Animal experimentation: A rational approach towards drug development

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Man’s observation of animals as objects of study undoubtedly began in prehistoric times. The first recorded attempt involving the use of live animals for research was by Erasthratus in Alexandria in 300 B.C. Animal investigation has clearly made possible the enormous advances in drug development in this century. A cursory review of any modern text book of pharmacology or medicine will attest the many drugs currently available to benefit mankind in the struggle to eradicate and control diseases. The main purpose of this article is to describe some of the experimental work on animals which contributed to the discovery and development of drugs benefiting human beings and other animal species. Since animal experimentation has occupied a focal position in all the research leading to useful drugs, one will appreciate that it will be necessary to limit the discussion to certain aspects of this broad and interesting topic. With this in mind, an attempt is made to relate briefly the nature of animal investigations which were instrumental in the development of major classes of drugs. Some attention has also been focused on legislation’s on animal experimentation of some developed countries with emphasis on India and to views on animal experimentation. We hope this article will stimulate the minds of the scientists for a rational debate on the future of animal experimentation.

The use of animals in scientific investigation has been traced back to ancient history. For instance, the writings of Aristotle (384-322 B.C.) and Erasistratus (304-258 B.C.) indicate that they had studied the anatomy of various animals1. Early investigations such as these were the beginning of the basic sciences that today form the foundations for new drug development. Until the end of the last century, experiments using living animals were carried out on domestic or easily captured wild species. The choice was usually limited and based on availability. By the end of the nineteenth century, the concept of the laboratory animal had begun to emerge as an animal deliberately chosen for its inherent suitability for the purpose. It was especially bred in captivity or obtained from its environment not merely on grounds of convenience but rather for its usefulness for the particular investigation at hand.

Tests on intact animals are necessary to understand how a drug will work in the context of the myriad metabolic and homeostatic mechanisms that are active in vivo. Screening tests are commonly conducted with in vitro systems and isolated tissues or organs to identify pharmacologically active agents. However, the variable processes of absorption, distribution within the organism, metabolism to either inactive or more active products and excretion will modulate the expression of pharmacologic activity in vivo. The only way this modulation can be estimated is by studying the new drug in intact animals. Aside from studies of pharmacologic activity, side effects of new drugs must be identified and an initial assessment must be made of their risk-to-benefit ratio. Again, mechanisms of action and effects on specific organs can be studied by using in vitro techniques. However, to identify unexpected adverse effects and to estimate the dosages that are pharmacologically active without producing unwanted effects, in vivo studies must be conducted.

For most substances, the mechanism of action will be the same in humans and other mammals. Therefore, quantitative rather than qualitative differences in response are most common. Humans may be more sensitive to some drugs than certain laboratory animals but usually certain animal species are more sensitive than humans. For example, the mouse and cat are sensitive to atropine, and the dog and rabbit can tolerate atropine at doses 100 times higher than what humans can tolerate. Species differences in sensitivity can be explained by differences in metabolism, including quantitative and qualitative differences in the ability to detoxify drugs and also differences in the rates of absorption, transport, distribution, and elimination of chemicals. After oral administration, absorption in laboratory animals is generally considered to be similar to that in humans, although there are quantitative differences for some compounds. For example, species differences in the absorption and action of some compounds are related to differences in the bacterial
flora of the gastrointestinal tract. The distribution and storage of drugs are reasonably consistent among mammalian species, including humans, although plasma binding tends to be more extensive in humans than in small mammals. Species differences in response to drugs appear to be related mainly to rates of biotransformation, which are generally more rapid in small laboratory animals than in humans.

**Animal experimentation in drug discovery and development**

Thirty years ago the initial screening of new compounds for pharmacologic activity was conducted using whole animals or tissues and organs isolated from animals. Today most of the initial screening for new drugs is done in vitro using the techniques of biochemistry and molecular biology. Only after a new drug candidate has been identified in vitro, studies are initiated in animals. The purpose of animal studies is to verify the pharmacologic activity of the new drug, identify any unexpected pharmacologic activity and develop initial data based on the action of the drug in vivo. An ideal approach would be to have an in vivo screening program designed to allow for the detection of unique profiles of activity or combinations of activities. Therefore, in addition to a set of initial screening models, relevant secondary tests would be conducted to generate additional information on specificity, mechanism of action, and possible side effects. A complete in vivo pharmacological screening program would include models for the detection of the major therapeutic classes of compounds shown in Table 1.

