

**VOLUME 5**

Editor

**Allan M. Lefer**

**ADVANCES  
IN SHOCK  
RESEARCH**

**Alan R. Liss, Inc., New York**

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**ADVANCES  
IN SHOCK  
RESEARCH**

**VOLUME 5**

**Proceedings of the Third Annual Conference on Shock  
Lake of the Ozarks, Missouri, June 1980  
Part 1**

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## Preface

Research in the area of shock and trauma has recently intensified and new findings and concepts are being brought forth continuously. Against this background of increased research activity and the uncovering of new avenues of investigation, the newly formed Shock Society has convened annually in an attempt to codify and unravel many of the unknown aspects of shock research. This volume contains selections from the Third Annual Shock Society Meeting held at Lake of the Ozarks, Missouri, June 11 – 13, 1980.

The volume includes a series of papers probing important questions in two vital areas of shock research:

- 1) Pathophysiology of Shock
- 2) Therapeutics of Shock

The first area contains a series of five papers on metabolic alterations in shock followed by three papers on new insights in cell and organ responses to the shock state. In this section, new work on lipid and carbohydrate metabolism is investigated and linked with hepatic function. Several of the papers signal a rekindling of interest in the reticuloendothelial system, including leukocytes and Kupffer cells of the liver.

The second area contains a set of three papers on mechanisms of the protective actions of glucocorticoids in shock, followed by four papers on interesting new aspects of fluid and prostaglandin therapy in shock. The first area is well established, the second is one that may hold great promise for the future. Although this volume is not a definitive treatise on these subjects, it represents a good cross section of current interest in these interesting and important areas of shock research and will be of value to the reader interested in shock research.

Allan M. Lefer

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## Keynote Address: Legal Threats – Real and Potential – to Shock Research

Maurice B. Visscher

When Dr. Hinshaw, your Chairman, wrote me asking whether I would be willing and able to present a speech at your annual banquet and said that I could choose the topic myself, I was quick to respond in the affirmative. I am very pleased to be able to share with a group of active investigators, most of whom must use living animals in order to make meaningful progress in their research, my concern over the threats to impose great impediments to such research in the future.

There are too few among our medical research colleagues who recognize the danger signals that have been growing in number and seriousness in recent years. I hope that I may be able to analyze the problems in a way that will encourage medical scientists like yourselves to take a more active part in stopping the attempts of the animal humane groups to throttle progress by legislative action at all levels of government. It is not only in the U.S. Congress that threatening bills have been introduced and actively lobbied for by misguided humane societies and their members, but state legislatures have already passed damaging laws, and even at local levels, restrictive legislation is interfering with medical research progress. We all know about the Cruelty to Animals Act passed in 1876 in Britain which has hampered both research and teaching in that country. Biomedical research persons in the United States have been lulled into a sort of trance with a feeling that "it can't happen here," by the fact that for more than a century the U.S. Congress has resisted the passage of legislation like the Cruelty to Animals Act of 1876 in Britain. Only those of us in America who have carried out research in Britain know what a handicap the 1876 Act represents. For one thing it has greatly increased the cost of dogs and cats because of the prohibition of use in research or teaching of unclaimed impounded animals, which are consequently killed in the pound without any benefit to man or animals. For another thing it makes the use of any animals by science students illegal. It also makes use

in practice surgery illegal. Furthermore, it encourages subterfuge by calling more or less routine teaching experiments or surgical practice, scientific research. These subterfuges are always in danger of being exposed and stopped or even prosecuted, thus endangering both the scientists and the regulators in the British Home Office, which bears the responsibility for enforcing the antiquated statute.

However, times are changing. Most amazing and unexpected factors are entering into the age-old controversy between the antivivisectionist element in the so-called animal humane movement and the practicing animal experimentation community. As I have already intimated, the latter community has been living in a "fool's paradise" of what I propose to call "innocent ignorance."

The innocence comes about because biomedical investigators have always believed that what they were doing was in the essence of righteousness. For example, when Banting and Best performed fatal experiments on hundreds of dogs and rabbits, the thought never crossed their minds, I am sure, that anyone could seriously criticize them for what they were doing, because they saw progress toward the control of diabetes to be a self-evident good. Of course, time has proven their "innocence" to be unshared by many. So it has been with thousands of other *innocent* investigators.

The "ignorance" to which I refer has to do with the lack of attention paid by most persons who employ living lower animals in research to the rising tides of opposition of many varieties that threaten to engulf them. Less figuratively, one can say bluntly that attacks from numerous angles threaten to stop their studies.

