

The use of animals in nursing research

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WITH NURSING reaching maturity as a research-based profession, nurse researchers need to give more consideration to the use of animals as experimental subjects. To date, the use of animals in nursing research has been limited. Frequently research ideas are discarded, or less-than-perfect experimental designs are adopted because to do the desired experiment on human subjects would be unethical. We have found that when animal subjects are used, there are many more opportunities to test new ideas, generate hypotheses, and control confounding variables. There are both advantages and disadvantages in using animals as research subjects, and animal research is more appropriate for some types of questions than for others.

We do not propose the use of animals in research because we are insensitive to ani-

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mal suffering; rather, we are extremely sensitive to human suffering. Carefully planned and ethically done animal research serves to improve the quality of life for both humans and animals. (Consider for a moment that many pets have benefited from antibiotic therapy or suturing of wounds.) In addition, we believe that animals should be used in research *only* after thoughtful consideration of the issues described later.

ANIMAL MODELS AND ANIMALS AS SUBJECTS

In discussing the use of animals for scientific experimentation, it is important to clarify terminology. The phrase *animal model* is used to refer to either animal populations that have been bred to have diseases similar to humans or to animals in which a condition has been induced that is similar to a human condition. For example, several strains of rats with a genetic predisposition to high blood pressure have been bred in an effort to duplicate human essential hypertension. The hope was that these animals could then be used to determine the cause, natural history, and appropriate treatment of high blood pressure. Similarly, Brattleboro rats, a breed with a genetic predisposition to diabetes insipidus, are used to study the numerous physiological effects of vasopressin (antidiuretic hormone).

Rabbits injected with antibodies against acetylcholine receptors to produce a muscle weakness known as experimental autoimmune myasthenia gravis are an example of the second type of animal model.¹ Similarly, a condition resembling

adult respiratory distress syndrome is produced in dogs by injecting them with linoleic acid. There may be several animal models for one human condition because models are developed by different research groups, and a particular model may not be totally representative of the correspondent human condition. When planning to use an animal model for a research question, it is imperative to determine how much is known about how closely the model resembles the human condition.

Often there is not a specific animal model for a particular research question, and a researcher will choose any convenient animal. In this case, we will use the terminology *animals as subjects*. If, for example, one wished to study the effect of sleep disruption in wound healing, a variety of animals including rats, mice, hamsters, pigs, dogs, sheep, and nonhuman primates could be chosen as experimental subjects. The choice of an animal subject would be influenced by budget, availability of animals and appropriate housing, previous experience with handling a particular species, and most importantly, by how closely the animal resembled humans in sleep patterns and wound healing. A researcher may begin exploring a topic using small rodents as subjects because of their availability and relatively low cost. The use of rarer and much more expensive animal subjects, such as nonhuman primates, would be reserved for later, more specific phases of the research program.

HISTORY OF THE USE OF ANIMALS IN RESEARCH

A survey of medical history reveals that the earliest scientific use of animals was for

anatomical dissection. Both Aristotle (322–384 BC) and Galen (130–201 AD) described the anatomical features of a variety of animals including pigs, oxen, sheep, and apes. Evidence of live animal use is found in Andreas Vesalius' treatise, *De Fabrica Humani Corporis* (1543), the final chapter of which is entitled "The Dissection of Living Animals."^{2(p126)} In this chapter, Vesalius describes the dissection of a live dog and makes references to using pigs and tailless apes. Animal experimentation was used extensively by William Harvey in the early 1600s to prove that blood circulates. This monumental leap forward in medical science would have been impossible without the study of animals. The animal subjects used by Harvey included toads, frogs, serpents, fish, crabs, shrimp, snails, and chick embryos, as well as dogs and pigs.²

Animal research has been prominent in health care professions, most notably in medicine. In nursing there has been considerably less work with animals, either as research subjects or as animal models. Since nursing, medicine, psychology, and all basic biomedical sciences share many areas of research interest, the contrast between nursing and the other disciplines in their history of animal research is striking. Why should this be so? Are animals irrelevant to the perspectives of nursing?

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Are there historical proscriptions against such methodologies? Is the use of animal subjects contrary to the values of the discipline?

A historical review of the limited animal studies reported in the nursing literature and comments regarding animal use in nursing research textbooks will place these questions in historical perspective. Reasons can then be suggested for the paucity of animal research.

