ADVANCES IN VETERINARY SCIENCE AND COMPARATIVE MEDICINE

Edited by

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Urbana, Illinois

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University of Florida
Gainesville, Florida

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VOLUME 22

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PREFACE

Constituting this volume are selected reviews and evaluations of recent significant advances in knowledge of areas of veterinary science and comparative medicine. The authors deal ably with widely diverse yet often inseparable factors (e.g., environmental, physiologic, immunologic, and infectious) that impinge on the well being of man and others in the animal kingdom.

Emphasized in the initial chapter is the lack of "exquisite" control of the environment in which experimental animals are held, e.g., physical factors such as chemical contamination may entirely vitiate the data obtained from biologic experiments. Indeed, the impact of minor changes in environmental temperature, humidity, and light, even as influenced by tier cage location in an animal room rack may significantly influence the outcome of well-planned biologic research.

In the second chapter consideration of less well-known effects of hyperthermia on prenatal development, teratogenesis, and mortality among numerous mammalian as well as avian species is interestingly revealing. Also significant scientifically and economically are newer findings that exposure to temperature and various other adversities seriously jeopardize adaptation of the fetus from intra- to extrauterine existence, thereby contributing to fearful perinatal mortality rates among many animal species. Newer evidence confirms that differences in such reported losses among species and countries are associated with defects in the diagnostic approach, and in the recording and evaluation of accumulated data, thus suggesting the urgent need for a comprehensive and judicious attack on the problem, something that Australian workers have initiated.

Next recorded and evaluated are recent advances derived from study of the characteristics of losses from the following: (1) a number of viruses that widely attack the respiratory tract of cattle to inflict major morbidity and mortality losses; and (2) the current epizootiologic enigmas typifying viral bluetongue and epidemic hemorrhagic disease among wildlife species of the globe. Restressed is the risk that domesticated animals and wildlife species may become mutual reservoirs as well as sources for human contagion. Reviewed are important clarifications of the synergistically complex causation of swine dysentery (treponemal, anaerobic bacteria, and possibly other intestinal residents) as well as more precise means for its control. Recent major forward strides have derived from identification of the coccidial nature of *Sarcocystis*, the agent(s) of a formidable zoonosis, and are reviewed here; yet, confusion in nomenclature of the parasite(s) befogs the literature, thus impeding progress toward conquest of the disease.

Lack of progress from protracted studies toward elucidating the defects that result in autoimmune (AI) disease in man has actuated critical research using dogs as experimental models. An increasing concern and effort has also stimulated sophistication of approaches to AI disease in practical canine medicine. Transcendingly important to the human situation has been the investigation of the central immunologic obstacle causing rejection and destruction of transplanted tissues and organs. It is pointed out that the formidability of the problem which has spawned "extensive experimental use of broad spectrum immunosuppressive drugs has made clinical transplantation feasible but at a plateau of achievement that has remained unchanged for at least a decade." Consequently, the search for possible alternative means of immunologic manipulation, especially in dogs, has been intensified.

Another author updates the interest in and development of farm animal disease data banks during the past 15 years. The writer feels such interest reflects the optimism and enthusiasm that go along with novelty. In addition, he feels that the impression that all applications of computerized data banks are working well and are of great utility is in all probability a false one. Actually, it appears that veterinary medical applications have been no more or less successful than those in other areas, commercial and technical. Logically then, the author opines that the time is now right to take a more critical and euphoric view of veterinary data banks so that the design of future systems can benefit from past experience.

The final chapter deals with findings of recent initial studies on taste perception and discrimination in the dog; revealed thereby is a substantial preference by dogs for animal rather than cereal food products. The research was prompted not only by scientific inquiry, but by the predicted competition between man and other species for animal-tissue-based food.

The editors of this serial publication are highly grateful to the authors whose able talent and effort have contributed toward creating this volume; they are also indebted to the continued discerning counsel of the Advisory Board members of this publication and for the ever helpful guidance and assistance of the staff of Academic Press.

C. A. Brandly
C. E. Cornelius

ADVANCES IN VETERINARY SCIENCE AND COMPARATIVE MEDICINE

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I. Introduction

The study of animals as experimental models is a major way by which investigators have contributed to our knowledge of biologic phenomena. Great contributions to improvements in the physical well-being of man and animals alike have resulted from application of this base of knowledge. We are on a track wherein the quest for knowledge in all disciplines will continue as long as there is freedom to pursue inquiry and to meet in open forum for exchanges of information. There is no known limit to the amount of information to be uncovered through biologic experimentation. Yet, limitations of certain types prevail. The increasing dollar expenditures required to perform experiments have already slowed the

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rate of growth of biologic research, and it is a limit that is likely to prevail. The emotional anguish that some persons experience when they think of the use of animals for experimental purposes has led to actions that continue to limit the experimental process. The anguish of these persons is not apt to subside, although humane considerations are very much a part of every biologic research endeavor.

