and physically defective through malnutrition. They also ask how we can justify spending billions of dollars a year to put a man on the moon when there are children among us who don't go to school because they lack shoes and clothing. As a result of student concern, certain kinds of research have al-

ready been made unacceptable on a number of university campuses; e.g., activities supported by the CIA and by the Department of Defense, many of which have included substantial laboratory animal programs. Because scientists have generally supported such activities, they have come to be viewed increasingly by students as amoral and unconcerned about the social significance of their work. As a result, we may expect that further efforts will be mounted to exert social control over what scientists do.

In the face of these pressures for social reform, it may be asked whether laboratory animal programs can compete successfully for resources. Since it is only proper that the support of any program be commensurate with its relative importance, it behooves us to examine the need for laboratory animal programs in the light of future as well as existing requirements.

FUTURE OUTLOOK FOR ANIMAL RESEARCH

Viewed in historical perspective, the use of laboratory animals in research has never been more important or promising. The crucial position it enjoys today in many fields (e.g., science, medicine, industry, and agriculture) results from the culmination of centuries of inquiry, which has only recently established the kinship of all living creatures. This kinship, which was postulated by the theory of evolution, has since been verified by recognition of the unbroken continuity of life in DNA. Awareness of this relationship has transformed man's attitude toward other species, in that he no longer regards plants and animals as alien creatures. On the contrary, he now conceives of them as kindred organisms, dependent on the integrity of the same overall ecosystem and prone to similar diseases and disabilities. Laboratory animals have thus taken on enormous importance as models for elucidating and predicting behavior, health, and disease. In a larger sense, research on animals has become an essential part of man's age-old quest to understand himself, his origin, and his relation to the cosmos.

In wrestling with many of the biomedical and social problems we face today we must turn increasingly to animal models, and we must reach beyond the currently recognized investigative approaches. This is particularly true of our ecological difficulties, which stem from the growing conflict between our expanding industrialized population and our finite and dwindling natural resources. This problem and its ramifications are unprecedented in their urgency and complexity. Their solution will call for vastly expanded study of animal models in the laboratory as well as of ecological interactions throughout the biosphere. Some of the dimensions of this problem, along with other timely questions calling for expanded laboratory animal research, are set forth briefly in the following:

Population Control and Overpopulation Hazards

The single most urgent crisis confronting man today, and one that may decide the survival of the human species, is the population problem. It overshadows all other issues and compounds them in many instances. If this problem cannot be solved, the others will soon become merely academic.

The present concepts and techniques of population control are far from satisfactory; they have, in general, met with failure on a global basis. Improvements in contraceptive technology will clearly require sophisticated studies in carefully selected animal species before optimal approaches are perfected for human use. Certain animal behavior studies have already shown promise in predicting the human behavioral adjustments to be expected in an ecological niche of constantly increasing population density. They may be expected to be used increasingly in studies seeking an understanding of population dynamics.

Environment

Related to the problem of the population explosion, but also stemming in no small part from the technological revolution, is the accelerating deterioration of the environment. The exploitation of technology is necessary for survival of the vast numbers of people who inhabit the earth. Hence, we can no longer return to the simple life. Instead, we must strike a balance between technology and conservation. This will require enormous intensification of research on ecology and on the adverse reaction of living organisms to perturbations in their environment. Of particular importance are insidious and delayed effects on higher organisms, such as the induction of cancer, mutations, degenerative changes, teratologic abnormalities, and behavioral disorders, which may not manifest themselves until months or years following exposure, when damage to the entire population may have become irreparable. This problem is staggering in scope and can only be attacked by systematic and comprehensive studies on many diverse populations in the wild as well as on widely selected laboratory animals.

One promising direction may be the development of sentinel species with low thresholds to adverse effects of pollutants, e.g., the coal miner's canary. An unfortunate example is the peregrine hawk, which we have unwittingly exterminated by DDT, this species acting as the final biological accumulator of the insecticide in its food chain. The destruction of these and other birds has played an important role in prompting legislated control over the use of DDT and related insecticides.

Insecticides and Pesticides

As exemplified in the foregoing, we now recognize that, in the development of methods for controlling agricultural insects and other pests, each new solution may generate in turn a new ecological problem. This entire question is thus more complex than hitherto suspected and will have to be explored and evaluated in suitably sophisticated animal and ecological models.

Industrial Wastes

The far-reaching consequences of environmental pollution by industrial wastes are just now beginning to be recognized for their gravity and complexity. Mercury poisoning is a timely example. Another aspect of this problem, thermal pollution of the atmosphere and waters, is almost totally unexplored. These environmental perturbations cannot be adequately analyzed without comprehensive studies in animal populations, both in the laboratory and in the field.

Food Additives, Food Processing Agents, and Agricultural Chemicals

The production and processing of foodstuffs, from farm to table, now involves a prodigious number of chemicals, which is continually increasing. To protect the consumer, vastly expanded programs dealing with the acute, chronic, and intergenerational toxicologic consequences of previously unevaluated, underevaluated, and newly developed food additives and processing agents must be undertaken. These studies will require extensive use of laboratory animals as well as ecological investigations.

Drug Toxicity

Study of the biological consequences of newly developed drugs need to be vastly expanded. Only in recent times, for example, have deleterious effects on future generations been considered. Examples such as thalidomide, cyclamates, and LSD suffice to indicate the scope of the problem and the urgency of the need for intensified evaluation in animals.

Noise Pollution

The full effects of noise pollution are only now beginning to be suspected. Behavioral experiments on animals, with morphologic correlations, will be

necessary to explore and quantify the psychologic and psychosomatic consequences of exposure to noise. These studies will require techniques and animal models yet to be developed.

Cancer

Although the essential basis of the neoplastic transformation may be found to reside in macromolecular changes within the cell, full understanding of the cancer process will require extensive studies on laboratory animals as well as on human beings.

Epidemiological data imply that more than half of all human cancers result from environmental agents and are thus potentially preventable. Hence, we must redouble our efforts to detect the carcinogenic agents in question and to eliminate them insofar as possible. This will require extensive testing of suspect compounds in carefully selected laboratory animals. Since, however, some agents cannot be entirely eliminated, such as certain naturally occurring carcinogens and chemicals that are converted to the active form by metabolism within the body, efforts to block or reverse the action of these agents are called for. These studies will require systematic investigation of the metabolic pathways of such agents and of their action at the cellular and subcellular levels in appropriately selected experimental animals, as well as in human subjects. Related investigations on the etiologic action of ionizing radiation, of viruses, and of other oncogenic agents will require comparable animal explorations.

Efforts directed toward improvements in cancer therapy, whether by means of experimental surgery, radiation, immunological methods, or drugs, will likewise require expanded use of laboratory animals for investigative purposes.

Bioengineering

Advances in metallurgy, ceramics, plastics, and electronics, coupled with those in surgery, have led to promising developments in the design and construction of prostheses of various sorts, many of which are intended for implantation within the body. In the testing and perfection of these devices, experimental trials in animals are essential. This field, like experimental surgery itself, may be expected to call increasingly for appropriately conditioned animals of diverse species, particularly dogs and primates.

Degenerative Diseases

With the gradual conquest of infectious diseases as a cause of death and disability, the developmental and degenerative diseases command increasing attention. These conditions, most of which arise through the interaction of genetic and environmental factors, can usually be studied in full detail only in animal models. It is important, therefore, that relevant animal research be encouraged and supported to an extent commensurate with the magnitude of the problem. This will require the development and maintenance of a wide variety of gnotobiotic and genetically-defined stocks to supply the models in question.

Behavior

Within the remainder of this century, research in the neurosciences and in the behavioral sciences may be expected to become increasingly productive. To the extent that this may help us to make fuller use of our intelligence, to grow in wisdom, and to live more harmoniously with our fellow men, few lines of study could be more deserving. Other promising aspects stem from the recent discovery that certain physiologic processes controlled by "involuntary" mechanisms (e.g., blood pressure, heart rate, temperature, etc.) are in fact susceptible to self-modification using classical Pavlovian conditioning. This discovery has enormous medical and social implications.

Research in these areas will require extensive use of experimental animals for investigation at all levels of biological organization.

ROLE IN SUPPORT OF EDUCATION AND RESEARCH

Laboratory animals have become an important part in the education of most students at the high school and college levels, whether or not they are embarked on careers in the life sciences. Today's students accept the laboratory animal as a standard tool for the study of biological processes.

At the same time, there is growing concern for the comfort and well-being of laboratory animals, with the result that it is now considered unacceptable to subject them to needless suffering or deprivation. Standards for the handling and care of experimental animals are becoming increasingly comprehensive and rigorous.

In the future, those responsible for laboratory animal resources will be called upon more and more to provide informed guidance in the housing, care, and handling of laboratory animals. It will be incumbent on them to help ensure that students and laboratory workers do not approach such matters

haphazardly but are schooled systematically in sound principles and provided with ready access to expert consultation in animal husbandry, medicine, and technology. To meet these requirements, existing training programs must be expanded enormously, and the services available through most laboratory animal resource programs must be greatly broadened.

With evolving sophistication in biomedical research, moreover, the need for specialized expertise and diversification in laboratory animal resources is becoming continually more exacting. Contemporary experiments tend to require animals of elaborately defined genetic background and environmental status, the details of which may vary widely, depending on the purposes of the study in question. Only with meticulous control of the many interacting variables that are involved is it possible to elucidate most biological processes, and ultimately to formulate meaningful generalizations that are applicable to man. Increasingly, therefore, it will be necessary for laboratory animal resource programs to maintain pedigree stocks of great specificity and diversity so that various genetic combinations can be available as needed for the study of gene action in mammalian cells, organs, organisms, and populations. Furthermore, because of the epigenetic action of certain viruses, as well as the difficulty caused by microorganisms that are pathogenic in the traditional sense, all pedigree stocks ideally should be microbially defined insofar as possible and should be safeguarded against crossinfection from other animals or from man. Although few colonies of this type are being propagated today, they will be required in growing numbers in the future. Hence, it is essential that steps be taken at once to develop the advanced technology, resources, and manpower that are needed to keep pace with these developments.

SUMMARY

Laboratory animal research, which has come to play an indispensable role in modern science, medicine, and industry, will be even more vital in approaching the urgent ecological problems that now confront us, arising out of the conflict between our expanding industrialized population and our dwindling natural resources. Hence, despite the pressure of mounting social needs that compete for national support, it is essential that we equip ourselves to carry out the animal studies needed to ensure the preservation of our environment, our ecological balance, and our survival.

The challenge posed by these problems is staggering in its urgency and complexity. This challenge, coupled with the evolving sophistication of contemporary biomedical science, calls for prompt broadening and deepening of laboratory animal research, resource, and training programs on a national scale.

Evolution and Current Status of Laboratory Animal Resource Programs

Bennett J. Cohen, Edward C. Melby, Bernard F. Trum
(Presented by Bennett J. Cohen)

SUMMARY

Animal resource programs have played a major role in the evolution of present standards guiding animal research. The standards were derived from a practical application of good husbandry, scientific principles, and humane considerations. Adequate support of animal resource programs in relation to overall institutional priorities for biomedical research is essential if long-range stability of these programs is to be ensured.

Support should be based on the following considerations: (1) The funding of research using animals must include provision of adequate funds to meet current standards; (2) Present standards reflect the needs and interests of individual scientists, their host institutions, and the granting agencies supporting their work. All of these groups share a responsibility to provide the support necessary to implement the standards. (3) Experience has indicated that veterinary services, as required by current standards, are better provided when financed as a core activity not dependent upon a cost recovery process; (4) Animal resource programs must meet high standards of efficiency, fiscal accountability, and responsibility to ensure wise use of limited funds for animal research; (5) The priority for funds used to support animal care resources must be considered as high as for any other phase of research using animals.

INTRODUCTION

Recently we have noted a retrenchment of financial commitments to animal resource programs by scientists who previously supported these programs very strongly. As best we have been able to determine, the problem is how to pay for animal care in the face of reduced grants, and those involved are seek-

ing clarification of a difficult economic situation. Whether or not programs in support of laboratory animal facilities and resources have enjoyed a preferred position in recent years with respect to funding is difficult to determine. However, it is not difficult to understand that the more efficiently operated programs, those that are functioning with little or no surplus of operating funds, are the ones most seriously affected by the current curtailment of funds for research. Clearly, reduction of support cannot continue if these programs are to continue to exist.

Scientific, legal, and ethical considerations have prompted a significant elevation of standards for animal research during the past 20 years. This is reflected in Public Law 89-544, in various state and local laws, in the voluntary accreditation program of the American Association for Laboratory Animal Science (AAALAC), and in the *Guide for Laboratory Animal Facilities and Care* (U.S. Department of Health, Education, and Welfare, 1968). The development of institutional animal resource programs to implement the standards is one of the most significant factors responsible for the improvements in animal care during the past generation. The state of these programs up to 1968 is well described in a recently published national survey of animal facilities in medical research (Trum, 1970).

However, we now face a new situation. Financial support of biomedical research has declined or, at best, has reached a plateau (Kelly, 1970; Marston, 1970) and this, coupled with a rising cost of living, has sharply reduced the dollars available for implementing animal care standards. No one really wants to overturn the beneficial effects on animal research that higher standards have brought; but what is to be done if scientific institutions no longer can find resources to support these programs? We seem to be facing the unpleasant choice of reducing the amount of research that can be supported in order to pay for these higher standards of animal care, or of lowering animal care standards in the hope that this will spread research dollars further. The challenge we must meet is to find alternatives so that we can maintain and even improve upon existing standards without making it financially impossible for investigators to continue their work. This is really what this conference is all about. Our objectives in this paper are to review the varying roles of laboratory animal resource programs, to identify how these programs are supported, and to indicate possible future directions in the light of present restrictions on growth.

PRESENT STATUS OF ANIMAL RESOURCE PROGRAMS

The nature of animal resource programs varies among scientific institutions; but two patterns of organization predominate. The first pattern evolved

during the period of rapid growth in federal support of biomedical research during the 1950's. Many medical schools and universities organized centralized animal care departments, usually under veterinary direction, to deal with the logistics of animal care and with other problems that accompanied the great increase in use of animals during this time (Cohen, 1960). The function and objective of these departments was to provide more knowledgeable, better animal care than could be provided by individual departments or investigators; their raison d'être was as service units. Today they perform some or all of the following services:

1. They ensure compliance with PL 89-544, with state and local laws, with AAALAC requirements, and with institutional regulations.
2. They provide for the day-to-day procurement, management, housing, husbandry, and breeding of numerous animal species.
3. They provide a variety of laboratory animal medicine services such as animal health and quality control, isolation and quarantine of animals, veterinary clinical care of animals, laboratory diagnostic services, surgical services, and postsurgical care.