HISTORY OF ANIMAL STUDIES IN NURSING

Only papers published in nursing journals or accessible proceedings are considered here. No attempt was made to survey unpublished master's or doctoral theses or publications by nurse scientists in the journals of other fields. The rationale for this decision was that articles most likely influence the discipline of nursing if they appear in publications that are relatively accessible to active nurse researchers. Although the contributions of nurse scientists publishing in other fields are valuable to science as a whole, it was assumed that those articles most relevant to nursing science would appear in nursing journals.

The history of animal work by nurse researchers is longer than one might expect. It was anticipated that nothing would be indexed until the 1960s, with the advent of the training of nurses in the biological and social sciences, supported by the federally funded nurse scientist programs. This expectation was partly correct; however, the first study indexed that used animals was conducted as a doctoral dissertation by a graduate nurse, Ruby

Bohart, and published in 1930.³ She used guinea pigs to evaluate killed tuberculosis antigen.

Three more dissertations based on animal or insect research were indexed between 1930 and 1940 and one in 1952, but none were published in the nursing literature.⁴⁻⁷ Three of the four authors studied nursing subsequent to obtaining PhDs in physiology, and this fact may explain why they were not published in the nursing literature. However, Henderson⁸ noted that it was difficult to find publishers in nursing who would accept reports of *any* research, a problem not remedied until 1952 with the establishment of *Nursing Research*. Henderson's own "modest investigation of medical and surgical asepsis" involved animals⁸ but was not mentioned in her review of the literature regarding asepsis.⁹

Despite the establishment in 1952 of a nursing publication devoted to research, no further reports of animal studies appeared until 1965. Half of those published prior to 1975 appeared in the *ANA Nursing Research Conference Proceedings*, a publication that is not indexed in general scientific indices, and that is not readily available outside large health science centers. It is entirely possible that relevant articles have been omitted from this search because of the inconsistency with which the nursing indexes do or do not use the heading "animals, laboratory," and nonappearance of articles under the appropriate heading.

The studies reported in nursing journals or published research conference reports fall into four categories: (1) methodological articles, (2) studies of nursing therapeutic measures, (3) studies of one or more aspects of the caring or nurturing process,

and (4) studies by nurse researchers of basic scientific phenomena.

Methodological articles

An early nursing article on animal research was published in 1968 and discussed issues and practical considerations in using animal subjects, based on the author's experience in studying techniques of tracheal suctioning.¹⁰ Vredevoe¹¹ and McKinnon-Mullet¹² both advocated the use of animal research. Four other articles that addressed animal research as a method were critiques of Hadley's studies of the effects of care delivery organization on postoperative recovery rate and discomfort.¹³⁻¹⁶ Three of the four authors supported greater use of animal research; the fourth discounted the value of animal subjects involving psychosocial variables.

Nursing therapeutics

Therapeutics may be broadly defined as those measures intended to intervene in problems of human activity such as rest and sleep, activity, comfort, elimination, and oxygenation. Such interventions may include manipulation of the physical environment, technical procedures, and in some cases, direct or indirect manipulation of the internal environment. Although manipulation of the interpersonal environment can also be considered therapeutics, the only studies that included such variables are more appropriately discussed later in the category of care delivery.

The majority of papers in this category can be considered physical therapeutics regarding thermal applications,¹⁷⁻¹⁹ oxygenation,²⁰⁻²⁵ feeding,²⁶⁻²⁸ intramuscular injection,

tions,^{29,30} and methods of noninvasive measurement of physiological function.^{31,32}

Caring and nurturing process

The roots of the word *nursing* and the pervasive historical concern of the profession have been in the nurturing and caring area. Despite our intuitive sense that one can care for and nurture animals as well as persons, only two animal studies were found, both of which are part of Hadley's famous beagle pup studies.^{33,34} In these studies, Hadley and her colleagues tested the effects of various conditions of nursing care delivery on postoperative recovery rate and discomfort. Although Hadley claimed to be testing the effect of "the nursing process," the study seems actually to test organizational variables—varying the number and constancy of caretakers and varying the amount of physical contact.

Gill and Atwood³⁵ attempted to conceptualize a study of wound healing in terms of Rogers³⁶ concepts of reciprocity and helicy. The principles that describe mutual interactions of human beings and their environments can be considered central to the caring or nurturing processes as they affect innovative change (helicy). It is not clear, however, that the design of this study is any different than it would have been had it been derived totally from the framework of regulating wound healing.