The most unexpected new factor which has been introduced into the antivivisectionist argument is the attempt to make the growing scientific evidence that some mammals, such as the higher apes and dolphins, for example, have more human-like mental abilities than was previously thought — a new basis for criticizing the sacrifice of any lower animal life for human good. A whole new philosophy about "animal rights" has developed. The designation of any animal group as "lower" is being called "speciesism," and comparable in obnoxiousness with racism and sexism. Thus the fact of an evolutionary scale in the animal world is being made the basis for condemning the species that is obviously at the top of the ladder, for recognizing the fact. It seems strange that otherwise sensible people could fall into such a trap of simplistic logic as this, but it is, unfortunately, the case. People like Jeremy Stone, for example have swallowed the "animal rights" dogma, almost hook, line, and sinker. Witness his Special Report for the Federation of American Scientists, entitled "Animal Rights," in which he expounds the thesis.

As an aside, I should say that Jeremy Stone, who is the executive officer of the Federation of American Scientists, is a mathematician, not a scientist, and that although the FAS boasts of many Nobel Laureates among its list of prestigious sponsors, its elected board of directors has only one recognizable biological scientist on it. When Stone's Special Report on "Animal Rights" appeared I wrote to that person and asked whether it was true, as claimed by Stone, that the board of directors had approved of the position taken by Stone for the FAS. That person said yes, it was true, and went on to say that, although he recognized the necessity of animal experimentation, he was himself very much distressed by the careless ways in which many bioscientists treated animals.

Stone set up a new organization which he called the "Scientists' Center for Animal Welfare." SCAW has become part of the alphabet soup that is the diet of Washington bureaucrats in and out of government. The significance of this new entity in the Animal Rights movement is illustrated by the fact that the March, 1979, issue of *BioScience*, the house organ of the American Institute of Biological Sciences, devoted a five-page article by Robin Henig, its feature and news editor, to SCAW and other related organizations promoting the animal rights philosophy.

It is impossible to comprehend the gravity of the current situation with respect to the use of live animals in research without seeing exactly what types of legislative restrictions and impediments the animal humane and welfare organizations are promoting. The most important bill now in the Congress dealing with the problem is undoubtedly H.R. 4805, introduced by Congressman Richmond on July 19, 1979. It proposes to set up a "National Center for Alternative Research" and provides that it may be called the "Research Modernization Act." It initially had only three co-sponsors in the House of Representatives, but the pressures from the animal welfare groups for its enactment became very great, more than forty other Congressmen have added their names as co-sponsors.

The stated intent of H.R. 4805 is, "To establish a National Center for Alternative Research, to develop and coordinate alternative methods of research and testing which do not involve the use of live animals, to develop training programs in the use of alternative methods of research and testing which do not involve the use of live animals, to disseminate information on such methods, and for other purposes." The most significant aspect of the Bill is its Section 10 on funding. This provides, "Effective in fiscal year 1981, each agency represented in the Center shall direct to the development of alternative methods of research and testing no less than 30 percentum and no more than 50 percentum of all appropriations made available to such agency for all research and testing programs conducted or sponsored by such agency involving the use of live animals." In

other words, the Act provides that no special additional appropriations of money by the Congress will ever be needed, but that every agency of the Federal establishment which carries on, or supports by grants or contracts, research or testing involving live animals will automatically have 30 to 50 percent of funds appropriated for that purpose transferred to the Research Modernization Institute for the support of its program. The Act defines in Section 11 what such programs are intended to be: "*alternative methods of research and testing* includes, but is not limited to, the use of mathematical models, isolated organs, tissue or cell cultures, chemical assays, anthropomorphic dummies, simulated tissues and body fluids, mechanical models, computer simulations, or lower organisms." It might almost appear that some mathematician, a computer manufacturer, or tissue-culture promoter wrote this section. Actually there has been an international body, the Council of Europe, which took the recommendation of a tissue culture laboratory director for setting up a kind of international Alternative Methods program.

In a special section of the Bill, dealing with training, it is provided that, "(a) Each agency which conducts or sponsors research and testing involving the use of live animals shall make grants and enter into contracts with educational institutions to establish courses for the training of scientists in methods of research and testing which do not involve the use of live animals. (b) Each agency referred to in subsection (a) of this section shall make training programs available to scientists for the purpose of educating them in alternative methods of research and testing."

To make sure that the Alternatives bill has teeth, there is a Section 6 saying, "(a) No Federal funds may be used to conduct or sponsor research or testing involving the use of live animals in cases in which alternative methods of such research and testing have been published in the Federal Register under Section 5 of this Act. (b) No Federal funds may be used to sponsor or support research or testing involving the use of live animals if such research or testing duplicates work performed by an agency."