The following five points clearly demonstrate the many and varied ways in which animal experimentation has contributed to the discovery and development of drugs:

1. **Role of animal experimentation in the development of drugs useful in diseases of known etiology**—Animal experimentation has been particularly useful and rewarding when the cause of a given disease has been established and when the disease can be reproduced in small animal species. Under such circumstances, the experimental pharmacologist can establish a reliable screening procedure which will permit a team of investigators, trained in several disciplines, to search for agents to either prevent or cure the disease. Several specific examples of important classes of drugs developed by such animal experimentation will serve to illustrate the point.

**Chemotherapy of infectious diseases—antibiotics, sulfonamides and other antimicrobial synthetic drugs**—Animal experimentation has been useful in man's quest for drugs to control infectious disease of bacterial origin. At the close of past century, animal experimentation played a dominant role in establishing the etiology of many infectious diseases. Fortified with such informations and with reliable screening procedures by infecting small laboratory animals with known pathogens, investigators attempted to find drugs which would be more toxic for invading bacteria than to the host cells.

In 1935, Domagk, working with experimental streptococcal infections in mice, announced the discovery of prontosil, the first of a number of remarkable sulfonamides and other synthetic drugs, useful in the prevention and cure of bacterial infections in humans and animals. Today the sulfonamides continue to be very valuable in the management of certain bacterial and viral infections. However, in many instances, the sulfonamides have been replaced by antibiotic therapy, the second major development in the chemotherapy of bacterial as well as certain viral and fungal diseases. Indeed, the development of antibiotics for the treatment of infectious disease constitutes one of the most remarkable advances in modern medicines. Currently

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there are a host of known antibiotics which are clinically useful. Among the most widely used are penicillin and its derivatives, streptomycin, aureomycin, chloromycin, tetracycline, achrromycin, erythromycin, bacitracin, polymyxin, griseofulvin, nystatin and amphotericin B. All of these antibiotics were discovered and made available by the combined use of in vitro and in vivo screening procedures designed to detect agents which would inhibit the growth or kill pathogenic microorganisms. The in vivo experiments were performed mainly in mice infected with various gram-positive and gram-negative bacteria. At times, special studies were undertaken with pathogenic fungi or with tuberculosis infections in mice and guinea pigs. The list of infectious diseases of animals and humans, which have yielded to the sulfonamides, other antibacterial synthetic agents and to the antibiotics, is long. It includes tuberculosis, syphilis and leprosy, three diseases which have been the scourge of mankind for many centuries. However, much experimental work remains to be done in the area of chemotherapy of viral diseases and the recent animal experiments dealing with interferon bear watching.

Chemotherapy of parasitic diseases—antimalariais, thiobendazole and amprolium—Parasitic diseases due to protozoa and metazoa are extremely widespread in humans and animal species. According to present estimates, over two billion helminth infections exist in man throughout the world today. In the lower animal species, parasitic diseases are even more prevalent.

Obviously it will not be possible to discuss in depth the important contributions animal experimentation has made to the treatment of these widespread diseases. The approach to finding drugs for chemotherapy of parasitic diseases has been essentially the same as outlined in the forgoing section on bacterial chemotherapy. Where possible, the disease is established in laboratory animals and a systematic search is made to find drugs which are more toxic for the parasite than for the host. Once leads are uncovered, skillful chemists modify the structure of the lead compound and attempt to increase toxicity for the parasite and/or increase safety for the host. Thousands of compounds were screened for antimalarial activity in ducks, chickens and even monkeys, and several highly potent drugs were found which were useful to suppress or cure the devastating disease. Quinacrine, chlorquine, chloroguanide and primaquine are among the drugs resulting from these studies.