General scientific phenomena

The remaining studies can be classed as investigations of phenomena of general scientific interest. Although some could be considered more central to patient care, such as regulation of appetite,³⁷ other areas

of general scientific interest were wound healing and skin circulation,³⁸⁻⁴⁰ gastric ulcers after burn,⁴¹ thrombosis formation,⁴² cardiac contractility,⁴³⁻⁴⁵ neurophysiology of epileptic cells,⁴⁶ and neuroanatomy.⁴⁷

Of the 38 articles indexed and reviewed, 20 have been published since 1975. Of the total published, only half appeared outside published conference proceedings. Two reasons for the relative paucity of articles in nursing journals may have been the limited number of nursing journals devoted to research prior to the 1970s and the reluctance of journal editors to accept articles previously published at length in proceedings. As nursing research meetings and proceedings increasingly follow the format of other disciplinary societies and use short articles, this procedural barrier is disappearing.

The number of animal studies conducted is obviously small, perhaps related to costs, limited facilities, and the absence of training in the technical skills necessary to carry out such research. We believe that a more fundamental barrier to the conduct and publication of animal studies in nursing is based on a devaluation of the applicability of findings from animals to humans. If one accepts that a central focus of nursing science is the interaction of caring and nurturing and human responses to states of health and wellness, it is most appropriate to question the relevance of the experience and response of nonhuman animals to that of humans. Abdellah and Levine have suggested there is too little applicability to humans to make animal studies worthwhile.⁴⁸ Although over 15 years old, their text was the research "bible" for generations of nurse scientists.

More recently, Murphy expressed a common opinion that to consider psychosocial variables in animal subjects is inappropriate reductionism and therefore the value of animal studies is limited to physiological or neuromuscular phenomenon.¹⁶

We disagree with these positions and find them curious, since the knowledge base in nursing is grounded to a large extent in animal research in other disciplines. For example, the concepts of maternal-infant attachment and loss, so important in parent-child nursing, derived not only from the work of Bowlby with human infants⁴⁹ but also from that of the Harlows with infant rhesus monkeys and their cloth or wire surrogate mothers.^{50,51} Bowlby described the effects of maternal loss on child development; the Harlows pursued the questions regarding which elements of mothering were crucial to normal growth and development. If the components of nurturing or mothering are not psychosocial support, what is?

The physiological and psychosocial components of what is commonly called "stress" are prominent in most nursing textbooks and are derived largely from animal studies. Mason's work with nonhuman primates⁵² was pivotal in testing Selye's hypothesis that emotional factors produced stress, equally with physically noxious stimuli.⁵³

The findings of animal studies should not be accepted without question. Their applicability must be tested as in other disciplines. Carefully designed animal studies allow one to test selected variables, including appropriate psychosocial variables, in a more controlled setting than is usually possible with human subjects.

ADVANTAGES OF USING ANIMALS IN RESEARCH

There are a number of significant reasons for using animals in research. The researcher has much more control over various aspects of a project if animals rather than humans are utilized as subjects. The time, place, and number of experiments can be arranged to suit the scientists' needs. There is no need to advertise for subjects, to wait for them to be admitted to a unit, or to work only during clinic hours. More importantly, the researcher has much greater control over intervening variables that may influence the experimental results. Variables as disparate as time of day, diet, and blood pressure can be controlled, thus making the results easier to interpret.

When animals are used for experimentation, there is greater freedom to make physiological measurements that involve invasive techniques. For example, the influence of meaningful vocalizations on intracranial pressure can be studied in awake nonhuman primates; such an experiment would not be feasible with humans. It is also possible to gather more extensive data either by extending the length of an experiment, by repeating it on another day, or by making more measurements in a given time period.

Human populations cannot ethically be used to try out new procedures, medications or surgical procedures. The use of animals has allowed the development of scientific advances such as vaccines to prevent communicable diseases, open-heart surgery to correct congenital defects, and kidney dialysis machines to treat renal

failure. The use of animals allows the researcher to test new ideas and determine whether there are any unknown side effects that would preclude subsequent testing in a human population.