In many respects, these service departments relate to the institutions they serve as the teaching hospital relates to the medical school, and the director of the animal service program occupies a position comparable to that of the director of hospital administration.

During the 1960's, a second organizational pattern for animal resource programs evolved, usually, but not invariably, as an outgrowth of the first. The academic potential of institutional animal resource units was recognized to permit and encourage involvement of their staffs in teaching and research as well as in service activities. Today, many of these units have become full-fledged academic departments in their respective institutions. Their staffs hold regular academic appointments, and the program director functions as a department chairman or its equivalent. In these departments, teaching activities include the offering of graduate and professional courses in areas such as use and care of experimental animals, experimental animal surgery, animal models for biomedical research, comparative pathology and medicine, zoonotic diseases, and others. In addition, in some of these departments, graduate training programs in laboratory animal medicine, comparative pathology, gnotobiology, and other related fields are well established (Clarkson, 1961 a, b); and in others, undergraduate level educational programs for animal technicians have been developed (Hoag, 1969). One need only scan the current scientific literature to document the scientific productivity of these recently established animal resource programs. These two aspects, service and professional or academic functions, may be separated for support considerations.

FINANCIAL SUPPORT OF ANIMAL RESOURCE PROGRAMS

The patterns of financial support for animal resource programs vary among scientific institutions as do the programs themselves. In general, institutions have made commitments to these programs of animal care based on the idea that in an educational institution the full cost of research should be borne by the funding that supports it. Expenditures are recovered from three principal sources: government funds, foundations and other private granting agencies, and institutional support.

Traditionally, the expenses of an animal care program include the cost of the animals, food and bedding, and maintenance labor. Occasionally, charges are made to include cost of replacement of equipment. In most institutions, these expenses are directly charged to the research on a per diem basis (Cohen, 1960; Deits, 1968; Jones *et al.*, 1970; Trum, 1970; Watkins and Cohen, 1964).

Despite the importance of income from recharges, we do not know of any major animal resource program that is supported entirely from this source, and the results of the recent ILAR survey (Trum, 1970) confirm that some degree of subsidy usually is provided. Professional services, supervision of care, and administration are not usually charged to the research but are supported from supplementary funds. The amount of the subsidy usually depends on the range of such services required, or on the extent to which the staff is engaged in other directly supportable activities such as teaching and research. Thus, the salary of the program director may be subsidized, and direct support may also be provided for other professional personnel, equipment, supervision of animal care, and for the professional services associated with the health care of animals. The sources of the subsidy include institutional funds of various kinds as well as funds of federal origin such as institutional indirect cost income and general research support. In addition, a most significant type of subsidy has been provided through the laboratory animal resource grant program of the Animal Resources Branch, NIH. This has enabled many institutions to upgrade their animal resource programs and to provide professional services that could not otherwise be made available. Finally, training and research grants in laboratory animal medicine and related fields indirectly have provided a measure of support that has enhanced the overall animal care program in a significant number of institutions.

FUTURE DIRECTION OF ANIMAL RESOURCE PROGRAMS

Institutional administrators are finding it increasingly difficult to provide support for animal resource programs. Other programs urgently need help, too,

and there is increasingly sharp competition for limited funds. This has brought about a search for new funds or alternative methods of financing animal care.

The alternatives seem to be

1. Increase direct charges to include all costs of animal care. This, of course, will be resisted because the original estimates of research costs may not have included these increases. Simply to increase animal care charges without supplementing grants or providing a general commitment of increased support could only result in an overall reduction in research. It might partially solve the problem for animal care, but at the expense of other aspects of research.
2. Provide direct support from grant fund sources to supplement funds obtained through recharges. For example, funds could be provided on the basis of the total dollar amount of research involving animals at an institution.
3. Provide funds for distinct functions in a variety of ways and from several sources such as (a) funds available upon application for replacement of equipment or facilities based on a deterioration formula; (b) considering support and service supervision together with administration of animal research facilities as a reimbursable item to be included in the cost computation used in the negotiation of the indirect cost rate and therefore to be spread over the whole research enterprise.
4. Consider the other alternatives not now clearly apparent. One would be to finance the supervisory costs from institutional funds without any attempt at recovery on the grounds that an institutional pledge has been made to adhere to standards and that this expenditure is one way of honoring the pledge.

In mentioning these alternatives, we have assumed that quantitative reductions in animal care services relative to reductions in research using animals will be made; but this can be done only up to a point. Ultimately, the requirements of efficient administration and good animal care practices make a further reduction of animal research resources impractical.

Accordingly, we ask What does the future hold in store? and Where should we go from here? This is not a good time for prophecy, but we believe our path to the future is reasonably well marked. We all know that scientific and educational institutions throughout the country face overwhelming financial problems. With specific reference to biomedical research, there is little likelihood of substantial increases in the level of federal and nonfederal funding in the immediate future (Jones *et al.*, 1970). Consequently, scientific institutions and granting agencies have no alternative but to review their priorities for support of all programs in this area, including animal resource programs. We have no reason to fear this re-examination. Indeed, this is the best way to

promote understanding of the fundamental, essential support these programs provide to animal research. The future of animal resource programs depends upon a careful, systematic evaluation and recognition of their roles in biomedical research. Those who represent this area should be prepared to assist in this evaluation in every possible way so as to promote the necessary understanding and recognition.

What considerations should guide those who must determine priorities for support of animal resource programs?

1. The experience of the past generation should have taught us that animal research cannot be promoted at the expense of animal care standards. On the contrary, the maintenance and further improvement of present standards is essential to good research. Efficient methods for the attainment of the best animal care can and should be sought; but our fundamental legal, scientific, and ethical standards, as expressed in PL 89-544, in the voluntary accreditation program of AAALAC, and in the *Guide for Laboratory Animal Facilities and Care* must not be compromised.

2. Our present standards are an outgrowth of the experience of every scientist having a stake in animal research. They reflect the mores of the scientific community and the public-at-large. The standards have been tested and proven in the arena of everyday usage and are now a demonstrable aspect of research itself. Thus, any lowering of animal care standards would inevitably have adverse effects on the quality of animal research. Inasmuch as the standards reflect the needs and interests of a broad community, including individual scientists, their host institutions, and the granting agencies sponsoring their work, the support necessary to implement the standards should come from the various elements of that community.

3. A key requirement of present standards for laboratory animals is that of adequate veterinary care. The term is not precisely defined in the standards, but most institutions now consider it essential to provide for veterinary participation in the health care of their research animals. Of paramount importance is the mechanism(s) by which veterinary services are supported, since this has a crucial bearing on the nature and scope of the animal resource program.

We strongly support the recommendation in the recent ILAR survey (Trum, 1970) that core financial assistance be provided directly. The idea of recovering the costs of veterinary services by recharges to grants and contracts, as is commonly and properly done to recover husbandry costs, seems to us to be wrong both tactically and philosophically. In our experience, recharging for professional services tends to repel investigators rather than attract them to the animal resource unit. It transforms what should be a colleague-to-colleague relationship among investigators and veterinary staff

into a mechanical association with a technical service. Finally, it denies the veterinary staff the financial stability it must have if it is to maintain a meaningful animal care program with the necessary range of services. It makes more sense for institutions and granting agencies to acknowledge that veterinary services are an essential adjunct of animal research and should be supported directly. The obvious sources of support are institutional indirect cost funds, when the costs of the animal resource program are included in the computation thereof, general research support funds, and direct grants or contracts to animal resource units. The principal advantages of this approach are that it ensures a measure of stability to the animal resource program, allows the staff to concentrate on providing "adequate veterinary care," and provides an effective method of monitoring the quality of the program.

4. Animal resource programs cannot be turned on or off like water spigots. The development and training of a competent staff takes much effort and time. If a good staff is to be retained, there must be some assurance of long-range program stability. This stability is lacking in many programs today, even though the host institutions want their programs to be good ones. What is needed is a careful review of the institution's priorities and objectives with respect to biomedical research and a decision about the role of the animal resource program in relation to those objectives. We are confident that out of such a review will come wider recognition that animal resource programs are not "camels in the tent" and competitors for scarce funds. Rather, their role is that of collaborators in biomedical research, and through judicious support of good programs, limited funds will in fact be spread further while continuing to raise animal care standards.

5. In the face of current financial limitations on animal research, animal resource programs have a powerful obligation and incentive to keep service costs down. Careful cost accounting, automation, close supervision of husbandry, and other methods of conserving limited resources must be implemented wherever possible. The chairmen who have been complaining about the high cost of animal care on behalf of their departments have every right to expect the same budgetary restraint in the animal resource program that has been imposed on their departmental operations and research activities. Given this restraint, however, and a reasonable documentation of the actual costs of animal care, few investigators who have experienced good animal resource programs would choose to turn back the clock to the time when such programs did not exist.

CONCLUSION

We have stated the facts as objectively as possible, considering the fact that we are as involved in the problem as we are knowledgeable about it. Animal

research has changed enormously during the past generation, and its requirements are likely to grow increasingly complex in the future. Among the future challenges that must be met are the development and characterization of new animal models for biomedical research, more direct participation by laboratory animal specialists in teaching and research in comparative medicine, and further elevation of the efficiency and standards of laboratory animal husbandry and disease control. If these and other challenges are to be met, however, animal resource programs must have some assurance of long-range stability. The requirements for stability and survival are to be found in the following propositions based on the considerations we have just discussed:

1. We must continue to meet legal, scientific, and ethical standards requiring good care for laboratory animals.
2. We must require fiscal responsibility and accountability from our animal resource programs to ensure wise use of limited resources.
3. Institutions and granting agencies must recognize that they share fiscal responsibility for implementing present animal care standards, and that investigators must participate in recovering total costs of animal care if research grants are to be renegotiated to include such costs.
4. With specific reference to the provision of "adequate veterinary care," direct support of this activity is essential.
5. Institutions must assign sufficiently high priorities for support of their animal resource programs to promote their long-range stability. The costs of a good animal resource program are nominal in proportion to the total investment in animal research and the payoff from good programs. We believe that prudent investment in good programs is a wise use of limited resources and is in the interest of all institutions that conduct biomedical research.

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DISCUSSION

DR. SCHNEIDER: The first two papers reflect the scope of this conference. On the one hand, Dr. Upton clearly pointed out that we will need increasingly sophisticated models for animal research in the future. Dr. Cohen's paper, on the other hand, dealt with the "nuts and bolts" of supporting this sophisticated effort. Here is the difficulty. When we were not under any hard fiscal constraints, we could move with great flexibility; now we are pressed financially. What is to be saved? How much is to be fought for? Where shall we concentrate our efforts to win support and recognition from administrators and budget makers?

DR. DAVID DREILING (Mt. Sinai Hospital): The problem we face is shrinking funds at a time of increasing costs. Dr. Cohen suggests that the institutions support the central animal facility. This is not the total answer. Our medical school does provide direct support of the central animal facility, but this is inadequate. Realistically, the only way the problem will be solved is to obtain more money from the federal government. To do this we must convince the general public that money spent for biomedical research is justified. If we convince the public, they in turn can influence government policy.

DR. THURMAN S. GRAFTON (State University of New York at Buffalo): Please comment further on the use of indirect cost income to support animal resource programs.

DR. COHEN: Indirect costs associated with the research of a university are negotiated annually based on all of the factors that make up these costs. Perhaps some of the costs of animal care administration could be negotiated as part of the indirect costs. For example, radiation control services in many institutions are now an aspect of the indirect cost negotiation. Certain of the animal care activities might be financed in the same way.

It would be better to defer any detailed discussion of points such as these until we hear Mr. Meadow's presentation.

DR. JOHN A. CAMPBELL (Chicago Medical School): Dr. Upton discussed the need for animal models and plans being made to develop breeding

colonies of endangered species, such as certain nonhuman primates, e.g., the orangutan. What plans are being made to develop breeding colonies?

DR. SCHNEIDER: Dr. Clarkson, would you respond to this question as current Chairman of ILAR?

DR. CLARKSON: The domestic propagation of useful species in research is a concern of all of us who are involved in laboratory animal resources. The ILAR Committee on Conservation of Nonhuman Primates is now considering this problem. Primate species are of special interest to the national primate center programs. For example, the Yerkes' laboratory has been particularly successful in propagating orangutans in captivity. We are now identifying those species that are truly endangered, and that are indispensable to biomedical research. When this task is completed, I am certain the means for domestic propagation will be found.

Priorities for University Research Programs in Biology and Medicine for the Seventies

Fred C. Davison

At a time when mankind is plagued by a number of clearly defined crises, it is tempting, and it would not be too difficult, to address ourselves to a set of priorities for specific programs of research in biology and medicine for the seventies. On the other hand, because our crises are rather clearly defined and because there are communities other than the university involved in research, I would like to discuss what I regard as some very basic considerations where university research programs are concerned.

It is important that we redefine, emphasize, and preserve the special relationship of research to the university community. For here it fills a function beyond that of research in the private institute or in the corporate research and development center. This may sound elementary, perhaps, but it becomes increasingly important in that research in a university context has a far greater dimension than anywhere else, and this dimension must be protected jealously.

The American university has, in little more than a hundred years, become the almost exclusive source of trained scientists and research men in the nation. This seems only natural to us today in that teaching and research are so inseparably bound up in our institutions–along with a third function–that of continuing education for a vast number of constituents.

We cannot forget that the research program of the university today is the graduate teaching program for tomorrow's scientists and researchers. The professor who is engaged in research is not, usually, working in splendid isolation and complete freedom. Nor is he pursuing on schedule the answer to a specific problem laid out for him by a hierarchy of decision makers. He is not working merely to improve or promote himself professionally. He is engaged in a high and complex calling that should involve intimate relationships with graduate students who are in effect serving apprenticeships with the master. From him they absorb more than techniques and ideas, they are observing the value of speculation and learning to project ideas. They are observing and practicing the systematic approach to investigation and recording of facts.