Other limitations are imposed by the very nature of the experiments themselves. The leading edge of research today is extremely intricate, and often the experimentally induced changes are subtle and in danger of going undetected in any other than the best of controlled conditions. The emphasis placed on the need to study cancer has led to the evaluation of chemical and viral carcinogenesis. These procedures require special containment facilities and well-defined protocols in order to perform critical experiments. It is the concern for the last two limitations, the need for finely controlled conditions and biohazard containment, that will constitute the major portion of this chapter.

William Harvey's experiment using turkey quills to measure the blood pressure of a horse was a classic in physiology but short on biometrics. The same could be said of the studies of Aristotle and others. The information they generated were starting places and relatively crude approximations of what we know today. New information has always been built on existing information; and the limitations, the concerns for finite environmental control, have been generated through the biologic experimental process. The further we advance in seeking information, the finer will be the tuning that is necessary to reveal intricate facts. Animals are complex organisms, sensitive to their environment. The intricate processes functioning within the animal are the objects of our scientific inquiry. To reveal these processes requires controlled conditions heretofore unmatched.

II. Environmental Changes and Their Effect on Specific Biologic Phenomena

The use of laboratory animals in biomedical experimentation has resulted in a better understanding of the biologic processes. The knowledge that has been gained has led to the need for more sophisticated studies. Fortunately, animal experiments have also provided the technology needed for the production and maintenance of the defined animals that are needed in these studies. Improvements in laboratory animal facilities and husbandry to a large extent were prompted by the need to decrease the incidence of disease in experimental animals. More recently, advances have been made in the definition of the environmental influences, and investigators are requiring environmentally defined animals to assure the integrity of critical studies.

1. Light

Visible light occupies a very small part of the spectrum of electromagnetic irradiation, yet light is a powerful stimulant and synchronizer of the reproductive system. This stimulus probably is mediated through the hypothalamus, causing the release of neurohormones which control the secretion of gonadotrophic as well as adrenocorticotrophic hormones from the pituitary (Weihe, 1976). Light acting via these neuroendocrine pathways plays a key role as a stimulator of cyclic diurnal changes of tissues and physiologic functions. This is borne out by the fact that seasonal changes in reproduction disappear completely with a constant photoperiod, providing that thermal and other conditions are kept constant. Continuous darkness depresses reproduction and may result in reduced ovarian and uterine weights in rats (Hoffman, 1973). In contrast, continuous light results in an overstimulation of the reproductive system (Weihe, 1976). In mice and rats, permanent vaginal cornification develops, and many follicles reach the preovulatory stage; but corpora lutea do not form (Weihe, 1976).

The arrangement of the cages on the rack and the positioning of the rack in the room can influence the intensity of light that reaches the animal in the cage. It has been shown that the intensity between the cage on the top shelf of the rack and the cage on the bottom shelf of the rack may differ by more than eighty times (Weihe *et al.*, 1969). The effect of different intensities is varied. Albino rats maintained under continuous illumination of between 540 and 980 lux for a period of 65 days suffered complete degeneration of the retina. Pigmented rats exposed to the same continuous light did not suffer retinal degeneration (Reiter, 1973). In hamsters maintained under different light intensities varying from 15 to 200 lux on a 12-light-hour, 12-dark-hour schedule, reproduction was not affected (Weihe *et al.*, 1969).

The light spectrum also has been shown to have a significant influence on the behavior of animals (Mulder, 1971).

2. Noise

Noise is an environmental variable that occurs in animal rooms as a part of the day-to-day activities and operations. A certain degree of continuous background noise is generated by ventilating and air-conditioning equipment. This has been measured in empty rooms and has been found to have an overall intensity of 60 to 70 dB over a range of 20 to 1000 Hz (Serrano, 1971a). When animals are present, the degree of noise is not constant but varies with the husbandry activities being performed and the animal species involved. In one facility, it was demonstrated that the intensity of noise in a dog room reached 102 dB from the barking of dogs during the time people were present (Fletcher, 1976). In the same facility where the ambient noise level was 42 dB in a rabbit room, the intensity rose to 68 dB during the cage cleaning and feeding activities.