H.R. 4805 justifies its provisions by asserting in Section 2: "The Congress finds that (1) direct support for the development of alternative methods of research and testing is an appropriate and necessary role for the Federal Government; (2) development of alternative methods of research and testing does not require additional expenditures of Government funds; (3) cooperation and coordination among agencies will result in more effective use of resources for research and testing; (4) continued reliance on animal experimentation delays the development of new, more effective procedures; and (5) there is growing public concern over the suffering of large numbers of animals in research and testing."

The statement of Congressional Findings is in general simplistic, and in part misleading, if not knowingly false. For example in subsection (2) it is simply not true that no additional funding would be required if currently funded programs in biomedical research were to be continued. The assertion in subsection (4) is totally unsubstantiated. Furthermore, subsection (5) is simply a confession that the bill is politically motivated.

It seems obvious that no working scientist using live animals in his or her research or toxicity testing on crucial problems in medicine had any part in writing H.R. 4805. No one who understands the complexities of problems in physiology, pharmacology, immunology, pathology, toxicology, would want to work with the prohibitions that this bill makes.

Workers in the shock field, and I still consider myself one of you, although as you know my own active participation ended some years ago, recognize that one must deal with the whole organism in analyzing the realities of the shock problems. One may and does work with specific organs, specific cells, or even specific chemical reactions in the analysis of mechanism, either of pathophysiology or therapeutics, but so frequently it is the interaction of cells and organs and organ systems that determines end results, and failure to study the whole animal can lead to entirely erroneous conclusions. To suppose that mathematical models or sophisticated computer analyses will displace empirical studies in a situation like endotoxin shock would be laughable if it were not for the real danger that the animal rights activists might win the battle over the "alternative methods" issue.

There are several actions which I believe biomedical and other biological scientists should take in order to prevent the passage of legislation like H.R. 4805. First and foremost, all institutions or organizations whose effectiveness in research and teaching would be seriously hampered by passage of such legislation should act in unison in opposing such bills as H.R. 4805. I am especially distressed that a serious attempt has been made by Jeremy Stone of FAS to split the bioscience community over the matter. The simplistic pseudologic of the attempt to equate "speciesism" with racism and sexism as equally abhorrent behavior patterns should be explicitly analyzed and exposed as fraudulent. We should challenge the baseless thesis that speciesism is as unethical as racism. There should not be continued silence on the part of scientists whose work requires the sacrifice of lower animal life in the face of implications or actual charges of unethical conduct in carrying out such studies. We should expose the absurdity of the supposed logic that says that because some higher mammals can be taught to respond to particular auditory or optical symbols in definitive ways, that such animals' lives are as worthy of protection as is any human life.



There are a few specific points which I very much hope that you will remember:

1) The Metcalf-Hatch Act in New York State has already been repealed, hampering live animal research by increasing its cost.

2) Michigan, New Jersey, Mississippi, and other states have regulations that are severely hampering to the useful employment of unclaimed impounded animals.

3) There are several bills in Congress, one or more of which will very likely be enacted in the not too distant future, which would, like H.R. 4805, cripple scientific research or toxicity testing on living animals.

4) The "Animal Rights" movement is definitely growing. New York Mayor Koch, for example, was responsible while he was in Congress, for a bill which was of the same "Alternative to Living Animals" type as H.R. 4805. Even Congressman Father Drinan has introduced such a bill. Persons like Jeremy Stone are lending their prestige to attempts to divide the bioscience community on this issue.

5) I believe that it is imperative to get every medical school, research institute, and research hospital financially behind the only truly broad-based organization we have in this country to defend humane live animal studies, which is the National Society for Medical Research. Too many organizations have already let financial problems cause them to discontinue support. A very few have dropped their support because they have fallen for the "Animal Rights" doctrine.

6) It is naive to believe, or even to hope, that the pressures for legislative action at the national, state, and local levels are going to subside. "True believers" do not need rational bases for their beliefs. Do not forget that Huxley and Darwin accepted the British Cruelty to Animals Act of 1876, not because they liked it, but because they became convinced that political pressures for its enactment were too great to resist. The same thing is happening again in Britain on the "alternative methods" issue. It has not been passed yet, but the Labor party is for passing it! And without a really united bioscience organizational front opposing it and supporting rational educational efforts to forestall it, the same thing is going to occur in the United States. We scientists all support humane methods and facilities. Let us not allow animal welfare zealots to continue distorting the truth to achieve their ends, which are to make the study of living animals so expensive as to achieve their antivivisectionist ends without calling them that. The Animal Rights movement is flawed by fallacious logic. The "alternative methods" bills are, as I have pointed out, based on false or misleading assertions of supposed Congressional findings.