They are testing the value of questioning, experiencing the satisfaction of learning, and tasting the excitement of being on the frontier of knowledge. One of our first priorities is to preserve this relationship, for once we permit it to lapse, by carelessness or design, we strike at the roots of the tree of man's knowledge.

Since World War II, tremendous public and private resources have been poured into research and development programs, and where universities are concerned, these resources have helped to strengthen graduate and research programs. They have served to create and strengthen ties between professional groups and the laboratories. On the other hand, they have tended to focus attention and inevitably to shape priorities in terms of short-range goals and, oftentimes, in terms of problem solving. As we can readily see and acknowledge from the standpoint of medicine and biology, particularly, such work is badly needed, and results have been dramatic. However, the point I should like to emphasize here is that the university is and must be interested not only in man's basic problems but also in all that he does not know. There is no other community in which there is such sharp realization that no matter how much man may have learned, he is still confronted by a vast sea of the unknown. There is undoubtedly a case to be made for the university professor who can lend his time and competence in a time of need to the solution of specific problems, but the point must never be lost that within the framework of the university, his primary obligation lies in the pursuit of knowledge and the education of another generation of seekers.

More than a decade ago, Lee DuBridge voiced the question "Should a professor do research?" His answer was another question "Should a fish swim?" Then he went on to explain that if a university is true to its concept as a center of learning, the professor will inevitably want to learn. But he warns that the institution must do more than tolerate the professor's pursuit, it must actively encourage and stimulate. The professor, in turn, excites the student-learner, and through his example the student sees that learning is a lifetime pursuit. I might add that our attention to continuing education is bringing this last point home to men and women of another generation who might have lingering ideas that diplomas, units, and course requirements are the measure and the terminals of learning.

While some of our accomplishments in research may have caused a heady feeling among various groups of people, we must sustain a realistic position that at best we can hope to extend man's understanding a bit for the next generation and lay the foundations for the next generation to do its own extending.

Money and emphasis on problem solving and short-term success in research are not the only pressures that are felt as we try to shape research programs in the university community. There is the question of specialism and vested inter-

est along with the effects of expanding bureaucracy that has attended the growth in size and complexity of our institutions.

In many instances an institute within the university community is the vehicle used for bringing together representatives of a variety of disciplines and experiences to work together. In some areas the development of study centers under the university umbrella has brought together teams of researchers. One of our priorities should be to encourage this kind of development, for here, again, the university community is peculiarly suited to interaction. No other community has a greater variety of skills and backgrounds. And while undoubtedly a great degree of specialization will still be needed as we push into the unknown, more and more communication and relationship among our various disciplines will be needed to cope with our findings. More and more, we find that man's quest for understanding cannot be confined by inflexible, departmental school or college lines.

To preserve and extend the concept of research in a university framework, we must encourage the understanding that learning operates with a different efficiency than does business. Research cannot be done on an assembly-line basis. The learning of one generation of students, the quest of one generation of teachers will differ markedly from that of another—and neither can be measured by an immediate profit and loss statement. It is commonplace to point out to a group like this that our technology today is the fruition of other generations of learners. But this is something that our constituencies are prone to forget.

Having sketched in these preliminary thoughts, let me turn now to some of the ways in which we can and must strengthen research generally in our universities and in particular, of course, our efforts in medicine and the biological sciences.

First, we must reallocate our dollars to bring about cooperation and long-range stability. I think we all realize that funds from public and private sources must continue to be channeled into research if we are to maintain the momentum that we have built. We must not permit concern with specific problems—many of which are urgent and which should be dealt with generously—to rob programs of basic research of support sufficient to continue and strengthen them. As many buffers as possible must be built in to prevent annual fluctuation of programs because of the uncertainty of budgets or the failure to produce measurable results over a given period.

We must continue to seek the resources to provide university communities with the best and most complete means of communication, and we must encourage the exchange of information and ideas across disciplinary as well as institutional lines with a minimum of red tape and as a normal chain of events. The broadest possible dissemination of information is necessary. The com-

puter, television, and many other extensions of man's senses are indispensible in research efforts today.

And, of course, most important of all—at the center of all these considerations—are the men and women with whose work we are concerned with. We must turn our attention to expanding our pools of imagination and talent. We must recognize that there are many ways in which the researcher pursues his quest, and while the philosopher-scientist no longer occupies the ivory tower, he is not geared to an 8-hour day, a 40-hour week, or a tidy office and clean desk. He obviously must work alone at times, at other times in tandem, and oftentimes in teams. Our obligation is to understand this, to select and encourage dedicated men, and to protect them from the internal and external pressures that might force them into routines that would result only in defeat and failure. This is perhaps one of our most urgent priorities, and it may require some of our most penetrating thinking and hardest work. The results of the massive technological application of scientific knowledge to a space shot are dazzling but equally impressive are the concepts that came from quiet laboratories and studies that made it possible.

It is true that for more than a century, people of the United States adapted the findings of European researchers. But, in less than a half-century, our research efforts outstripped those of European institutions. I am not sure that we are not underselling our constituencies when we emphasize problem solving and short-range goals. It is true that basic research is a high-risk investment, but so has been the development of North America.

As important as the men and women who will continue to plan and carry out our programs of university research are the students who will be recruited or who will become teachers and researchers themselves. We are at a juncture when we are having forced upon us for high-priority consideration the manner in which we are discharging our stewardship here.

Are we designing programs for students of an earlier era? The world tomorrow, we all know, will be as vastly different from the one in which we are living as this era is different from early years of the century. A recent conference in the far West inspired a news story that began "Forty innovators met in this mountain community recently to plot a creative revolution aimed at unleashing young inventive minds . . . " Corporations, universities, and other institutions were represented in a meeting to consider what one scientist is reported to have called "the gravest moral crime in the world." A biochemist has declared that "humans are born with something beautiful—creativity—and we are not allowing it to develop."

We all know that we must attract students of potential, but are we doing everything we can to develop their potential? The institutional forms of the university frequently encourage mediocrity—even at the advanced graduate

level where our future scientists and researchers are working. Old forms and traditional practices often tend to limit and bind, and anything which may challenge conventional frameworks is discouraged. Subtle and not-so-subtle emphases are placed on success, when all of us know that real research and scholarship carry high risk of failure.

I feel very strongly that the major points I have touched here are basic to any consideration of university research in the next decade. Perhaps I am restating what John Gardner once termed "an interesting question": whether the university, in meeting the demands upon it, will exhibit qualities of statesmanship or function as a sort of badly organized supermarket.

I am firmly convinced we must function as statesmen, not as technicians or supermarket staffmen. To lose our perspective as to the relationship of teaching and research, to shorten our vision down the future, to permit the scope of the university community to be narrowed, to build further impediments to interaction and communication of the various disciplines and areas of knowledge and wisdom, to fail to question traditional practices and to consign our teachers or students to assembly-line procedures would be poor statesmanship.

On the other hand, if we accept the opportunities that go with the responsibilities of a community of learners, dedicated to learning, research will thrive and flourish, and the next generation will have a little more upon which to build and extend its knowledge than we have had.

Laboratory Animal Resources and Research in Medical Schools

George T. Harrell

The use of laboratory animals is absolutely essential for the program of education and research in a modern medical school. A dependable supply of stabilized animals, properly housed in facilities that provide a controlled environment, and adequate resources for the teacher or research investigator to use or call upon must be available. The educational and research programs in a modern curriculum inevitably intertwine and overlap.

EDUCATION

The student in medicine at all levels needs to learn and be constantly reminded of the difficulty in obtaining reliable, reproducible data in living systems. The reason for this difficulty is the inherent biologic variability of living things. The student must learn the need for meticulous care in the design of studies to meet scientifically acceptable statistical criteria. Only by studying groups of individuals can the individual variations be smoothed out.

Animal studies put the quantitative collection of data in a basic science setting into perspective with the laboratory work subsequently performed in a clinical setting on human patients. The student from the beginning of his studies in medical school should recognize that the intellectual process followed by the physician in practice is essentially one of problem solving. Animal experiments offer excellent training for this pattern of thinking and emphasize the necessity for careful execution of the plan for collection of data. Detailed planning in advance of the laboratory exercise is necessary to point out that attention must be given to the species of animal used, its preparation to provide a stable base, and the techniques and materials used to see that they are appropriate. The student should learn that in dealing with living things, he should use the best methods available and perform at the highest level of which he is capable. The formation of professional attitudes, which he will follow the rest of his professional life, must begin early at the student level. If he accepts no difference in the quality of care given to surviving animals from that given to human patients in the educational setting, he is

not likely to accept a double standard between private and nonpaying future patients of his own in practice.

RESEARCH

The causes of death in this country have drastically changed in the last forty years. Formerly, people in all age groups died of acute infectious diseases. Now the chief causes of death are chronic illnesses—heart disease, stroke, and cancer—in which the life history is measured in terms of years rather than of days. Students, faculty, and the public as well, must recognize that the basic biologic information on the pathogenesis and mechanism of development of the chronic degenerative diseases is not known. The increasing recognition of genetic factors in determining the susceptibility to chronic illness and the probability of development of complications from which the patient may die must be taken into account in the planning of future research. Only in animal experiments can the genetic factors now recognized be controlled. Other variables that influence the course of chronic illness can be reduced in controlled laboratory animal experiments as compared to clinical research on human beings.

The increasing emphasis on the repair of congenital defects and the replacement of damaged or nonfunctioning organs requires increasing attention in research. It is likely that artificial organs and prostheses will offer more achievable solutions in the future than transplants of tissue from living donors or cadavers. The solutions must be worked out in animals before they are tried in human beings. The materials used must be biologically nonreactive, the mechanical devices dependable without repair or replacement over periods of months or years, and the techniques for insertion and maintenance easily achievable. Such studies involve long-term experiments in which the standardization of animals before the beginning of the experiment is imperative. The facilities for maintaining animals should be optimum and the environment should be controlled to reduce the number of variables.

COST

This quality of research is expensive. In the past, the proportion of cost allocated to animal care has been totally unrealistic. The attitude that the purchase and care of animals should represent only a small part of research grant requests unfortunately persists. The most expensive item in research of any type is the time of the faculty member devoted to the experiments. The experimenter's time is wasted if animals are not reliable and stabilized before

the beginning of the experiment or properly cared for afterwards, especially if observation will continue for a long time. The next most expensive item is technical assistants trained to help perform the specific experiments. Budgets for research grants often include an item for animal care that is a fraction of the cost of a single technician. As a rule of thumb, it is realistic to expect that animals and their care should cost at least as much as the technical help provided. With the current size of the animal items in research grant applications, only a fraction of the true cost of provision of quality animal care is provided. A medical school now must subsidize not only the cost of construction and maintenance of facilities, but make up deficits in the provision of day-to-day care. Few schools in these days of financial restriction in general operating funds and particularly in research grants can afford such subsidies. The cost of research animal care must be recouped as a charge against grants.

The caliber of people supervising a central animal facility and providing day-to-day care should equal the professional and technical qualifications of the research investigator and his staff. Professional advice in design of experiments, help in performance of them and supervision of animal care should be provided by veterinarians and animal technicians specially trained in laboratory animal medicine. If intelligent, dedicated, properly trained personnel are provided, overall labor costs can often be substantially reduced. The problems of nutrition and cross infection are best met by placing responsibility on a school-wide supervisory administrative unit located in a central facility.

ONE SOLUTION

In the planning of The Milton S. Hershey Medical Center, provision was made for a central animal resource facility that is part of an academic Department of Comparative Medicine. The medical school has a site of 216 acres on the edge of the community; approximately 30 acres have been devoted to an animal research farm, dairy barn, pastures, and corrals. The animal research farm comprises 38,356 gross square feet of new construction, 28,235 in the central animal quarters and the pre-existing barn 7,788 for a total of 74,379 gross square feet. The research farm building was constructed at a cost of approximately $1.9 million, including moveable equipment. Descriptions of its philosophic concept and details of its design have been published (Lang and Harrell, 1969; Harrell, 1969). The animal research farm is connected to the central animal quarters in the basic science wing of the medical sciences building by a tunnel to provide all-weather access for movement of animals or personnel. The central animal quarters in the basic science wing comprise 28,235 gross square feet out of a total of 200,170. This building cost $11.6 million equipped or approximately $58 per gross square foot. The central

quarters represent, conservatively, a capital outlay of $1.6 million. In addition, small animal holding rooms for one or two cages of animals for overnight observation or short-term holding are provided on each floor of both the basic science and clinical science wings of the medical sciences building. These figures give some indication of the importance attached to animal care facilities by the administration of this new medical school.

The budget for the Department of Comparative Medicine and the animal resource facility for the 1970–71 fiscal year is approximately $200,000. Roughly half of this budget represents a subsidy by the college of medicine for teaching and the provision of research resources. The other half is supported by income from grants for provision of specific research animal care. This overall budget is in the same range as that of the traditional basic science departments in this school.

The chairman of the Department of Comparative Medicine serves as the director of the animal resource facility. The dean of the college of medicine requires that all research grant applications be reviewed by the chairman of the Department before submission to the granting agency. Thus, the investigator is assured that space is available to meet his requirements for animals and that necessary environmental conditions can be achieved. The review also includes scientific evaluation of the suitability of the species proposed, the design of animal aspects of the experiments, and the number of animals proposed to obtain statistically valid data. If the dollar figure is not adequate to provide for the purchase and per diem maintenance of the required number of animals, the draft of the research proposal is returned to the investigator for revision. Experience in three years of operation indicates that the provision of properly prepared, well-cared-for animals reduces the number of animals required for an experiment. Staffing with intelligent and well trained personnel indicates that our overall labor cost is less than in many other comparable facilities. In addition, no epidemics or detected cross infections have occurred in the three years of operation.

The educational responsibility for medical students is met through provision of laboratory and surgical facilities for problem-solving projects and for elective research experience. In addition, a master of science program in laboratory animal medicine is in operation at the postdoctoral level for holders of the doctor of veterinary medicine degree. This program requires completion of a research project and thesis and balances the research emphasis with training in animal care.

Research is performed by the members of the Department of Comparative Medicine alone or in conjunction with faculty from other departments. Facilities are provided for a wide variety of species, ranging from rodents and other traditional laboratory animals through large domestic farm species. Provision of this laboratory animal resource has been instrumental in obtaining sub-

stantial project research grant support and has been instrumental in attracting a young, enthusiastic faculty.