Two relatively new drugs, found by selective screening procedures in animals and which were introduced primarily for the treatment of parasitic diseases of animals, are worthy of mention. The first, thiobendazole, is a highly effective, broad spectrum anthelmintic, developed and introduced for the treatment of nematode infections of sheep. For the past several years, the drug has been widely used in sheep and other animal species to control many types of roundworm infections. More recently thiobendazole has been found effective in several types of roundworm infections in man. The second drug, amprolium, is a unique example of a class of drugs useful for the control of coccidiosis, a parasitic disease which affects a wide variety of animal species and if untreated, the disease lead to high morbidity and mortality. The disease is particularly devastating to chickens and turkeys. Since it is not possible to culture these organisms in vitro, the infected experimental animal has been the only means available to search for drugs which will control this disease. Similar examples could be offered of experimental animal screening programs which contributed to drugs currently used in the treatment of amebiasis, trypanosomiasis, leishmaniasis, schistosomiasis, filariasis and tapeworms. However, like the viral diseases, certain protozoan and metazoan diseases of man and animal species do not respond well to current treatment. Therefore the search for better drugs to treat these diseases continues at an ever-increasing pace. The success of these programs depends in large measure on the availability of satisfactory animal assay procedures.

Drugs useful in Allergy: The clinical manifestations of these diseases are known to be due to antigen-antibody reactions in the host. Among other things, these reaction cause the formation, or release, of histamine and other biologically active materials which produce inflammation, contraction of smooth muscle and tissue injury. Allergic diseases are rather common in human beings and probably occur frequently in all animal species, although the incidence in lower animals is not known. Moreover, allergy appears to be the basis for a number of disease currently classified as diseases of unknown etiology. Animal experimental models have been developed which have permitted scientists to search and find drugs highly useful for the symptomatic treatment of diseases of allergic origin. Compounds were found which protected guinea pigs against several lethal doses of histamine. Moreover, these compounds antagonised histamine-
induced spasms of various smooth muscles and most significantly, lessened the symptoms of anaphylactic shock. As a result of such animal experimentation, a group of drugs known as antihistamines were developed and found to have value in the symptomatic treatment of various allergic diseases. Pyrilamine maleate, diphenhydramine hydrochloride and tripelenamine hydrochloride are examples of useful antihistamines for humans and animals.

Using in vitro and in vivo screening programs, global attempts are being made, to find drugs which will suppress antibody formation or block the union of specific antigens and antibodies. Such drugs may find wide utility in the prevention and treatment of diseases brought about by autoimmune reactions. Hopefully, compounds with selective action may prove useful and permit successful organ and tissue transplantation.

(2) Role of animal experimentation in the development of drugs useful in diseases of unknown etiology—Among the most difficult tasks for the experimental pharmacologist is the designing of a meaningful assay in animals, which allows investigators to search for effective drugs when the cause of the disease is obscure and when the disease does not occur spontaneously in nature in lower animal species. In spite of these great difficulties, animal experimentation has paved the way for scientists to find drugs of considerable benefit for many of these diseases of unknown etiology. In such instances, pharmacologists have established assay procedures which permitted scientists to screen for drugs active against one or more symptoms of the disease. These drugs are often highly effective in relieving the patient’s distress but do not necessarily prevent or cure the disease. For example, using normal animals, one may find drugs which will lower blood sugar, or blood pressure, respectively. These drugs may be useful for the treatment of diabetes or hypertension respectively, but they have no real curative effect on the disease processes per se.

Animal experimentation leading to anti-inflammatory drugs-adrenal cortical steroids, indomethacin, butazolidin and aspirin—Inflammation is an important component of a wide variety of diseases of humans and animals. It is notable symptom of rheumatoid arthritis and other so-called connective tissue diseases. Polyarthritis occurs in all large animals and the condition is best known in horses. Arthritis disorders are not common in dogs and cats. The cause of these disorders is not known although many clinicians believe immune mechanisms give rise to inflammation.