When people develop a problem or disease condition, they are not available for research until they have been diagnosed, which sometimes occurs years after the initial stages of the disease. With an animal model, research can be done on the initial stages of the disease or problem long before significant symptoms appear. Data

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gathered from such research might then be used to identify who is at risk for developing the condition, and to initiate early treatment to prevent onset or to reduce severity. Nonexperimental studies of groups of animals have been used to describe the phenomena of aging, development of social bonds, evolution of feeding behavior, and other social group behavior. Clues to the key variables are obtained by observation of animal groups in their natural environment. Subsequent experimental studies can be used to manipulate these variables. Because the life span of many species is much shorter than that of humans, the effects of environment, social variables, and physical variables can be more rapidly evaluated.

PROBLEMS WITH THE USE OF ANIMALS IN NURSING RESEARCH

When deciding whether animals would be appropriate for a project, the investigator must consider several issues. Depending on the type and number of animals used, animal research can be expensive. The cost of both animals and their daily care is rising rapidly, and substantial grant money is necessary to sustain a long-term project. At the University of Washington a dog currently costs \$70 to \$100 for initial purchase, and a nonhuman primate costs from \$500 to \$600. Daily care and feeding for animals currently ranges from \$1.50 to \$3.

Decreased availability of some animal species, especially nonhuman primates, may pose a problem. Previous indiscriminate use of some animals resulted in shortages and soaring prices. To cope with this problem, primate centers and breeding colonies have been established throughout the country. These centers have established criteria for the appropriate use of nonhuman primates.

Emotional attachment of the investigator to the research animal can pose a difficult problem, especially when an animal is studied for a prolonged period. The researcher needs to anticipate this problem and to consider carefully whether this aspect of animal use will be tolerable. It is neither possible nor practical to take every animal home after the experiments are over. We believe that some degree of researcher discomfort is beneficial and necessary to prevent the development of callousness and disregard for the animal's

comfort. The decision to use animals may expose the nurse scientist to criticism and condemnation. To counter and cope with this type of negative input, the nurse investigator must make the decision to use animals with conscious recognition of the potential difficulties.

Animals have limited use in experimental questions that require a subjective response or for which there is no animal model. For example, if the researcher were interested in the effects of a biofeedback technique on headache, it would be difficult to determine whether or not an animal had a headache initially, and then to what extent pain responded to treatment. Similarly, research on menopausal hot flashes requires human females because adequate animal models are not available.

A key issue with animal use is whether the results obtained are transferable to humans. As mentioned previously, there are several animal models for essential hypertension. It remains to be determined which of these, if any, is analogous to human essential hypertension. Data from experiments with these models must be interpreted with caution. When using animals as subjects, the choice of an appropriate animal requires careful consideration of how closely the animals being considered resemble humans in the area of research interest. For example, dogs are dissimilar to people in some aspects of cardiovascular regulation and thus should not be used for cardiovascular studies. The cardiovascular systems of pigs, however, closely resemble those of humans. But pigs are somewhat more difficult to handle in the laboratory. Similarly, since the temperature-regulating systems of dogs are dif-

ferent from those of humans, it is inappropriate to use a dog as the subject when studying the effectiveness of thermal applications for human problems such as inflammation.

Ethical issues require the most careful deliberation when considering the use of animals for research. Animals should not be exposed to undue pain or suffering. For example, much needs to be learned about responses to burns and trauma, but there is growing concern about purposefully exposing animals to such painful conditions. In areas such as these, we do not consider the use of animals to be appropriate. During the planning phase of a project, the researcher needs to address the following questions.

- Is this research necessary?
- Is this an appropriate question for animal research?
- Has the correct animal species or model been chosen?
- Will the animals be treated humanely?

Peer review during the funding process helps to assure that the investigator has considered the above questions and will receive additional input from a panel of experts.

APPROPRIATE QUESTIONS FOR ANIMAL RESEARCH

What are appropriate questions in nursing that lend themselves to animal research? Some critics of animal studies in nursing imply that, since animals do not share human communication and social systems, only mechanistic questions can be asked.¹⁶ Others visualize a wide range of appropriate questions, including those of a

psychosocial nature.^{14,15} We see several avenues that lend themselves to animal work, ranging from studies of physiological control mechanisms at the cellular level to ethological studies of animal populations.

One aspect of a practice discipline is the development of prescriptive theory,⁵⁴ theory that guides intervention in health and illness. To derive prescriptive theory, there must be some understanding of the mechanism underlying the phenomenon under consideration. Descriptive studies of the phenomenon itself are an important first step, and in a discipline that seeks to understand health behavior of humans, such studies are appropriately conducted with human beings. These descriptive studies delineate the factors or variables that might be manipulated in order to derive prescription or intervention. However, until the mechanisms or relationships among the variables are understood, prescriptive theory proceeds in a vacuum. Study of animals whose characteristics are similar enough to those of humans in the crucial areas is one way to establish the mechanisms sufficiently to permit the design and testing of prescriptive hypotheses.