SUMMARY

Medical schools must give increasing emphasis to the provision of well-designed central animal facilities with supporting resources to ensure a proper learning environment for students and research capability for faculty.

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The Impact of Laboratory Animal Research and Resource Programs on Veterinary Medical Education and Research

L. Meyer Jones and W. Morgan Newton

INTRODUCTION

The profession of veterinary medicine is responsible for the health and care of animal patients and for protecting the health and welfare of man. Veterinary medicine also protects the nutritional and ecological welfare of man and animal; it has come to rely heavily upon laboratory animal medicine in meeting the above professional goals.

During the past two decades, the use of laboratory animals in veterinary teaching and research has reached a new height. Laboratory animals are used in innumerable ways—some of the more prominent as follows: for the teaching of comparative medicine in colleges of veterinary medicine; for identifying and controlling intertransmissible diseases of animals and man; to study the methods of disease prevention in all species of animals and man for improved health, nutrition, and economic advantage; to provide more humane care for animals; and to provide new experimental models and methods for studying disease in man and animals.

Veterinary educational institutions have responded well to the need for development in laboratory animal programs in recent years. However, there is still the need for additional development in laboratory animal medicine on the part of the colleges of veterinary medicine and research laboratories before the challenge can be fully met. We can only wish that our college had responded more quickly and more extensively, but funding of the laboratory animal facilities and programs has not been easy because of competing needs for the same dollars by patient-oriented projects and general institutional needs. It has always been difficult to obtain support for a laboratory animal facility designed to improve the health and care of mice in preference to supporting a clinical project that is responsible for the health of man or a food-

producing animal, such as the cow. Nevertheless, each is important in its way. The support of the mouse program can reveal new information that would augment the effectiveness of the other programs many times.

IMPACT OF LABORATORY ANIMAL PROGRAMS ON VETERINARY MEDICAL EDUCATION

In 1949, the Animal Care Panel, dedicated to fostering laboratory animal medicine, was started by four veterinarians who were associated with different midwestern institutions. This pioneer organization has matured and changed its name to the American Association for Laboratory Animal Science (AALAS) to encompass members from many areas of biology, as well as from veterinary educational institutions.

In 1957, the American College of Laboratory Animal Medicine (ACLAM) was recognized as a specialty board by the American Veterinary Medical Association. ACLAM has grown from a very small nucleus to the present membership of 160 diplomates, of whom a large percentage are associated with veterinary educational institutions.

Laboratory animal resources have had an impact also upon the curriculum of veterinary medical institutions. In 1964, there were two veterinary colleges that offered formal courses in laboratory animal medicine. In 1968, seven veterinary colleges offered such courses. In addition, six other veterinary colleges gave appreciable attention to laboratory animal medicine in courses not devoted solely to the subject.

Postdoctoral training programs giving special training in laboratory animal medicine to veterinarians constituted a natural development during the past decade. Currently, four of these programs are found in colleges of veterinary medicine, seven in colleges of medicine, one in the Veterans Administration, and one in the U.S. Air Force. Again, there is clear-cut evidence that the science of laboratory animal medicine has had an impressive impact on veterinary medical education.

Another way of illustrating the impact of laboratory animal programs on veterinary education is to ask how many newly-graduated veterinarians are entering the field of laboratory animal medicine annually. Information of this nature is not readily available to us for the nation as a whole, but we can indicate what has happened during the past four years at the College of Veterinary Medicine at the University of Illinois. In 1967, two graduates went into laboratory animal training programs. In 1968, there were three; and in 1969, five of our graduates entered such programs. Not enough time has elapsed following the graduation of our class of 1970 to give a specific answer, but it

appears to be the same as for 1969. We believe that laboratory animal medicine will continue to attract at least 7 to 8 percent of our new graduates because it is a dynamic area of veterinary specialization.

IMPACT OF LABORATORY ANIMAL PROGRAMS ON VETERINARY MEDICAL RESEARCH

The overall use of laboratory animals in veterinary medicine has increased sharply within the last decade, but the greatest increase came in research in a response to available funding. The 1970 survey (on FY 1967) on animal usage by ILAR has shown that in colleges of veterinary medicine about two thirds of the laboratory animals were used in biomedical research projects. The remaining one third were used in teaching, with a few allocated to diagnosis and testing procedures.

The significance and benefits from using animal models for the experimental study of disease have become widely recognized in recent years. The help and guidance of funding agencies during the past decade have had a pronounced stimulating effect in focusing the attention of all scientists, particularly veterinarians, on the strategic role of the experimental animal model in studying diseases. However, the identification of research animal models is still a challenge that the veterinary scientist and administrator must pursue. The identification of research animal models is dependent in large measure upon an effective diagnostic laboratory for identifying and utilizing the unique laboratory animal disease. The diagnostic laboratory provides surveillance for many kinds of laboratory animals to identify the aberrant biological condition that may be used for study of a disease process of man or other animals. The research scientist, the veterinary clinician, and the veterinary diagnostician should always be looking for a potential animal model, and the administrator must be ready to supply the necessary budgetary support. Animal models are not only highly effective tools for accumulating information in veterinary research, but they may be used to achieve great economy. For example, the recent substitution of the mouse for the cow in research on bovine pleuropneumonia offers great advantage in economy, ease of usage, availability of larger numbers of animals, and a greater acceptability of species for humane reasons.

SPECIFIC INSTITUTIONAL PROBLEMS IN LABORATORY ANIMAL PROGRAMS

In identifying guidelines for setting priorities for laboratory animal programs, it would seem helpful to discuss the program and some of the problem areas,

at a specific institution. For this purpose, we refer to the University of Illinois at the Urbana-Champaign (U-C) campus with which we are familiar.

1. *Administration* There is strong administrative support in the University for the laboratory animal care program, and the concept of a centralized program is firmly established. The immediate goal of the University is for the entire U-C campus to qualify for accreditation by The American Association for Accreditation of Laboratory Animal Care.

2. *Facilities* The U-C campus of the University of Illinois has been attempting for three years to construct a central laboratory animal holding facility on the campus. To date, insufficient moneys have been available for the construction of the facility. It is anticipated that during the next session of the state legislature additional funds of state origin can be obtained enabling the construction of an animal holding facility costing less than $1 million and containing approximately one fourth of the presently needed floor space. No matching funds from federal sources are currently available to aid in this construction. Nevertheless, the University of Illinois intends to proceed with its effort to improve the conditions for laboratory animals on the U-C campus with the hope that at a later date more funding for additional space will become available to meet the current and augmented future needs for accommodating experimental animals.

At present, many of the facilities for laboratory animals on the U-C campus should be realistically described as inadequate and congested. Present facilities consist of isolated units scattered across the campus in various departments. Many single operations are satisfactory and maintain a relatively high level of sanitation and general management. Not infrequently, however, these units tend to be congested, poorly ventilated, and with highly variable levels of husbandry.

3. *Educational Need* The University-Wide Committee, which serves in an advisory capacity to the director of laboratory animal care, is convinced of the need for a centralized animal holding facility for the campus and generally holds an enlightened view of the total operation and needs. A need to educate the scientific investigators to the value of appropriate care of laboratory animals exists in many departments and at all levels on the U-C campus. The educational problems are manifold, and generally arise from the lack of current information about approved procedures of animal care. These investigators may be of two extremes: (a) the older and more experienced investigator who has learned by trial and error a minimum of experimental animal husbandry that may or may not meet current standards of humane care and experimental control for the collection of valid data; and (b) the investigator who knows

little or nothing about experimental animals and views them as inanimate test tubes not influenced by environmental factors that can invalidate the data collected. Many young students in the biological sciences seem to have had no contact with animals or experience in the care and use of laboratory animals.

On our campus, greater educational emphasis should be given to formal instruction to students on laboratory animal handling and care. Enrollment in such a course should be part of every graduate student's program before he is allowed to participate in experiments involving laboratory animals. Such a course might also be in the curriculum of advanced undergraduate biology majors.

Education of animal caretakers has not presented many difficulties. At Illinois, the Office of Laboratory Animal Care holds regular training sessions for instructing animal caretakers. In addition, they receive on-the-job instruction from their scientific supervisors.

4. *Evasion of Regulation* Outright evasion of USDA regulations sometimes takes place, e.g., when a department chooses to declare that all of its animals are "on research" when they are unloaded at the departmental dock. This procedure is a simple evasion of the intent of the Animal Welfare Act and is self-defeating in the long run. We think it is important that all investigators recognize that Public Law 89-544 protects them from unscrupulous and illegal dealings in experimental animals.

5. *Diverse Needs* The U-C campus, with nearly 34,000 students and an emphasis on the advanced undergraduate and graduate training programs, presents a diversity of laboratory animal needs that challenges the ingenuity and knowledge of the Office of Laboratory Animal Care. The construction of the projected central animal-holding facility will help a great deal, but there will still be the many individual laboratories with special needs and varying facilities. It is imperative that the individual investigator's scientific freedom and needs are not jeopardized by needless regulations; yet, a coordinated program of animal care is essential to ensure that quality animals are available for the collection of valid scientific data.

CONTRIBUTIONS OF NON-STATE AGENCIES TO LABORATORY ANIMAL PROGRAMS

The laboratory animal research and resource programs funded by the federal government have stimulated and made possible vast improvements in the care and use of laboratory animals. These programs have greatly improved the col-

lection of valid scientific data from experiments using laboratory animals.

The provision of funds by the National Institutes of Health for construction and remodeling of animal quarters and for training of personnel has had a greater impetus in improving laboratory animal care and the scientific accuracy of animal data than any other single factor. The rapid advances in the education of veterinary scientists for improving and protecting the health of man would have been impossible if the colleges of veterinary medicine had been restricted to available state funds.

The leadership of the Institute of Laboratory Animal Resources has been essential in the establishment of standards and the dissemination of information on laboratory animal care. Such efforts provided the basis for the regulations currently in force under the Animal Welfare Act. ILAR has greatly aided laboratory animal users, producers, and funding agencies in their development of constructive programs in laboratory animal research.

PRIORITY GUIDELINES FOR SUPPORT OF LABORATORY ANIMAL RESEARCH AND RESOURCE PROGRAMS IN COLLEGES OF VETERINARY MEDICINE

1. A strong administrative structure should be evident that provides

a. A centralized program of laboratory animal care,

b. A flexible program to meet the needs of each project and not interfere with the scientific freedom of investigators,

c. A scientific advisory committee to guide the program director and to provide public assurance that all research utilizing animals is appropriate and significant to the welfare of man and animals;

d. Thorough fiscal accountability.

2. Programs directed to identifying, characterizing, standardizing, and using experimental animal models in health research projects deserve special encouragement and support.

3. The establishment and maintenance of a diagnostic laboratory service for controlling disease in laboratory animals would enable the collection of more valid experimental data. The diagnostic laboratory would also provide surveillance of experimental animals for identifying research animal models of spontaneous origin.

4. Education of biology students, veterinary students, and postdoctoral specialists in laboratory animal programs is essential. The training of animal caretakers and animal technologists is an important concern, but on some campuses it is not a responsibility of the college of veterinary medicine.

5. Funding for research projects in the following areas is important but difficult and, therefore, may deserve special consideration:

a. The influence of the environment on laboratory animals kept in confinement, namely, animal housing design, humidity, air-exchange standards, and various automation devices such as the centralized watering system, which may be substituted for the individual water bottles.

b. Special nutritional problems. Nutritional deficiencies still occur in laboratory animals despite the use of controlled fortified rations.

CONCLUSION

Laboratory animal research and resource programs constitute a general support of teaching and research which is sometimes not recognized and frequently taken for granted. It is difficult to overemphasize the importance of these programs which support other projects in the collection of valid research data on health problems. Not until after the establishment of a sound laboratory animal program in a research center does one have assurance that productive, valid experimentation may follow.

DISCUSSION

DR. BUSTAD: We have a little time for discussion, but before this I want to call on Dr. John Platt whose presentation at the First National Biological Congress impressed me very much. I have asked him to tell us about genetic copying by parthogenesis.

DR. JOHN PLATT (Mental Health Institute, University of Michigan): I want to emphasize a direction of research that has been neglected, has a very high payoff and that is particularly appropriate to the interests of those attending this meeting; that is research on the kinds of animals best used in research. The neglected area is genetic copying by parthenogenesis or by other methods such as nuclear transplantation. Parthenogenesis is now known in reptiles, birds, amphibians, and other species. Parthenogenetic birds have been developed at Beltsville. Parthenogenetic frogs have been studied extensively by Fishberg and by Guerdon.

Fish have been studied at the University of Michigan, and about 30,000 goldifsh are used annually in experiments in memory and learning. These are experiments injecting protein into brain, or injecting various other compounds into the brain to see what effects there are on learning, memory, and reten-

tion. The goldfish are trained to jump over some barriers. Recently we discovered a strain of goldfish in the Ozarks that appears to be parthenogenetic. Sperm are necessary to trigger the development of the egg. Sperm from a related species are adequate; they do not penetrate the egg and thus do not contribute genetic material. The offspring are a clone that is genetically identical with the mother. We are trying to develop this goldfish strain in Florida.

The advantage of this approach should be apparent. If we could develop these genetically identical goldfish, much of the variance in the psychological experiments could be reduced. Similar advantages would occur in testing new drugs. Not all drugs should necessarily be tested on a single identical strain of animal, but in primary evaluations or comparison of two drugs much of the statistical variance due to the animals could be eliminated.

If one could perfect a rat for laboratory purposes and then make a thousand or a million copies of him, this would be a great advantage for many laboratory research purposes.

The time is ripe for a concentrated effort on this because of the high payoff this approach could bring. Parthenogenesis may depend on particular chemical compounds that interfere with the haploid division in the oogenesis stage, so that one gets a complete set of maternal chromosomes in an egg. If we could determine what those chemicals are and determine how the sperm of related species triggers the development of an egg without actual penetration, it might then be feasible to extend these studies to mammals or animals.

Guerdon at Oxford has succeeded in genetically copying frogs by removing the nucleus from the egg, and replacing it with the nucleus from intestinal epithelial cells from another animal. However, about two thirds of these nucleus transfers fail. Failures probably occur because of gross mechanical damage and the loss of chromosome bits and important connecting membranes. Fully fertile animals are produced in successful transfers. The result is a genetic duplicate of the animal from which the intestinal epithelial cells were transferred.