For many years clinicians and experimental investigators have attempted to find therapy to prevent or cure these diseases. The first major breakthrough in the development of new drugs for the alleviation of these diseases resulted from the clinical observations of Hench and his associates in 1948. These investigators reported prompt and striking subjective improvements in patients with active rheumatoid arthritis given cortisone. Among other actions, cortisone had the capacity to suppress the development of local heat, redness, swelling and tenderness, which are gross signs of inflammation. Unfortunately, cortisone was in very short supply and also caused a number of undesirable side effects when administered for long periods of time. Therefore, a massive research effort was initiated in an attempt to find new steroids which could be made available for the millions disabled by arthritis. It was recognised at the outset that no progress could be made without the availability of a simple animal assay which would detect anti-inflammatory action of minute amounts of new steroids. Simultaneously, the animal investigation provided a guide to the side effects which such steroids might induce. Since the steroids appeared to suppress all types of inflammation, regardless of the cause, a quantitative animal assay was developed by implanting a small cotton pellet, of known weight, under the skin of rats. This foreign reaction which could be readily suppressed by cortisone and other anti-inflammatory steroids. The potency of the compound was a function of the dose and the anti-inflammatory activity of the steroid. This assay and other more recent animal assay procedures, have played a major role in the development of all the adreno cortical steroids. Within the last few years, a new nonsteroidal anti-inflammatory agent called indomethacin was discovered and made available for the treatment of rheumatoid arthritis, osteoarthritis and gout. This compound is far more potent than butazolidin and aspirin and cause none of the characteristic side effects of the adreno cortical steroids. Here again, animal investigations, much like those performed to find new steroids, laid the foundation for the work leading to the discovery of indomethacin.

Animal experimentation leading to drugs useful in Cardiovascular-Renal diseases — Cardiovascular-renal diseases are among the most prevalent diseases of
unknown etiology in human beings and animals. Accumulation of electrolytes and fluids are common in many of these diseases and may lead to considerable distress and even death. The story of experimental work leading to discovery and introduction of new, potent drugs which aid in the mobilisation and excretion of these fluids is a classic example of the important role animal experimentation may play in making beneficial drugs available to human beings and animals.

The animal experimentation leading to the discovery of new potent, oral diuretics called chlorthiazides began with investigations by Beyer concerned with kidney function in normal animals. For many years it was recognised that the kidneys fail to carry out their function properly in such disorders as hypertension, congestive heart failure, cirrhosis of the liver, kidney disease, toxemia of pregnancy and premenstrual tension. Simultaneously, it was known that salt free or low salt diets were helpful to patients with diseases associated with edema.

Taking all the foregoing facts into consideration, investigations were initiated in animals to find a safe drug which would act orally to remove the excessive salt and fluid from the body. Oral drugs could be given conveniently to ambulatory patients. Animal assays were designed to measure the effect of drugs on the excretion of salt and water and in cooperation with organic chemists, an exhaustive search was made to find a compound with the foregoing properties. Hundreds of different compounds were designed and assayed. Their chemical structure were correlated with biological function. The fruitful results of these investigations and the usefulness of this class of compounds is now known to millions. Since animals suffer from cardiovascular-renal diseases too, these diuretics are also beneficial for them.

The major pharmacological actions of a large number of drugs are based on their ability to alter the cardiovascular system. Digitalis and certain closely allied drugs have a powerful action on cardiac tissue for the treatment of congestive heart failure. Various samples of powdered digitalis leaf differ widely in their glycosidal content and potency and therefore, digitalis preparations must be standardised by animal assay. The official method is the USP biological assay, which requires that digitalis preparations be assayed in pigeons. Although this assay has a number of limitations, digitalis would not be available for human and animal use if preparations could not be standardised.

Animal experimentation has been also useful in attempting to understand, prevent and treat atherosclerosis. In recent years much attention has been given to the role of plasma lipids and lipoproteins. There is as yet no definite evidence that lowering of plasma lipoprotein concentration by drugs or diet is effective in the prevention of atherosclerosis.

Other diseases of unknown etiology: Animal experimentation played an important role in the investigations leading to drugs useful in the systematic treatment of diabetes, rheumatic fever, certain types of cancer, thyrotoxicosis, convulsive disorders, hypertension, addison’s disease, several types of anemia and others. Through animal experimentation in recent years, great strides have been made in finding drugs useful for the symptomatic treatment of the psychoneuroses and personality disorders. Today, psychotherapeutic phytomedicines useful as mood elevators are widely used and serve a very useful purpose.

As may be expected, there are a number of diseases of unknown etiology which do not respond satisfactorily to therapy. In almost all instances, animal experimentation is being used to learn more about these illness. Hopefully, investigators will establish assay procedures which will allow scientists to search for useful drugs. Animal investigations concerned with the chemotherapy of cancer; certain diseases of central nervous system, such as multiple sclerosis and psychoses and others, continue to receive enormous attention. Based on past experience, one may look forward with some optimism to the availability of new drugs useful in the treatment of these diseases too.