An example of the usefulness of both human and animal research in deriving intervention hypotheses is found in the current work of the second author. In a clinical descriptive study of the relationships between ordinary nursing care activities and intracranial pressure in acutely ill persons, turning the patient in bed was found to be associated with increases in intracranial pressure in a high percentage of persons.⁵⁵ An extension of the study confirmed the observation in a larger sam-

ple.⁵⁶ A study is now in progress with nonhuman primates (the African baboon) to better delineate the physiological mechanisms underlying this potentially detrimental relationship. When these mechanisms are better understood, nursing intervention to prevent such increases associated with bedside care may be designed. The baboon was chosen because its intracranial proportions and mechanisms of cardiovascular adaptation to postural change are most like those of humans. The laboratory setting allows greater control over situational variables such as noise, ventilation, and invasive physiological monitoring systems than is customarily possible in intensive care units.

A similar refinement and testing of mechanisms underlying clinical observations is evident in the series of studies by Powaser and others in which clinically apparent hypoxemia related to suctioning was documented. First in dogs, mechanisms were identified and two means to prevent the hypoxemia were tested. Then the methods of prevention were tested in humans following cardiac surgery.^{20,22,24,25} The tradition of using both the human and the "bench" laboratory in nursing research has not been well established, but it is encouraging to see some evidence of fledgling efforts in nursing literature in the past five years.

The studies and approaches used as examples thus far have been both experimental and concerned with control mechanisms of physiological systems. This is the nursing profession's richest tradition, as evidenced by the concentration of published nursing studies in those areas. Animal studies are appropriately used in

investigating certain questions of social relationships—mechanisms of physiological response to psychosocial stimuli. Only Hadley has published in this area, and the complexity of her design makes it difficult to separate variables as examples. Consequently, examples must be sought from other disciplines.

Ethography as a method is most commonly thought of in anthropology, studying human cultures. However, Henry et al have for years used this approach in studying physiological consequences of social dominance interactions in mice.⁵⁷ Colonies of mice in population cages are allowed to establish their patterns of dominance and subordination, with repeated measurements taken of their blood pressure and enzyme levels reflecting the hormones most often implicated in stress research. These values are correlated with the observations of the behavior of individuals and the colony as a whole.

Although the mouse is not a good model for humans, the variables isolated in his work have served as the basis for the extension of the design to nonhuman primates (*macaca mulatta*: the rhesus monkey).⁵⁸ Until recently, nearly all of the work regarding the biochemical response to stress was based on studies with nonhuman primates. The potential of observing colonies and social groups of animals and the effects of manipulating key variables has been untapped in nursing. Attachment, effects of physical and cognitive disability on subsequent development, enrichment or deprivation of the environment, and development are all important areas to be studied in nursing. To the extent that key variables can be identified in animals and

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Considering the ethical issues previously discussed, the use of animals in nursing research is limited only by the creativity of nurse-researchers. How many nursing therapy programs and activities have a sound research base? The community health nurse is counseled to ambulate a patient with breast cancer to prevent or minimize a reoccurrence of hypercalcemia. The community health nurse asks the question, "How much activity is necessary?" The answer is unknown. Perhaps with the development of animal studies, guidelines can be developed. What is the most effective interval for stripping chest tubes? Is stripping necessary? What variables influence the necessity for stripping a chest tube? How does alcohol affect the functioning of the maternal-placental unit? Can nutritional therapy prevent or compensate for changes caused by alcohol consumption? The answers to these and many other key questions are available through the use of animals in nursing research.

RECOMMENDATIONS

Consideration of many issues is involved in the decision to use animals in research. The development of nursing science would

be advanced by the increased use of animal subjects and animal models in nursing research. The authors do not, however, propose indiscriminate use of animals by any nurse who thinks it might be advantageous. Doctoral programs in nursing should include preparation in the use of animals in research as part of their curricula. Nurse scientists whose academic

careers did not include such preparation could seek mentors skilled in the care and use of laboratory animals prior to initiating a project. Research involving animals supplements and precedes but does not replace research involving humans. The judicious use of animals in research should result ultimately in improved care for all living creatures.

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