Guerdon's colleague, Christopher Graham, also at Oxford, has been working along similar lines with mice, using fertilized egg cells treated with colchicine and colchimid.

This research is still highly experimental at the moment but Dr. Clement Markert, of Yale University, thinks that a concentrated effort with ten or twenty labs working on this problem could make genetic copying of mammals practical within five years. This would have important advantages to the animal industry with respect to meat animals.

In the case of the food animals, this could lead to accessibility of improved varieties of animals, of more animals of certain selected types, of identical strains of animals. We could conceivably double meat production if we could copy champion animals. It might also permit a reduction in the number of certain animals now needed in drug research. Members of this conference

should give serious consideration to genetic copying as a future auxiliary animal resources.

Copying of man will not be mentioned because this subject has been discussed at numerous conferences on the ethics of science and on the future of science. Joshua Lederberg has repeatedly discussed the subject in these terms and I think this has turned off an enormous number of biologists who might have been doing useful work in this field mainly because they did not want to get into the question of morality. My own opinion is that to forego a potentially important method of animal husbandry because of the fear that in the long run it might be applied to man would be a grave mistake. Consider it as animal breeding management.

DR. BUSTAD: Thank you, Dr. Platt.

DR. RONALD E. FLATT (Iowa State University): I would like to direct attention to the point about the loss of confidence by society in our learning institutions. What has brought this about, and what can be done to correct it? This problem, I think, gets at the basis of many of our problems in animal resources today.

DR. MORRIS POLLARD (University of Notre Dame): We must keep in mind that financial support of research is generated by investigators. If we do not cultivate the sources of support, it will not come our way. Many of the laboratory animal resource units are service organizations; their support comes from investigators in the individual institutions that they serve. If those investigators do not go out and seek support for their research programs, or if they do not have research programs that merit support, then certainly the service organizations, which derive their support from the investigators, will suffer. Thus it really is not entirely the responsibility of the laboratory animal services within an institution to generate the support. It is the responsibility of the entire academic community to see that the support is forthcoming.

Institutional Options, Programmatic and Fiscal, in Providing Optimal Care for Laboratory Animals

Henry C. Meadow

INTRODUCTION

I have listened to the presentations of the previous speakers with mixed feelings—with pleasure that there has been such a lucid and complete presentation of the problems and opportunities and with concern that as the picture has been unfolded there is less and less for me to say. In any case, at least a part of the title of my talk today is a misnomer—there are really no programmatic options left to any institution concerned with biomedical research. Apart from the fact that federal regulations place a floor under the level of care and facilities which must be made available, the ever-increasing needs of the research programs for more sophisticated data demand the best available professional care and management of the most suitable animals.

Dr. Upton, in his opening statement, discussed the demands which research in the future would place on the laboratory animal system. Dr. Cohen pointed out that we must today improve on standards of laboratory animal care at less cost and for a great variety of programs. Dr. Cohen also pointed out that for an educational institution to have the ability to make decisions with respect to the application of generally available internal resources it must strive to make each of its programs pay its own way. Dr. Cohen, in his examination of the fiscal problems of our present programs, has said many of the things I planned to say, as has Dr. Harrell. Accordingly it will come as no surprise to you that our conclusions are similar.

I am grateful to Dr. Cohen, especially for painting in vivid colors a most complete picture of both the problems and the most available alternative solutions. Within the framework he has so well established, my remarks may serve to emphasize some of the issues already brought to our attention. I do not plan to discuss overhead or indirect expenses, although if I can be helpful in answering questions in this area I shall be glad to do so. I shall also

disappoint those who have been hoping for a detailed cost-effectiveness scheme which will solve all our present problems. There isn't one.

The whole subject of the use of laboratory animals in relation to modern biomedical research is broad and complex. Fortunately, we have available the "Report of a Survey of Laboratory Animal Facilities and Resources Supporting Biomedical Research 1967–68" conducted by the Institute of Laboratory Animal Resources and reported in Part II of Volume 20, Number 4, of *Laboratory Animal Care*, August 1970, to help us in describing and defining the situation as it now exists.

According to this study almost half the money ($408 million out of $920 million) expended for biomedical research by those institutions eligible to receive federal funds during the fiscal year 1970 was expended for research that involved the use of laboratory animals. According to the same survey, the cost of the animals used and of their care before and after their involvement in the research programs was approximately $50 million. About 63½ percent of this $50-million expense was met by direct charges (including *per diem* charges) to the various research programs. The balance of more than $18 million was provided by the institutions involved. About $1½ million of this is chargeable to teaching programs, leaving a balance of $16½ million used to support the research animal programs that the institutions provided from other funds available to them. It is to this aspect—the $16½ million—of the funding of our animal care programs that I should like to call to your attention today.

To permit me to do this in the time available I should like to make certain assumptions:

1. That our animal care programs are operated in accordance with the federal regulations established under Public Law 89-544 and that all those who use and care for animals subscribe to the principles of the *Guide for Laboratory Animal Facilities and Care*;
2. That we agree that individual circumstances will determine the desirability of centralized versus decentralized facilities or for "staff" veterinarians versus the purchase of veterinarian services;
3. That we can assume (perhaps rashly) a responsive and effective accounting system so that we may at any time determine our costs for salaries, supplies, animals, equipment, etc.

If you will permit me to make these assumptions, we can then proceed to look specifically at the problem of the $16½ million I mentioned earlier which is presently not being charged directly either as an animal purchase cost or on a *per diem* rate to the research programs in which the animals are involved but is rather being charged to other funds available to the investi-

gators or to the institutions. Generally speaking, the other funds available to the investigators or institutions are those that are being expended to meet the overall costs of maintaining the quality of the institution's animal programs. These "other funds" bear the cost of general services and expenses for the prevention, diagnosis, and treatment of diseases that occur in the laboratory animal population, the cost of the supervisory staff (veterinarians, superintendents of animal care, and supporting staff), and the costs of the operation of centralized facilities for animal care such as quarantine and conditioning, aseptic operating areas for general use, necropsy and morgue areas, centralized cage and rack washing equipment and storage areas. The critical issue is simply that these functions that determine and maintain the quality of the institution's animal care programs are not specifically supported by research animal-related grant funds. I need not point out to any of you that in times of financial stress these services and functions will be the first to suffer when other and higher priorities are assigned to the institution's and investigator's other available funds.

There are perhaps several possible solutions to the problem we are discussing today:

1. Tax the funds available to all investigators using animals to provide these additional "quality" services;
2. Charge for the services rendered on some equitable basis;
3. Include these costs in overhead; or, finally,
4. Provide specific funding to meet the costs of these "quality" aspects of the animal care program.

Of these several possible solutions, only the first and the last seem to offer promise.

One solution to the problem of self-sufficiency might be to raise *per diem* prices high enough to cover all expenses. According to the survey a 30 percent increase in *per diem* prices would be sufficient to eliminate the deficit—this type of increase would be within the ability of the system and the investigator to manage.

Let me briefly illustrate the impact of increasing the *per diem* costs of animal care by about 30 percent. The median cost of maintaining a rat for a day would increase from 3.6 cents to 4.9 cents. The median cost of maintaining an Old World primate would rise from 65 cents per day to 89 cents per day. I think you will agree that these seem to be modest increases. The fact that such a simple solution has not been successfully applied is in itself an indication of its inherent limitations. Such a solution places the total fiscal responsibility on that part of the system that is at present almost paying its way without attempting an equitable distribution of the cost of a quality

program over all those activities that benefit from the services.

Even if we were to ignore the equities involved, I must again point out what we all know, that we are currently in a period of severe financial stress and limitation of research funding and that each investigator must view all of his expenditures carefully with an eye to preserving the balance and integrity of his whole research program. Under these circumstances an increase in *per diem* rates to provide for essential central services may not be possible. The net effect might very well be to reduce the level of the institution's entire animal program so that fixed costs that are difficult to adjust downward might pre-empt the funding intended for the "quality" aspects of the program.

Only the last alternative seems to offer promise. I believe institutional administrators are well aware of the need and of their responsibility in these matters and are prepared to continue their support insofar as they are able to do so. Some have used General Research Support Grant funds to help in this area. These, however, are general purpose funds and are not appropriately assigned to specific continuing functions year after year.

I have no other choice but to conclude, albeit reluctantly, that we must again ask the National Institutes of Health to be responsive to this essential need that the institutions themselves may not be able to continue to meet. The fact that we have been encouraged and even required by federal regulations to provide these quality services in support of research involving animals is perhaps added justification for again turning to the National Institutes of Health.

Specifically, I would propose that there be established a special grant program in which the several National Institutes of Health would participate proportionately and that would be administered by the Animal Resources Branch, specifically for the support of central animal services, management, and facilities. I would propose that these grants be available to any eligible institution which applies for them, and that they be sized in relation to the institution's total NIH research support involving the use of animals over the preceding 5-year period. To provide for flexibility, I would hope that groups of institutions in the same geographic locality or various departments or parts of the same university or health center would be permitted or even encouraged to pool these grants to provide centralized services at a level that none of them could afford separately.

If these recommendations seem sensible to the members of this conference I would strongly urge that discussions be opened with the appropriate individuals and agencies of the federal government. As biomedical research demands more precise and accurate data the quality of the experimental animals involved and the provision for their optimal maintenance and care become ever more important to the success of the entire research endeavour.

An important aspect in the use of animals in research and teaching that has

moral, ethical, and financial overtones is the responsibility the academic community takes for the most efficient and effective design of experiments and/or teaching exercises using animals. I suspect that a broader familiarity with all the literature reporting animal studies would do more to improve cost-effectiveness than almost any other single step that could be taken. Perhaps effective faculty committees charged with review and approval of research programs involving animals could help bring collective knowledge to bear here.

How to bring the literature of importance to all those interested in mammalian biology—basic or applied—to the attention of each such individual be he biologist veterinarian, dentist, physician, ecologist, or animal husband—if that is the proper term—is a question I will leave with you.

DISCUSSION

DR. MELBY: Mr. Meadow has reviewed some of the problems we were discussing this morning. I was particularly impressed by comments at the conclusion of his paper concerning the quality of the experimental animals used in research endeavor. Isn't animal quality really the fundamental issue for us to consider? Isn't this why we are here today? If indeed this is the case, then solutions to our problems are not only important but mandatory to the well being of the entire research endeavor.

As one who has seen some of the animal resource problems at other institutions, I cannot agree with Mr. Meadow's assumption that all institutions are complying with the standards and guidelines contained in the *Guide for Laboratory Animal Facilities and Care.* Furthermore, not all institutions are in a position to comply fully with existing laws affecting animal research.

Many of us really don't know whether we are employing proper accounting methods within our laboratory animal programs. In the face of continually rising costs, this may be a reason for some of our financial problems. So many of the costs we face are indirect, would it not be better to use this indirect cost route to finance aspects of animal resource programs? Mr. Meadow, would you please comment on this?

Mr. Meadow has suggested the 30 percent increase in the *per diem* rate structure of the direct charges to users could wipe out our current problem. This might be true except for a couple of factors. One is the inflationary period we are in. A 30 percent increase today would have to increase to 45 or 50 percent next year, and in the following year it would be another 15 to 20 percent. At my own institution, for example, as of January 1, salaries of all union employees will be increased 15 percent and another 15 percent the following year.

MR. MEADOW: The whole matter of indirect cost reimbursement for re-

search activities in educational institutions is governed by the Bureau of Budget circular A-21. It has been in existence for about 15 years with rather frequent revisions recently. The circular sets forth accounting principles, and defines what can and cannot be included in research overhead.

Technically speaking, it would be necessary to again revise A-21 in order to support the quality aspects of the animal care program through the overhead indirect cost route. The suggestion that we try to do this is a good suggestion, and perhaps the organization under whose auspices we are meeting here today could press for this, although it is not going to be an immediate solution. I would like to see an opportunity for educational institutions to measure their needs for quality animal care programs against their available resources for these programs from year to year, and be able to apply to NIH for the support they need and that they cannot provide otherwise to their ongoing animal resource programs. I am not speaking necessarily of research or of innovation. I am speaking about the basic programs necessary to make productive the huge volume of animal research that is being carried on now and is going to be carried on year after year. If we let this go by the board, we have sacrificed a huge amount of money and effort, and this is what I don't want to happen, and I am sure that you concur.

DR. BERLINER: I am Dr. Berliner from NIH. What everybody is saying is that there are not any problems here that money won't solve. If we had sufficient funds, a mechanism could be worked out to pick up these charges in one way or another, whether it be as overhead charges, whether it would be by some special fund added to the general research support grants, or whether it was charged back as an increase in *per diem* cost for animals.

The problem is that no matter which of these mechanisms we select, we are going to take it out of the same pocket. It will all come out of the funds available for research, because the indirect costs are competitive with the direct costs. Every time the indirect costs go up, the amount of funds available for direct costs go down. If we put funds in the general research support area, they are in competition with funds in some other area. As a matter of fact, general research funds are very vulnerable under present circumstances.

It really all adds up to the same thing. There is no way of paying the core costs of animals except by either finding funds somewhere else or by charging them against the research in one form or another. We could discuss which would be the more appropriate way to do it, but it is going to end up having the same effect on the amount of research that can be done.

DR. MELBY: Dr. Berliner has presented us with a problem. There is limited money available. How can we most effectively use it? From our viewpoint, a most important area is the one we are considering today. We must make known the needs of animal resource programs.

What is our public image? Why are we having problems with the Bureau of

the Budget and the public at large? These questions were alluded to this morning. Perhaps we have misinformed the public, giving the impression that provided the proper amount of money, we could solve the problems of cancer, heart disease, and stroke. Now the public is saying, "We have given you so many billions of dollars over the years, and you have not yet solved these problems. Why should we continue to support you?"

This is a serious question that goes well beyond the question of supporting animal resource programs. It will require a cooperative and concerted effort to inform the public and to overcome the difficulty we now face.

DR. LES: Over the past ten years, there has been a gradual change in the type of service that the production department of the Jackson Laboratory has been providing.