(3) Animal experimentation leading to drugs useful in regulating organ function — More recently animal investigations have occupied a central position in the development of drugs which stimulate or depress specific physiologic activities of normal humans and animals. These drugs have not been developed for the treatment of diseases but are useful in many other respects. The most striking example of this broad area of pharmacology are the animal investigations leading to the development of drugs which regulate ovulation. Undoubtedly, the search for compounds and agents which will regulate other physiological functions will continue at an accelerated pace. Investigations are currently under way to seek drugs which will improve memory, increase ability to learn, enhance the rate of growth, reduce the rate of aging, stimulate pancreatic cells to produce insulin, control obesity, and so on.
None of these investigations are possible without animal experimentation.

(4) Animal experimentation as a guide to the isolation of hormones and other biological principles—Animal experimentation has been essential in supporting the work of chemists in their attempt to isolate active biological principles from naturally occurring materials in nature. It was work of this type that led to the discovery and isolation of most of the known hormones and vitamins. Generally, an assay was established in animals by the use of special diets deficient in a given nutrient, or a deficient state was produced in animals by surgical removal of an endocrine gland. The chemist was able to isolate and purify the active principles of interest based on the results of the animal assay. This same approach has been used to isolate all sorts of pharmacologically active drugs from plants, microorganisms and other natural sources. Animal assays offered basic guidance for the isolation of morphine and other opium alkaloids, reserpine, curare, the veratrum alkaloids, the ergot alkaloids, heparin and dicumarol. Most of the vitamins, hormones and drugs isolated from natural sources are essential to all well-being of man and other animal species.

(5) Animal experimentation in drug safety testing—Before a new drug can be given to people, it must be tested in animals to determine its side effects and the dose at which side effects appear. This testing must be done in vivo because the effects of the processes of absorption, distribution, metabolism, excretion, the interactions among these processes and the interactions among the various organ and neuroendocrine systems within the whole animal cannot be duplicated in vitro. To characterize the nature of the side effects to be expected from a new drug, it is usually necessary to give much higher dosages than would be given clinically and sometimes to give the drug over prolonged periods of time. This is because the dosages of drugs needed to elicit pharmacologic or toxicologic effects are often higher in laboratory animals than in humans and because the side effects of drugs suitable for clinical use are usually provoked only by exaggerated dosages. In some cases the drug may accumulate within the body or within particular organs or tissues and thus give rise to toxic manifestations. Some side effects appear only after long periods of repeated administration. In addition to the requirement to test new drugs in animals, it is also necessary to test on more than one species of animal, because extrapolation of the results of testing in animals to humans is less than perfect. Certain species may be more sensitive or predictive than others. To ensure that the safety of a new drug has not been overpredicted and that any potential side effects have not been overlooked, it is routine practice to test new drugs for safety in at least two species. In most cases these will be a rodent and a nonrodent species.

The variety of animal tests and the length of the studies required for a new drug depends on the nature of the drug (pharmacologic or chemical class), the intended clinical use of the drug (for example, length of the usual course of treatment) and to some extent, on the requirements of the countries in which the new drug will be registered for marketing. The following are various types of toxicity studies used for drug safety testing.

(i) Acute toxicity (ii)Subchronic and chronic toxicity (iii) Reproductive toxicity (iv) Mutagenicity (v) Carcinogenicity (vi) Primary irritation testing (vii) Antigenicity testing

Governmental regulatory agencies, such as the USFDA, have established guidelines describing the kind of safety tests that should be conducted in animals in order to have a new drug approved for use in clinical trials and in order to get approval of a New Drug Application (NDA). Among other things, animal experimentation allows the pharmacologist and clinician to become knowledgeable about the absorption, metabolic fate and excretion of each new drug. Such information is often useful in developing new forms of therapy or developing a better understanding of the disease being treated.

Legislation's on animal experimentation

Proper care of laboratory animals used in research is a basic requirement to assure the validity and reproducibility of the results obtained. Animals used in drug research are subject to stringent standards of care beginning with the animal supplier. For the most commonly used laboratory animals, these standards of care often apply for the entire life of the animal. Guidelines for proper care of research animals are provided by the Department of Health and Human Services. The American Association for the Accreditation of Laboratory Animal Care provides the service of certifying laboratories complying with those guidelines. All reputable industrial drug development houses strive to achieve and maintain certification by the association.