A recent review cites many papers dealing with both auditory and nonauditory responses to sound (Fletcher, 1976). Many of the experimental studies of the effects of noise have involved a wide range of frequencies of sound to limits exceeding 100 dB (Fletcher, 1976). Under experimental conditions, guinea pigs exposed to the noise of the firing of 500 caps in less than an hour showed histologic changes equivalent to those induced by 125 dB for 4 hours. The histologic damage that occurred involved the sensory hair cells of the organ of Corti (Poche *et al.*, 1969).

Nonaudiogenic responses are quite varied, and some responses seem to be genetically influenced. A number of different inbred strains of mice suffer from audiogenic seizures (Fletcher, 1976; Iturrian, 1971). The seizures may vary in severity, and death may occur following a maximal seizure (Iturrian, 1971). The age of the mouse at the time it is first subjected to a sound stimulus is a factor in its susceptibility to audiogenic seizures (Iturrian, 1971). Ninety percent of inbred DBA/2 mice had audiogenic seizures when first exposed to a sound stimulus, provided they were between 15 and 40 days of age (Iturrian, 1971). Also, brief handling of pregnant mice during days 10, 11, and 12 of gestation, for real or sham injections, produced stress sufficient to result in increased frequency of audiogenic seizures of the progeny (Beck and Gavin, 1976).

Auditory stress during gestation has been shown to produce a blockage to pregnancy, and reduced fertility of both male and female rats and mice occurred as a result of noise stress (Fletcher, 1976). Noise at 83 to 95 dB at 400 Hz, applied intermittently for 6 minutes out of each hour, resulted in reduced fertilization and increased preimplantation mortality in Swiss mice (Zakem and Alliston, 1974). Noise emitted from an animal house fire alarm system has been demonstrated to have a significant effect on the vaginal smear cyclicity of rats (Gamble, 1976).

3. Temperature

Body temperature is dependent on the interaction of heat production and the combined rates of heat loss or gain by evaporation, radiation, convection, and conduction (Porter and Gates, 1969). Within the limits of their regulatory mechanisms, homeothermic animals can maintain a relatively constant body temperature over a wide range of ambient temperatures. Within the wide range of ambient temperatures is a narrower range of temperatures at which an animal at metabolic rest is thermoneutral. At the thermoneutral temperature, no gain or loss of body heat occurs. When the animal is awake and active, the metabolic rate increases and additional body heat is produced. If the ambient temperature drops below the thermoneutral temperature, the animal must adapt to the change or suffer reduced body temperature. The temperature adaptation may consist in behavioral or physiologic changes to conserve or to produce more heat. In the wild, animals may adapt to the onset of cold weather by improving their insulation by developing heavy coats of fur and by burrowing or seeking other protection. Animals in the laboratory generally do not adapt by increasing their coats of fur, but they can adapt physiologically by constricting their peripheral blood vessels and raising their hairs. They can also respond behaviorally by huddling with other animals and by assuming body configurations that will reduce loss of body heat. When behavioral methods of adapting to cold ambient temperatures are insufficient, metabolic adaptation must occur to increase heat production. Increased metabolic activity is evinced by increased food consumption.

Mice housed singly and exposed to a 4°C temperature consumed 30% more feed than mice housed in groups of 5 and exposed to the same temperature, thereby demonstrating the difference in the heat conservation that can result from behavioral adaptation by animals when housed in groups. Within the range of 20° to 22.5°C and 40 to 60% relative humidity, much behavioral adaptation takes place with little requirement for metabolic adaptation (Weihe, 1971). The ability of animals to adapt metabolically to temperature changes is influenced by health, age, surgery, or treatment with drugs. In experimental procedures, when the thermoregulatory mechanisms are impaired, the body temperature of the animal tends to vary with changes in ambient temperature.

The toxicity of a great many drugs, particularly those with central nervous system effects, is influenced by the thermal environment. The details of how the metabolic changes are mediated are unclear, but they are linked with the metabolic and behavioral temperature regulation mechanisms. The effects of ambient temperature are most impressive in situations where behavioral regulation is limited and are minimal when temperatures are between 15° and 30°C and behavioral temperature regulation is provided (Weihe, 1973). These responses suggest that further studies are needed to define whether metabolic adaptation to temperature is a factor in the effect of temperature changes on drugs or whether the changes occur from alterations in the body temperatures.

Environmental temperatures are known to have additional effects on