Many laboratories that formerly bought animals from the Jackson Laboratory are now buying the parts of the animals that they need. For example, one laboratory that has been buying mice simply for the livers is now buying livers. This provides space that that laboratory formerly used for care of mice. This type of service has been expanding rapidly over the last ten years, and the Jackson Laboratory has found it is not capable of providing it, simply because the funds to develop the necessary facilities are not available. We have requests for animals that have been kept to age of three or four years for studying the effect of advanced age on various physiological parameters. In some cases we are able to comply with this type of request, but in most cases we are not. Those requests that require only short-term investment or that can be done fairly easily are complied with, and they are increasing in number. This is one way that research laboratories can economize, that is, by centralizing services of this type. Instead of each laboratory treating its own dogs or animals to where they can be used in research, a central facility might be more capable of supplying the animals after they have been brought to the point where they enter the research program. This is a way that might be more feasible to the organizations that support research.

DR. MELBY: Dr. Trum, may I now turn the meeting over to you for the last part of the afternoon program?

DR. TRUM: The ILAR survey has shown that approximately 30 percent of the cost of animal care is being supported by mechanisms other than recharges. A survey of the private institutions, at least, indicated that an average of $150,000 annually is being financed by the institutions from General Research Support Grant or unrestricted funds, to meet the quality requirements of animal care and animal care facilities. Ed Melby said that even this is insufficient for the purpose of complying with the present standards.

To summarize: Dr. Upton listed the priorities of society and the priorities of the institutions with respect to the continued need for animal research. Dr. Cohen stated that the quality factor in animal research centers and animal

facilities is being undermined. Quality is in jeopardy when its requirements are not considered at a higher priority in our research community. Dr. Davison emphasized that there must be a stability of operation and imaginative progress. Dr. Jones stated that on a University campus all of the academic units must make a commitment to quality animal care; it is not enough for the veterinary college only to make this commitment. Dr. Harrell pointed out that we have the information to do a good job of animal care. Now it is up to us to put this into actuality, and he showed how this could be done using his own institution as an example.

Policies of the National Institutes of Health in Relation to Animal Research and Resource Programs

Robert W. Berliner

The initial policies of the NIH regarding animal facilities and care largely grew out of its own intramural research support needs. In recognition of its responsibilities in a growing extramural grants program, in 1949 the Surgery Study Section developed standards for the *Care of the Dog in Medical Research* (U.S. Public Health Service, 1968). In recognition of the need to expand these standards to other animals used in medical research, a grant was made in 1952 to the National Academy of Sciences, Institute of Laboratory Animal Resources, to gather specialists from across the nation for discussions of their knowledge of the subject. Subsequent annual grants to the ILAR have resulted in the *Guide for Laboratory Animal Facilities and Care* (U.S.Public Health Service, 1968). The Public Health Service Policy Statement on Grants for Research Projects contains the following: "It is the responsibility of each person assigned or appointed to a project receiving any Public Health Service support to exercise every precaution to assure proper care and humane treatment of research animals, (PHS Publication No. 1024), should be followed. In addition, the grants policy statement makes reference to the animal care standards promulgated under Public Law 89-544 (The Laboratory Animal Welfare Act). Having preceded the law and its regulations, the Guide provided much of the substantive material upon which standards of the Laboratory Animal Welfare Act were based. In addition, the Guide will doubtless serve as a basis for any future legally-required animal care standards.

With the increased emphasis on support of extramural research in the late 1950's and early 1960's, NIH recognized that institutions required assistance in improving their animal resources. Well over half of NIH-supported research is dependent upon the use of animals. To maintain productivity and effectiveness of this medical research, high-quality animal resources are required. The first NIH initiative to support animal resources was a special program undertaken in 1960 to establish several regional primate research centers. At this time there was an obvious need to increase the use of simians in some specific research areas. The facilities and management knowledge for keeping

large numbers of these animals in a research environment had been determined to be lacking in most research institutions. Therefore, the Congress appropriated funds to establish and operate seven regional centers—each associated within a major medical research community—in which a core staff of experienced people would conduct research and provide the special skills and equipment for managing them for others on short-term basis. The research projects conducted within the centers are obtained through the regular competitive process, and the readily identifiable costs, including animal purchase and care, are charged to the project grants.

Concurrent with the establishment of the primate centers, there was a realization that individual institutions required assistance to improve many aspects of their animal resources. In 1960 a committee of consultants on medical research to the United States Senate Committee on Appropriations stated that there was an urgent need for improved research animal facilities, programs, and training throughout the country (U.S.Congress, 1960). This critical need was verified by an Institute of Laboratory Animal Resources survey made in 1967–68 that indicated that about 50 percent of the research animal resources of nonprofit, nongovernmental institutions could not meet all minimal standards for high-quality scientific studies (Institute of Laboratory Animal Resources, 1970). Therefore, in 1962 NIH established an extramural animal resource grants program administered by the Division of Research Resources. The purpose of this program is to assist institutions in improving or expanding animal resources needed for biological investigations and medical education. This is accomplished through grants for special animal colonies; research related to improving animal health care, disease diagnosis and control; studies directed to enhancing the usefulness of animal models for research, and general improvement of management and accommodations for institutional animal resources.

Essentially, the aim of the animal resource grant is to improve the scientific capabilities of the institution. Some grants are awarded to initiate and nurture new activities and improvements with the intention that these activities later become self-sustaining. Projects of this nature have assisted institutions in establishing centralized animal resource programs, dog and cat quarantine and conditioning programs, nonhuman primate colonies and breeding programs, improved animal health programs including clinical laboratory support, improved scientific management of animal resources, and purchase of cages and equipment and renovations to meet the standards of the *Guide for Laboratory Animal Facilities and Care*, and the Laboratory Animal Welfare Act. The objective in these projects is thus to capitalize a new or improved resource but not to provide a long-term source of funds for operations. Other activities often require long-term support. An example of this is the maintenance of a special colony of an unusual type of animal whose availability may be impor-

tant to a specific area of research. For example, recognition in the early 1960's of the value of inbred guinea pigs for study of many areas of immunology including contact hypersensitivity (Chase, 1960), tuberculin hypersensitivity (Bauer and Stone, 1961), anaphylaxis (Stone, 1961a), and the passive transfer of autoimmune encephalitis (Stone, 1961b) resulted in a sudden upsurge in the demand for inbred guinea pigs. This demand could not have been met if resource colonies had not been maintained when there was little interest in the use of inbred guinea pigs.

However, it has not been the purpose of the animal resource program to support total costs of all animal resource functions. It is our point of view that most of the animal resource costs should be borne by the research grant that uses the animals. A recent survey (Institute of Laboratory Animal Resources, 1970) indicated that 63 percent of animal costs are recovered on a self-sustaining basis. In the case of centralized resources, these costs may be recovered by fees for animals and services. The fee structure should be designed to recover costs that are readily identifiable and can be directly related to services provided to the user. These costs include animal caretaking labor and direct supervision; animal feed, bedding and consumable supplies; animal procurement costs; costs of processing animals, including vaccinations, routine tests, clinical treatments, etc.; and laboratory tests or surgery performed as part of an experimental procedure. These direct animal costs are obviously a legitimate cost of research projects. It is desirable that they be identified as such and reviewed by appropriate groups as part of the cost of the research project. Investigators must become informed as to the true costs of using animals in research. There is a great variation in the proportion of animal care costs identified and recovered among institutions. Greater uniformity in the recovery on animal costs would be desirable.

We recognize that some costs of resources do not rise and fall precisely with the volume of services provided. These are generally termed "core" costs and include such things as support for the director of the animal resource and his immediate staff and maintenance of central surgical facilities. These costs can be recovered through the fee mechanism when the resource is providing services at its anticipated level of utilization. However, problems arise when the level of use is temporarily below expectations, and the income generated from fees is not sufficient to maintain the core activities of the resource. While we recognize the problem, we do not believe it would be appropriate or practical for NIH to underwrite the core expenses of the 400 or so animal resources serving NIH grantee institutions. This we believe to be a responsibility of the grantee institution in the management of its own affairs. We are not unmindful of the financial problems faced by institutions; funds for these purposes are made available through payment of indirect costs, basic educational improvement grants, and general research support grants.

The General Research Support program provides support to advance and strengthen the medical and health-related research and training programs of institutions by complementing the research project system with funds to be used flexibly by the institution. Among the multiple ways a general research support grant may be used to benefit an institution is through establishment and operation of central research resources, such as animal facilities. Such resources should not be related to any one specific project or program, but should be essential to the general support of the health-related research and research training activities of the institution. In FY 1968, a total of $1,507,823 from general research support was expended for animal resources. These funds were used for purchase of equipment, animals, etc., and for support of personnel. General research support funds are frequently used as "seed" money for research projects. One example of how such funds may be used to advantage was the maintenance, last year, of a small, inbred guinea pig colony in which an endocrine abnormality similar to human diabetes was noted. Without this flexible means of support a resource to furnish animals for this important research might have been lost.

The animal resource and general research support programs are used for animal resources broadly utilized by investigators in a wide variety of research endeavors. However, categorical NIH research institutes have responsibility for supporting animal resources used exclusively for research within the institute's area of responsibility. For example, the National Institute of Child Health and Human Development is supporting an animal colony for the purpose of providing senescent rats required for its grantees conducting research on aging. The National Cancer Institute supports several animal colonies required by investigators in its Special Virus Cancer Program; and the National Heart and Lung Institute has provided support for development of animal models of myocardial infarction.

Thus, it is NIH policy to support research animal resources through a variety of mechanisms including animal resource grants, fees charged to research grants, institutional support grants, and support of categorical resources by the appropriate institute. We view the NIH responsibility to be the payment of animal costs clearly associated with its sponsored projects and the assurance that high-quality animal resources are available as required by its grantees. The resource should serve the purposes of the ongoing research and the associated costs of operation should be as nearly as possible related to project needs. Charging of fees for services to research grants makes the resource responsive to research requirements. Without such control, resources could tend to become ends in themselves. Where there are requirements for central control, such as general supervision, disease surveillance, air-conditioning and ventilation, general maintenance and legal compliance, the institutional responsibility is clear. Where there is a need to improve the scientific capability of an

animal resource or to maintain special animal colonies and capabilities, the resource grant is the most desirable mechanism because it ensures high quality in these efforts through the competitive peer review system. Resource grants are given a review similar to that given research grants. This has been an important stimulus to increasing quality of animal resources because only projects that are scientifically meritorious and administratively sound are supported.

The results of the recent national survey of laboratory animal resources conducted for the NIH by the National Academy of Sciences (Institute of Laboratory Animal Resources, 1970) shows that there is a substantial need for additional construction and equipment in order to attain the standards currently recommended. While large expansion of research activities, such as we have witnessed over the past 15 years, is unlikely in the near future, the data from this survey will be very useful in formulating budgetary decisions relating to laboratory animal programs.

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DISCUSSION

DR. TRUM: Dr. Berliner's remarks following Dr. Melby's session should be considered with his presentation. He clearly pointed out that all research funds, whether dispensed directly or indirectly, are from the same budget and are, in fact, in competition.

It is important to the overall research program to make priorities high

enough to effect the continuance of a quality program. A program dependent on "cost recovery" entirely does not have sufficient stability, and Dr. Berliner has pointed out that one dependent general research support, "is [in] a very vulnerable area under present circumstances."

Dr. Berliner, I think, I express the thought of all of the people who have worked in this area over the past twenty years. We are very grateful for the support that has come out of the NIH. This research support has helped in the upgrading of care. We are searching for the method to sustain the gains in this area and, unless a change is made in the policy, we are in for a serious downgrading.

I am not in any way castigating Drs. Berliner, Eyestone, or Bowery, but if they don't believe this lack of financial support can be downgrading then they should look at the NIH facilities. There hasn't been proper support in NIH and these conditions are apt to be reflected all through the country. Support of animal facilities deserves higher priorities and this is one of the reasons we are here today, to talk with each other and to try to convince others of the necessity for these priorities.

Policies of Private Granting Agencies in Relation to Animal Research and Resource Programs

Stefano Vivona

In the correspondence inviting me to present a paper at this conference, three related questions were suggested for my consideration:

1. How (do) private granting agencies, such as the American Cancer Society and others, determine priorities for support of animal research and resource programs?
2. Given present day standards for use and care of animals, what should be the role of private agencies in supporting implementation of the standards?
3. Are these agencies receiving adequate input regarding the complexities and costs scientific institutions face in assuring high standards?

So that the views of other private granting agencies, in addition to those of the American Cancer Society might be presented, letters requesting comments or answers to these three questions were sent on August 4, 1970, to the following:

American Heart Association, Inc.
Damon Runyon Memorial Fund for Cancer Research, Inc.
Epilepsy Foundation of America
Leukemia Society of America, Inc.
Muscular Dystrophy Association of America, Inc.
National Cystic Fibrosis Research Foundation
National Foundation
National Multiple Sclerosis Society
National Tuberculosis and Respiratory Disease Association
United Cerebral Palsy Associations, Inc.

The addressees were assured that the source of any information provided would be kept confidential.

As of the end of October, approximately three months after these requests for information were sent out, six of the ten agencies had acknowledged receipt of the request and five had provided some comments on one or more of the three questions.

In regard to the first question, four of the five agencies responding do not have rigid criteria for determining priorities for the support of animal research and resource programs. The fifth agency has a policy of not making awards specifically for the purchase of animals or for the establishment of animal colonies. The American Cancer Society does not have a written policy regarding support of such programs. However, the Society's awareness of its responsibility is demonstrated by three ongoing grants to

- The National Society for Medical Research: $1,500 per year from 1966–1970, for a total of $7,500.
- The Institute of Laboratory Animal Resources, from 1957–1970, for a total of $94,500. The 1970 contribution amounted to $14,000.
- Dr. Earl L. Green of the Jackson Laboratory, Bar Harbor, Maine, from 1959–1970, for a total of $188,506. Dr. Green's 1970 grant amounted to $24,000. These funds are provided for the maintenance and study of select mutant strains of mice and also make it possible for Dr. Green to provide these mice to other investigators.