The US Department of Health and Human Services publishes the "Guide for the Care and Use of Laboratory Animals," Publication No. (NIH) 78-23.
This was prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources of the National Research Council. The "Guide" contains recommendations regarding housing, sanitation, husbandry, veterinary care, personnel qualifications and occupational health.

The National Institute of Health (NIH) requires that grantees and contractors using live vertebrate animals in projects supported by NIH follow the guidelines prescribed in the "Guide". The Public Health Service further requires the grant-seeking institutions either be accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) or have an institutional committee that reviews its animal facilities and practices for compliance with the "Guide".

AAALAC is a non-profit corporation directed by representatives of 24 scientific and professional organisations that are members of the corporation. It was organised in 1965 to conduct a voluntary program for the accreditation of laboratory animal care facilities and program. AAALAC encourages optimal care for laboratory animals by providing a mechanism for peer evaluation of animal care programs by the scientific community. Humane treatment of laboratory animals, protection of personnel from hazards associated with the use of animals and control of variables that could affect animal research adversely are among the principal objectives of the accreditation program. Animal care facilities of applicant institutions are visited and thoroughly evaluated by two experts in laboratory animal science who submit a detailed report to the Council on Accreditation. Following the standard listed in the "Guide for the Care and Use of Laboratory Animals," the Council determines whether AAALAC accreditation should be granted. Accredited facilities submit annual reports on the status of their animal facilities to AAALAC and site visits to accredited facilities are conducted at least every 3 years. Then annual reports and site visits determine whether accreditation will be continued. Full accreditation by AAALAC is accepted by the NIH as assurance that the animal facilities are evaluated in accordance with their policy on laboratory animals.

In India, Prevention of Cruelty to Animals Act, 1960 and Wild Life Protection Act, 1972 contain provisions for prevention of animal pain or suffering and the condition for maintenance of animals as well as their use in scientific experiments. Several guidelines have also been published by Indian National Science Academy on experimental animals in 1992. Recently the newly formulated rules viz. "Experiments on Animals by Establishments and Breeding (Control and Supervision) Rules, 1998" for regulating animal use in experimentation were formed by the Committee for the purpose of Controlling and Supervising Experiments on Animals (CPCSEA) which was chaired by Maneka Gandhi, had 17 members of whom 12 were ex-officio. These includes Secretaries of the Departments of Biotechnology and Education, the Special Secretary of the National Informatics Centre, the Directors General of Health Services and Medical Research, the Drug Controller of India, the Directors of the Indian veterinary Research Institute and the All India Institute of Medical Sciences, the Chair of the Animal Welfare Board of India, the Additional Inspector General of Forests (Wildlife) and the Director (Animal Welfare) in the Ministry of Environment and Forests.

The overall objective of these legislation's and guidelines is to restrict the use of animals in the scientific experiments. However, experiments whose aim is the extension of new discovery of biological knowledge or knowledge useful for saving or prolonging life or alleviating suffering will be considered. During the experiments, where survival of the animals is expected, the procedure is governed by the pain condition which at most prohibits severe pain which is likely to endure. In many institutions, prior approval from the appropriate animal review committee must be obtained for any experiment, which may result in pain or injury to the animal. Surgical experiments can be performed only by individuals holding an academic degree and must be limited to the minimum procedures necessary to meet the objectives of the project. The use of higher animal species will be considered only when lower animal species cannot fulfill the requirements of the study. Experiments on vertebrates must be conducted under anaesthesia. Sacrifice of the animals at the end of the experiment is also precisely regulated and must be avoided when it is possible to keep the animal alive without further pain.

People views on animal experimentation & its legislation's

A recent report published in New Scientist reveals that the most important nation for animal experiments is the US and Americans are more comfortable than the British with the idea of animal experimentation. Polls conducted by Research American,
a group based in Alexandria, Virginia, suggest that around 70 per cent of people in the US believe that progress in medical research depends on animal experiments. A 1995 poll conducted for the Associated Press by ICR found that 62 per cent of Americans thought using animals to test medical treatments was "right under some circumstances", while 8 per cent said it was "always right". People seem to carry out sophisticated cost-benefit analysis before deciding whether an animal experiment can be justified. The experiment's goal and whether animals will suffer in any way are the most important factors. However, people do not find experiments in which animals might die any more objectionable than these involving pain, illness or surgery.