Three responses received to the second question, concerning what should be the role of private agencies in supporting implementation of the standards for use and care of animals, were somewhat varied. One stated "It is the policy of the . . . not to make awards specifically for the purchase of animals or for the establishment of an animal colony for research. Therefore, standards or qualifications for animal use and/or care have not played a role in the processing of our institutional grants." Another agency stated that it requires that signatures be submitted by responsible investigators and administrative officials guaranteeing that research involving animals will conform with the "Guiding Principles in the Care and Use of Animals" approved by the Council of the American Physiological Society. The third agency commented that a private organization that funds research does have a certain responsibility to ensure that high standards for the use and care of animals are maintained. However, this responsibility is secondary to that of the investigator and the institution where the work is to be carried out.

The American Cancer Society's position on this matter is very similar to this viewpoint. The Society's legal advisors have ruled that its obligations in regard to both human experimentation and standards for use and care of animals are met by the statement that appears in our policy brochures:

The American Cancer Society, in awarding such grants, does not assume any responsibility for the conduct of the investigation or the acts of the investigator, since both are under the direction and control of the grantee institution and subject to its medical and scientific policies.

Speaking as an individual and not as a spokesman for the American Cancer Society or other private granting agencies, I believe that the American Cancer Society's approach to implementation of standards is the only feasible one for most private granting agencies. In our case, our staff and our budget for administrative activities do not permit appropriate inspections and surveillance of our grantee's practices, no matter how desirable this might be.

Only one of the five spokesmen who provided statements commented on the third question, "Are these agencies receiving adequate input regarding the complexities and costs scientific institutions face in assuring high standards?" His position and that of the American Cancer Society are in complete agreement; namely, that it is the responsibility of the funding agency to make itself aware, through its scientific advisory committees, of the costs of doing research. These committees, if properly balanced, can provide most of the knowledge concerning the mechanics and problems facing the institutions and their attempts to maintain appropriate conditions and practices for the conduct of the research to be carried out.

In summary, I have one plea to make to the private granting agencies. It is that they include on their scientific advisory committees at least one member who represents the veterinary profession or who is well versed in the field of laboratory animal science. This would go a long way in helping the agency to maintain a continuing state of knowledge in the area of animal research and resource programs and to develop reasonable policies.

DISCUSSION

DR. COHEN: Assume that a grantee of the American Cancer Society had research under way of great importance to the Society, involving large numbers of animals. Assume further that the animals required veterinary care and diagnostic services that could not be paid for because these requirements were not programmed. In these circumstances, would the American Cancer Society provide support to assist a grantee such as this to protect the health of animals used in research sponsored by ACS?

DR. VIVONA: That is a good question. Those of us on the staff make almost no decisions concerning who does and who does not get support. The American Cancer Society is directed entirely by the volunteers. The senior vice president for research does have the authority to supplement a grant in

effect up to $5,000. We have had 23 granting periods a year but we are going to two. Approximately 50 to 75 grants a year are supplemented by from $50 to $5,000 each. This is a mechanism to take care of an emergency situation.

The work must be connected in some way or other with cancer research. Cell growth including normal cell growth is certainly related to cancer, therefore, we are not really bound to rigidly, but we do have to be mindful of our mission. Does this begin to answer the question?

DR.COHEN: I don't think it answers it at all, but you touched on the very heart of the problem. While the investigator who is faced with an emergency is desperately getting on the phone to reach Dr. Vivona or Dr. Mason saying, "I have a terrible disease problem in my mice, and the animal resource people would like to do some necropsies and provide veterinary care services, but they need to have these activities paid for," the investigator may lose his entire colony. We faced such a situation some years ago.

DR.VIVONA: Maybe I don't understand the problem too well.

DR. COHEN: Isn't ACS omitting an important area of responsibility by assigning funds directly to a grantee without taking into account his requirements for animal resource support that could make or break that research. The cost implications to the institution in providing these supporting resources must be considered.

DR. VIVONA: If an investigator has this big a problem coming up in his research, I don't see how he can continue with his research. Since he can take our money and use it in any way that he wishes in order to get his work done, if he can't continue his work because he has this big disease problem, and he has $30,000 left in this one year to do the work, he can use that $30,000 to fight this disease problem if he believes this is the best way to spend his money. Maybe I am missing a point. Our hands are tied in that this is an organization run by the volunteers, and we do have to be very careful. They collect the money, and they direct its use. If such a big disease problem were to be encountered, the proper thing to do would be to solve the problem, not to continue with the research. Otherwise, we have research of the quality obtained with a $5 mongrel dog.

It is most important, whenever it can be accomplished, that no research be done until a protocol has been reviewed by the statistician, the veterinary staff, and the animal care technician regarding proper care and housing to ensure that the design of the experiment is adequate, in view of the differences expected, and that the investigator does not use ten times the number of animals required to prove a hypothesis. We have seen this done, where many more animals were used than were required to prove the point.

MR. MEADOW: Dr. Vivona, the exchange between you and Dr. Cohen has brought out clearly that we can't handle these problems unless there is in existence a program in the institutions. If there is to be a program, there must be

continuity of support. Decisions must be made about expenditure of limited funds with respect to the direct costs of the animals, their care, and the maintenance of quality programs. Decisions within the institutions must be made in relation to this funding not available from research funds.

As pressure increases for other uses for funds over which the institutions have the power of decision, it may be that our programs of quality animal care are going to be reduced. I am suggesting that, since much of the national research program support is tied to animals, we might begin to involve some national decision making with respect to how money is used to support animal care programs in the institutions. It is not a question of more money. There isn't any more money. It is a question of how the money is to be used.

DR. M. B. STARNES: (University of Texas, Southwestern Medical School at Dallas) We have overhead money in connection with federal funds, but we don't have such overhead money in relation to contracts and awards from private sources. What are other institutions and schools doing about obtaining from private sources the kind of overhead grant money that they normally receive from federal funds?

MR. MEADOW: I think I can answer that question by telling a little story. When I was young and very new in research administration, Allen Gregg was then vice president for medical affairs of the Rockefeller Foundation. I went down to see Dr. Gregg about this very problem of overhead. We had just received a grant at Harvard from the Rockefeller Foundation, and there was no overhead attached to it. I went down and I very carefully explained the problem to him, and he shook his head in agreement, and he said, "You know, this is a real problem. It is one that certainly should be solved. I think the way we are going to solve it at the Rockefeller Foundation is the following: The first institution that turns down a grant of $5 million because there is no overhead is really going to bring the importance of this problem to our board of trustees in a way which will bring action.

Unmet Needs in Laboratory Animal Care— A Realistic Assessment

Willard H. Eyestone

INTRODUCTION

During the course of the past ten years, several developments have been instrumental in the assessment of resource needs for the management of laboratory animals used in research and teaching. These are (a) a survey conducted in 1961 on a selected sample of 561 nonprofit, nonfederal research institutions (Institute of Laboratory Animal Resources, 1964); (b) the passage and subsequent enforcement of Public Law 89-544 in 1966; and (c) a comprehensive survey in 1968 that focused on animal resource requirements of nonprofit organizations eligible for federal grants and also included certain data from federal agencies, commercial laboratories, and the pharmaceutical industry. (Institute of Laboratory Animal Resources, 1970). The criteria upon which most responses to the two surveys and, in large part, the regulations of Public Law 89-544 are based on is the *Guide to Laboratory Animal Facilities and Care* (National Institutes of Health 1968) developed by the Institute of Laboratory Animal Resources and sponsored and published by the (NIH). In addition, numerous articles on laboratory animal science, technology, and medicine have been published in the scientific journals, such as *Laboratory Animal Care*, and have provided further criteria upon which to base assessment of animal resource requirements.

The 1967–1968 ILAR survey (Institute of Laboratory Animal Resources, 1970) represents an enlightened estimate of animal resource requirements by institutions using laboratory animals in research and teaching. An assessment was made of the needs based on the 1968 requirements and on projections into 1973, presumably based on a growth rate in federal research funding similar to that during the years 1963–1968. For the present at least, it does not seem realistic to expect that the national expenditures for medical research will increase by 1973 much above the 1968 level, although the expansion of health professional education does appear likely to increase moderately. The survey indicates that roughly 20 percent of the animal care facilities of teach-

ing and research institutions are for animals used in teaching programs. Therefore, the estimates of need for 1968, plus a very modest annual operating increase through 1973 of perhaps 5 percent per year, would probably be a little closer to realism than the 1973 figures in the survey. Taking this into consideration then, the more realistic estimate of unmet needs for the present through 1973 are nearer the 1968 figures in the survey than those projected for 1973.

FACILITIES AND EQUIPMENT

The inventory of present space for animal facilities as related to research laboratories revealed about a 1:5 ratio. This is an actual ratio and is not necessarily optimal. If a judgment had been made on an optimal ratio, it would probably have been closer to 1:4. Some relief from pressures for space has been made by acquiring off-site facilities in nearby rural areas where building and maintenance costs are usually much lower. Quarantine and conditioning, plus long-term holding of the larger laboratory animals and farm-type animals, can be conducted in such facilities, often more advantageously as well as more economically. Currently, about 14 percent of research organizations have off-site animal centers, but almost three times this number report that they will need off-site centers by 1973.

Of the 7.6 million net square feet of animal space reported in the inventory, it was estimated that slightly over one million square feet, or about 25 percent, needed either renovation or total replacement. Again this figure represents 1968 estimates of need. The cost-estimate for new construction, and equipment, plus remodeling, and renovating, was $191,000,000.

In several respects, significant advances have been made since the 1961 survey of animal resources. Currently, 53 percent of the surveyed institutions have cage washers, compared to 32 percent in 1961, 77 percent have air conditioning, compared to 51 percent in 1961; 43 percent now have emergency sources of electrical power, compared to 27 percent in 1961.

TRAINING

Specific programs for postdoctoral training in laboratory animal science and medicine have developed during the past decade. Nine such programs are supported by the NIH, two by the military, and several by other agencies and institutions. The training periods provided are usually for 2 to 3 years, and most lead to advanced degrees. Most are designed to prepare the trainee for examination by the American College of Laboratory Animal Medicine, but several

emphasize laboratory animal pathology and prepare the trainee for the American College of Veterinary Pathologists' examination. Almost all trainees have been veterinarians, but an occasional one has been a physician or a PH.D.

It is interesting to note that of the 56 trainees who have completed the NIH-supported programs, 52 are now engaged in laboratory animal care activities, 28 of them being directors or staff members of vivaria, and 24 being engaged in research or receiving additional training. Presumably, those trained under the auspices of other agencies and institutions are also using their training in animal care activities. Military training programs are making a contribution to civilian institutions also, in that several trained veterinary officers have retired and accepted civilian positions in laboratory animal resources. It appears that, with the exception of laboratory animal pathologists, the training output of existing programs is coming close to keeping pace with present needs. However, the projections in the survey indicate a widening gap over the next 5 years.

In training, quality is probably a more important consideration than quantity. There is an evolution in training programs that reflects an awareness that the veterinarian's contributions to animal resources should extend beyond clinical care of animals and the professional direction of laboratory animal facilities. The specialist in laboratory animal medicine should be the animal resource specialist on multidisciplinary teams. He should be prepared to do research on animal resource problems, including the elucidation of new animal models. He should be prepared to offer advice and cooperation on experimental animal techniques and the choice of models for research projects. In an academic setting, he may teach courses of medical significance. Of course he is always an informal teacher of technicians, colleagues, and investigators. Training supported by the Animal Resources Branch of the NIH reflects a broad scope of activities through which individuals contribute to the use of animal resources for biomedical research and education.

The survey revealed that institutions ranked the training of animal care technicians as their number one training requirement. The training of these entry-level animal care technicians poses a special challenge. They are numerous, but comparatively transient. They must be trained in small groups soon after their employment and near to their place of employment. The training must transmit practical knowledge about work techniques and appropriate background information in animal biology and provide motivation and the desire to do a good job. These requirements cannot be easily met. The most realistic approach seems to be to develop an excellent program of instruction that can serve as a basis for use by a wide range of biomedical organizations to provide training to animal care technicians employed by them and other institutions in a geographic area. Such a course would probably make use of the techniques of programmed instruction, printed material, audiovisual devices,

direct instruction, and on-the-job experience. It should be sufficiently structured that many institutions could use it without the necessity of expending great effort in developing instructional and background material. Yet the course should be of sufficient flexibility that it could be adapted to a variety of institutional situations. The Animal Resources Branch of NIH is currently planning to support initial efforts to develop institutional material for training of animal care technicians.

RESEARCH

For the advancement of any field, discovery of new information is essential. Well-designed research projects must be conducted in important diseases of laboratory animals. Our knowledge of significant diseases, such as mucoid enteritis of rabbits, pregnancy toxemia of guinea pigs, chronic murine pneumonia, and respiratory disease of random-source dogs and cats is woefully inadequate. Research aimed at developing new and improved techniques relating to husbandry, reproduction, and management of laboratory animals is needed in order to match the needs of the scientists who use them. Environmental factors, such as caging, temperature, light, air flow, and exercise should be scientifically evaluated to establish meaningful standards for the care and maintenance of laboratory animals. Work is also needed to define more closely the usefulness of animal models for research on human diseases. Research on some human diseases is currently being impeded by a lack of suitable animal models. A partial list of such diseases include cystic fibrosis, chronic recurrent bronchial asthma, myocardial infarction, gallstones, rheumatoid arthritis, infectious hepatitis, pernicious anemia, and gout (Prichard 1968).

OPERATIONAL FUNDING

This symposium has dealt extensively with the funding of animal resource activities. Two facts that must never be overlooked are that well over half of biomedical research is dependent on the use of animals and about one-eighth of the cost of animal research is spent for animals and animal care (Institute of Laboratory Animal Resources, 1970). It is necessary to seek ways to reduce animal costs. There are several ways by which this can be accomplished:

1. Use of higher quality animals, thereby reducing death losses and random error in order to obtain significant results with fewer animals. For example, it has been documented that use of high-quality laboratory-reared dogs reduces death losses following prosthetic heart valve replacement by 20 percent, com-

pared to conditioned random-source dogs (Fletcher *et al*, 1969). Even with the greater initial expense of a better quality dog, savings in total cost of operative and postoperative expense per usable valve replacement are calculated to be approximately $50.

2. Reduction of covert and overt disease in animal colonies, thereby reducing costs due to death losses and possible misinterpretations of experimental results.

3. Greater emphasis on operational analysis in animal resources. Studies of cost effectiveness or cost-benefit ratios would aid greatly in economic management of animal resources. They could form a basis for such administrative decisions as the amount of investment to be made in animal disease control, installation of automated animal care systems, design of animal buildings, and purchase of animals and services from commercial sources as opposed to institutional production and services.

ANIMAL BREEDING

Another unmet need in animal resources is the greater availability of dogs and primates bred specifically for research. Over 75 percent of the rodents and rabbits used are bred specifically for research, as are half of the birds, ungulates, and other animals. However, 94 percent of the dogs and 86 percent of the primates are obtained from random sources (Institute of Laboratory Animal Resources, 1970). Increased emphasis should be placed on the use of colony-reared dogs and primates. Not only would such animals be of higher quality, but the dependence on random sources is hazardous because of public attitudes regarding use of animals that may have been pets and because of diminishing supplies of wild primates.

Numerous scientists and scientific groups (Fletcher *et al*, 1969) are becoming more concerned about the quality and quantity of nonhuman primates that can be obtained from the wild. It is becoming increasingly difficult to obtain many of the required species because of the destruction of natural habitats and nationalistic concern with conservation of species. For example, Colombia has begun to enforce regulations concerning export of primates, and this has greatly complicated the acquisition of owl monkeys (*Aotus trivirgatus*). Brazil currently prohibits the export of squirrel monkeys (*Saimiri sciureus*) except by special permit. Under the Endangered Species Act (P.L. 91-135) the United States is forced to exclude animals from countries where their exportation is prohibited.

We must obtain an accurate assessment of wild populations of primates and determine the most feasible methods of domestic breeding.

RECOMMENDATIONS

In summary, the unmet needs for animal resources are

1. Replacement of outmoded buildings, cages, and equipment still in use.
2. Continued improvement and understanding of animal disease control, nutrition, genetics, and environmental requirements in order to obtain superior research results.
3. Improved training of professional laboratory animal medical and scientific personnel.
4. Innovative methods of training animal care technicians.
5. Greater use of modern cost effectiveness management in animal resources.
6. Assurance of a reasonable supply of high-quality animals through domestic breeding of those species currently obtained from random sources and nature.

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DISCUSSION

DR. TRUM: Dr. Eyestone pointed out that at the present time there are in-house teaching programs for technicians. This is just another area in which there is no specific support given. This is a direct cost to each university or to each institution.

We seem to agree on the need for support of colonies of certain rare research animals. However, support for colonies of dogs, cats, guinea pigs, mon-

keys, or great apes depends upon the specific research in which they are currently used. We have yet to develop a policy through which the support of these colonies can be justified by potential scientific value.

At this moment, colonies of rare biological specimens and endangered species are being destroyed because we lack a policy in which the mere preservation of such valuable stock is sufficient reason for support. Must we wait to be forced by the public through legislation to do what we know is proper?

DR. GRAFTON (University of Buffalo): One of the things that seems to be a significant problem is lag time. This is part of the problem that is confronting us all. An investigator prepares a research grant proposal, based upon the best information at hand, and sends in the proposal, which takes months or a year to receive final approval. In the interim, the director of the animal facility finds that costs are going up, and by the time the investigator gets his grant and gets started in his program, he finds that costs exceed his projections. It would help if the time lag between cause and effect, proposal and receipt of grants, could be narrowed.

DR. COHEN: Dr. Berliner, did I hear you say in an earlier discussion, that it would be feasible for institutions to negotiate the indirect costs of certain animal resource programs? Mr. Meadow said, I believe, that the present regulations and policies in Circular A-21 do not permit such negotiations. Could this point be clarified?

DR. BERLINER: You heard us both correctly. I did not say, however, that this should enter into the negotiation, because the rules that determine the indirect cost rates are more or less rigidly fixed, and these must be modified before any changes of this sort could be made. I did say there was nothing to prevent the institution from using funds that they receive for indirect costs in part for this purpose. This in an institutional decision, and they have lots of things they want to do with those indirect costs. You may have trouble persuading them that this is where they should put it.

DR. TRUM: This approach is apt to be futile. All indirect costs have to be properly designated and justified before they are collected. Since only part of the justifiable indirect costs are being paid at present, we would be adding to that deficit without any guarantee that the institutional allocations would be made directly to the animal facilities or to buildings and grounds for maintenance in order to offset other losses in support of research facilities.

MR. MEADOW: There is not a single solution to this problem. In some institutions you may call the researcher's attention to the general benefits that animal services offer and persuade him that it is more important for him to put some money directly into these services than it is to spend it for dogs, cats, mice, or rats. In other institutions you won't be able to do this. You will have to work out another method of financing. Each institution should attempt to finance it the way that seems best, but there should be some rec-

ognition on a higher level, whether through the ILAR, the NIH, or others about the importance of these problems to the national research community.

DR. ROBERT W. OGILVIE: I am Dr. Ogilvie from South Carolina. Dr. Berliner implied that the general research support grant is a realistic source of funds to support the animal service, equipment, and personnel in the centralized facility. At the Medical School of the University of South Carolina, everyone is seeking such funds, but they are used up by those who are not funded. We do not have a policy whereby we grant these funds directly to the animal care department for any purposes they may have.

Is there anyone here with experience in which certain amounts of the general research support funds have been delegated before they are distributed to the investigators at large?

DR. HARRELL: In our school, we do take part of the general research support grant and allocate it before any other distribution is made to support the animal technicians, particularly in the central animal facility.

DR. CHEEVER: I am Dr. Cheever from the University of Pittsburgh. We follow the same general policy that Dr. Harrell has described. Some of the general research support goes directly to the support of a common animal facility.

Conference Summary

Thomas B. Clarkson

As Chairman of ILAR, I have been asked to summarize the conference on the future of laboratory animal resources. I have taken notes as all of the speakers have talked, and my summary will not only review many of the things they have said but, in addition, will include the impressions that I have gained today about the future in our field.

It is important as we think about the future of the laboratory animal resources that we think about fiscal problems as being only one of five major categories of concern that the speakers have touched upon today.

Fiscal problems which can be divided into funding as related to animal care activities and as related to the academic and professional core activities of the animal resources were discussed. Second, the matter of facilities was discussed, and the requirements for future facilities. Third, programmatic directions for the future were discussed. Fourth, the staff needs to meet these programmatic changes of the future were considered. Fifth, the communications problems, both as they relate to our public constituency and to our peer scientists who might be less familiar with animal resources problems, were reviewed.

FISCAL PROBLEMS

Turning first to the fiscal problems, Dr. Cohen commented that since the mid-1960's, the animal resource area has evolved to the point where we see increasingly that the units have responsibilities for administering not only the programs of animal care but programs of teaching and research as well. In order to clarify the budget problems of the future, we must separate these activities clearly. Looking first at the animal care financial problems of the future, I do not think that there should be major problems. It has been pointed out by many of the speakers that precise cost accounting will be increasingly important in order to identify the real cost of caring for animals and that we must take this real cost and see that it is charged back to the individual investigator or program on a *per diem* basis.

It has become apparent from the papers presented here that we are going to need improvement in personnel practices. Dr. Eyestone pointed out that

we need time and effort studies, studies of cost-benefit analysis, and the use of newer mechanical methods to reduce the labor cost of animal care. It seems clear to me that, if we do these things, we can reduce animal care costs. If we can identify them by good accounting, we can project these in research grant budget requests.

Concerning the financial support of the academic or professional core of the animal resources, I think there are two broad problems. The first of these relates to the teaching and research activities and other activities related to the professional core. The teaching activities are clearly the responsibility of the academic institution, especially if they are directed toward the undergraduate level. Support for the faculty members in the animal resource and for those things that are immediately associated with faculty effort—secretarial support, office supplies and so on—are clearly the responsibility of the academic institution. Research training related to graduate programs and postdoctoral education must continue to have federal support. Federal support of these programs should continue to be on the basis that is meritorious and is filling special needs as they relate to the animal resources.

Dr. Eyestone pointed out that we are presently meeting the training needs for laboratory animal specialists. It is essential that this continue, and that the Animal Resources Branch of NIH continue to support these programs.

The need for veterinary pathologists to support animal resource programs is increasing and, no doubt, will continue to increase. It will be important that the Animal Resources Branch of NIH find some way to provide the support necessary to fulfill these requirements.

In summary, the problem of financial support for teaching within the animal resource can be considered in two categories. If it is undergraduate teaching, it is the academic institution's responsibility. If it is graduate or postdoctoral teaching in an area of critical national need, and the unit has an unusually good capacity to meet this need, it should be deserving of federal support.

Research support for animal resources seems to me to be a relatively clear-cut question. The research efforts must compete with all other efforts for available research funds. No doubt, support in laboratory animal research will rise and fall with the fortunes of researchers in all of the biomedical sciences.

The second broad category, concerns the complex funding patterns for the professional core of the animal resources unit. Dr. Cohen has emphasized the complexity of the problem in his discussion earlier in the afternoon. Stated simply, how do we have continuing support of those core programs in a laboratory animal facility? It has become absolutely essential to those of us in laboratory animal resources to have good laboratory support, whether it is a diagnostic laboratory or radiologic support or surgical resources. It seems clear to those of us in the field that it is impossible to fund these on a recharge mech-

anism. We have all had experience with this, and I think anyone who has tried it will agree that we cannot support them adequately on a recharge basis.

If one accepts this as being the case, that leaves either of two sources: the academic institution or the grant agencies. The attitude of most institutions seems reasonable to me. That is, these core resources are needed primarily to support the research activities under support of the granting agencies, both federal and private. They are in large part not necessary for the teaching programs of the institution; thus support for them should in some way come from the granting agencies. The mechanisms for support of these core activities were reviewed by Mr. Meadows, but no single mechanism was identified as the best. It seems important that several be tried and the most effective one found. From the discussion, it would appear most of the animal resources feel the keenest need at this particular time.

FACILITIES

The problem of facilities was touched upon by several of the speakers. Dr. Harrell emphasized the need for the kinds of facilities and staff that would instill in the students a professional attitude toward the animals that would carry over to their attitudes toward patients. This is certainly a true observation, and I think the attitudes that students develop early do carry over to their attitudes toward patients in later years. This observation calls for new and better facilities and more thought about this problem in future years.

Closely akin to this observation is the idea of continuing and improving the quality, and the words "quality" and "standards" have come out many times in our discussions today. Many of us have spent many years in trying to define these standards and to further evolve them. It is absolutely essential that quality be maintained and that the standards continue to improve. This can be done only by continuing to improve the facilities in which animals are kept, seeking new and better ways to house animals, and better defining the environmental needs for the species usually used.

We have heard about the need for off-campus facilities, and I think those institutions that have experimented with off-campus facilities have found them to be one of the solutions for improving animal care. I think we will see this concept grow in the future to become an important part of almost all large animal resources.

As a part of this off-campus concept, we will be increasingly involved with breeding colonies of specialized kinds of animals. As research moves toward the seventies and eighties, experimentally induced disease will be much less frequently used, and naturally occurring diseases will be much more the subject of investigation. In order to have these disease models available to us, it

will be necessary that colonies of animals be maintained. This will require breeding facilities of types that we have not conceived yet and a wider use of off-campus facilities.

PROGRAMMATIC DIRECTIONS

It was of interest that almost every speaker spoke of the need for more and better animal models and of the need for further elucidation of the animal models that now exist. I have believed for some time that this will be an important programmatic area for the laboratory animal resources group in future years. It was pointed out to us that the short-lived diseases are now nearly a thing of the past and that our primary concerns, as far as human health is concerned, are for the chronic and degenerative diseases. Most of these must be studied in long-term experiments. Most are associated with genetic susceptibility and resistance. Most will require suitable animal models before they can be understood. So the animal model business is going to be a very important part of the future programmatic direction.

In addition to these special colonies of animals that have genetic characteristics associated with chronic and degenerative diseases, I expect in the future we shall have to meet a part of our need for animals that are becoming scarce in nature by domestic breeding colonies. We cannot depend upon a continuing favorable political climate in certain areas where essential research depends upon this climate, nor can we depend upon the haphazard supply of these animals in nature, where habitat destruction continues. We must prepare to meet these needs, either regionally, nationally, or institutionally, for species that are essential but appear threatened for one reason or another.

A third programmatic direction of the future will be an increased emphasis on ecologic and ethologic directions. Many of our society's problems presently, and as we project them in the future, have to do with the environment and behavioral aspects related to adaptation to the environment and to other pressures of our society. It will take some imaginative and creative efforts to find the correct comparative or experimental animal approaches to these problems.

Another problematic challenge is the evolution within our academic institution of mission-oriented institutes or study centers. Dr. Davison made reference to these problems. Increasingly, our universities are being asked to address themselves to some of the critical problems within our society, particularly heart disease, cancer, and strokes. One way of responding to these is to form interdisciplinary institutes or interdisciplinary study groups within the university. The size of these groups is going to be large in the future and is going to require a different type of orientation among those of us involved in the animal resources area, particularly at the interface of comparative medicine and

comparative pathology, and how we can best support these broad mission-oriented study centers is a matter of concern.

At the same time, it is important that we preserve the individual professor's approach, as Dr. Davison pointed out. All of us feel protective about the individual professor's freedom of investigation, his own approach, the fundamental and basic science approach, and we must continue to have the ability within our animal resources to respond well to these sorts of individual project-oriented research activities while at the same time developing our ability to respond to the center or institute mission-oriented activities.

PERSONNEL NEEDS

It is apparent that we must continue to study and broaden our scope of post-doctoral education in the areas of laboratory animal medicine, comparative medicine, and comparative pathology in order to meet these problematic challenges of the future. We shall need additional interested people and experts who can develop new animal models and the concepts on their use in solving future problems.

COMMUNICATIONS

The need for better communications between the whole area of the biomedical sciences and the public at large became very clear during this conference. This is particularly true with those of us using animals in research. I hope that all of us in laboratory animal medicine will be increasingly concerned about speaking to the public on this issue at every opportunity that we have.

An equally important aspect of our own communications problem is with our peer scientists who are not familiar with the animal resources area. Many of us have had the experience of serving on a review group considering grant applications where the quality of the animal care, the animal care staff, and the animal care facilities are very often the last thing to be considered in determining the merit of the proposal. It seems that we have not been entirely successful in our efforts to communicate to fellow scientists in other disciplines what their real stake is in the animal resources, how valuable these resources are to research productivity, how dependent their proposed projects are upon these resources, and how important the continued research productivity is upon the continued improvement of these research resources.

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