Mice are by far the most commonly used animal in British laboratories. They were used in 1.52 million of the 2.64 million licensed procedures conducted in 1997. The results show that a majority of people are prepared to accept that mice may suffer, if this helps to fight life-threatening diseases. There were clear majorities in favour of experiments to develop an AIDS vaccine or a drug for treating childhood leukemia. People were just as happy to support the final stages of testing to check whether drugs and vaccines are safe and effective as they were found in earlier experiments during their development.

But these positive views did not extend to all forms of medical research. Opinion was evenly divided over experiments to develop and test a painkilling drug if the experiment involved mice suffering pain—which is unavoidable in tests of a painkiller. Experiments on monkeys were viewed much more negatively than those involving mice. Indeed, only experiments to test or develop drugs to treat childhood leukemia were seen as justifying monkeys suffering. In Britain, experiments involving primates are very tightly controlled. Researchers must convince government officials that the knowledge to be gained justifies any suffering to the animals and that adequate data can not be obtained by using other species. In practice, this means that monkeys are unlikely to be used in leukemia research, as the disease can be studied in other animals. But attempts to develop AIDS vaccines depend heavily on experiments with related viruses in monkeys, in which some of the animals are likely to become ill.

If animal suffering can not be ruled out it may be hard to convince the public of the worth of continuing the fundamental biological research on which many scientists believe medical advances depend. In 1997, this category accounted for more than 800000 licensed procedures with animals in Britain. But it is possible that many were relatively benign and so might win public support if they were described in detail.

In India, the reactions of senior scientists like Ramalingaswamy and Nityananda voice the concern of those who are involved with biomedical research in India. The CPCSEA should function as a supervising body rather than trying to impose impractical conditions which will only serve to curtail the scientific research in the universities and retard the progress of the various time-bound projects, says Nityananda. V. Ramalingaswamy was appalled that the heads of research agencies concerned with biomedical research are shown as members of the CPCSEA. Apparently, the CPCSEA draws its authority from Section 15 of the Prevention of Cruelty to Animals Act, 1960. If the rules proposed by the CPCSEA are brought to Gazette notification, research into new vaccines and new drugs cannot advance in Indian laboratories. It will be a great pity if new drug and vaccine development is impeded at this juncture on account of the proposed rules.

Conclusion

The use of live animals as the subjects of research in science and medicine has a long history. The history of those who have protested against this practice is almost as long. The arguments of the two sides have changed very little the first original experiments were conducted. Since theories and practices may have developed enormously, but the ethical and social questions raised by experiments on animals remain unchanged. On the other hand, discussions about animal experimentation often appear unproductive and ritualistic. Thus, from the anti-vivisectionist point of view, the over-riding concern is that pain is deliberately inflicted on many experimental animals while many vivisectionist are equally convinced of the importance of their work for humane welfare.

It is apparent that animal experimentation has contributed greatly to the welfare of man and all animal species. Animal experimentation has played a major role in making drugs available to relieve pain and other distressing symptoms of disease. It has provided drugs to assist in the control of parasitic diseases. Some of the same drugs have reduced the load on chronic disease hospitals, while still others greatly decreased the population of our mental institutions. Animal experimentation has provided the
means to regulate the size of the world population, increase our food supply and make available nutrients to maintain good health. Based on the many investigations currently in progress and the pattern of past events, one can look forward with confidence to the availability of many remarkable new drugs which will enhance the well-being of humans and animals.

India’s Prevention and Cruelty to Animals Act of 1960 is an act of faith on the part of civil society and at the same time it tacitly recognises the principle that animals may have to be used in experiments if the much-needed information for advancing human health can not be obtained in any other way. Industrial nations have gone through the agonies of public debates on animal experimentation for the benefit of both men and animals and have adopted well-defined guidelines which will safeguard the interest of the scientists, the animals and the society without hampering useful biomedical research. The CPCSEA can invite reports from the institutional committees from time to time and conduct occasional inspections to the centers to ensure that animal welfare conditions are properly observed. We feel that a situation where each researcher and each institution is made accountable will be a practicable approach to promote healthy animal research in the universities and other research laboratories.

References