Title
Experimenting On Individuals Without Their Consent

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Experimenting On Individuals Without Their Consent[1]

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Summary

This paper discusses the harmful and fatal use of non-human animals in research. It argues and demonstrates that such use can be scientifically invalid if the results are applied to humans. Alternatives to such use are discussed in the context of being more defensible morally and scientifically. It calls for a change in attitude in order to institute available alternatives and develop others.

Keywords: alternative, animal use committee, animal welfare, compassion, ethics, human animal, informed consent, kindness, morality, non-human animal, research, scientific method, species differences

When people defend using non-consenting beings (in this case, non-human animals[3]) in research, they usually argue their position by listing all the 'benefits' which have been and are expected to be derived from such use. In a separate paper on moral concern, I argue why our own sense of morality should prohibit us from using non-consenting beings in research[4].

Incomprehensible and tragic is the dichotomy of our sensitivity towards, and treatment of, animals of the same species[5]. Society has anti-cruelty laws to protect our companion animals from abuse. If you poisoned your dog or burned her or him, you could be prosecuted and punished. If, however, you did the same thing to a dog in the laboratory in the name of science, you would not be punished. What changed when you and the dog walked through the laboratory door? Whereas you may balk at considering humans and dogs as moral equals, you cannot rationally argue that there exist morally relevant differences between one dog and another. All the substantive ethical considerations which would apply in protecting a dog who happens to be a human companion would apply equally to one who happens not to be.

It often is stated that animals harmed and killed in research are 'protected' by review committees and laws. If the same type of 'protection' was applied to you, you would appreciate just how vacuous statements of this sort are, especially when considering the extreme invasiveness and death inflicted upon animals and approved by those committees[6],[7].Would *you* consider it protection if someone was legally allowed to subject you to surgery unnecessary for your health or kill you as long as it was in the name of science? When a committee reviewing animal subjects determines that a particular project is 'reasonable,' the obvious question begged is, *Reasonable to whom*? Certainly, no animal, human or other, would knowingly submit to experiments, even if they

1 The intent of this review is to demonstrate that reliance on animal research is unnecessary, in addition to being immoral, to understand or treat diseases in people. Due to the substantial number of published studies that substantiate the various assertions I make, I have limited the citations to just a few in each case, and primarily to those that were published within a few years of revising this manuscript.

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3 Purely for the sake of convenience, I may refer to animals other than humans as "animals", recognising that all are animals of one kind or another; there is no intention to imply that any, even a human, is morally superior or intrinsically more valuable than another.

4 Buyukmihci 2022-12-01

5 Gronkiewicz et al 2017; Jaffer et al 2012; Jayaram et al 2014; Pulaski et al 2014; Spencer et al 2018; Tonetto et al 2016

6 Barra et al 2022; Berro et al 2022; Brown et al 2022; Gigliucci et al 2010; Heuer et al 2023; Heusser et al 2022; O'Callaghan et al 2009; Rather et al 2022; Sajad et al 2022; Silasi et al 2021; Zhou et al 2022

7 In extremely rare cases, a published study may be retracted by a journal after publication due to animal welfare issues (Zhong et al 2021). It is still the case, however, that the inhumane study had been approved by the relevant committees of the institutions involved and initially approved for publication by the reviewers and editors of the journal. In the particular case of Zhong et al 2021, it was only when I lodged a formal complaint with the editors of the journal that any action was taken (Lesa L. Aylward, PhD & Martin van den Berg, PhD, Co-Editors-in-Chief, *Regulatory Toxicology and Pharmacology*, personal communication, 26 April 2021).

were non-painful, if they knew that death was the endpoint. Informed consent is a basic ethical tenet of research involving humans, however we do not allow this with other animals even when they indicate in their own way that they are unwilling subjects, such as cowering in a cage, biting, stress vocalising, struggling to be free of restraint and so forth. There have been instances when individuals have taken 'defensive' action against a noxious situation[8] or have indicated their unwillingness through sign language[9]. Even if a person who is an advocate for animals is on a review committee, my personal experience on such committees has shown this to be a token gesture because the control of the vote is made up of people who in some way have a vested interest in having the projects done or who do not rigorously apply logical ethical principles in making decisions.

There is no legal 'protection' for animals used in research in the way you and I would like to be protected. Not only is it legal to do virtually anything in the name of science, bear in mind that essentially all animals used in research are killed at some point. In the US, the Animal Welfare Act, and its various amendments, is essentially the only law addressing this issue and it has exceptions to every rule. It primarily dictates from where animals can be obtained, how they are to be cared for during shipment and housing, what size cage can be used, and that they must receive food and water. *Even these minimal regulations are not applicable to the vast majority of animals used in research*. Invertebrate animals and so-called cold-blooded animals such as fish, reptiles and amphibians are excluded as are birds, mice, rats, horses, sheep, pigs, cattle and goats[10].

The Animal Welfare Act explicitly states that it is not allowed to interfere with the design or performance of research; this was reaffirmed in the substantive amendments in 1985. It is, therefore, legal to subject animals to unalleviated pain and suffering if it is part of the experiment. It is discouraging that, even though the Animal Welfare Act fails to 'protect' these animals, my colleagues in the biomedical community have consistently and vigorously fought it and all amendments to it, including provisions for non-human primate well-being and exercise for dogs, spending millions of dollars in the process. The research community also lobbied extensively to maintain the exclusion of rodents and birds who are produced for research purposes from being regulated via the Animal Welfare Act, and were successful in this[11]. Ironically, these same people profess to be concerned about the animals.

The National Institutes of Health (NIH) *Guide for the Care and Use of Laboratory Animals* (*Guide*), also falls short of providing any meaningful protection for animals used in research[12]. It states explicitly that it is not meant to interfere with the design or performance of research, and there are no restrictions on what can be done to animals. The use of analgesics, anaesthetics or tranquillisers is not necessary if the researcher deems that such use would interfere with the experiment. A brief search of the scientific literature provides numerous publications of studies which the authors stated were in compliance with the *Guide* and in which animals were subjected to survival surgery, pain and suffering, deprivation, severe restraint and more[13]. When animals are used in routine toxicity testing, no sedation or pain relief is provided in case this might impact on

8 Silverman 1978

9 I have been provided anecdotal information about a non-human primate housed at Yerkes Regional Primate Research Center. This individual had been taught to use human sign language. When he or she was placed in a study which involved a painful procedure, it is alleged that he or she signed to the investigator to "stop, it hurts".

10 So-called farm animals are excluded when the research being conducted is considered to be 'production' oriented. Although precise figures are not available, 'farm' animals appear to be used primarily in this type of research and are, therefore, exempt from the nominal provisions of the Animal Welfare Act.

11 APA 2002

12 NIH Guide

13 Benton et al 2022; Berro et al 2022; Burk & Sheinberg 2022; Gerak et al 2022; Heuer et al 2023; Kiguchi et al 2022; McCormack et al 2022; Rajalingham et al 2021; Sajad et al 2022; Simon et al 2021; Swift et al 2018; Zhao et al 2022; Zhou et al 2022

the results.

Groups which promote the harming and killing of animals in research routinely mislead the public about the issue of pain. For example, in an undated brochure entitled “Health Research to Benefit People & Animals”[14], the California Biomedical Research Association stated: “Procedures *require* the use of anaesthesia and medication to suppress pain and suffering” even though this is untrue[15]. (emphasis added)

The following are a few examples of painful or other noxious procedures or conditions that are imposed upon animals in the name of science: induction of cancer, gastrointestinal ulcers, inflammation of the eye and radiation exposure; poisoning, including routine toxicity testing; extremes of heat or cold; forced swimming test, sometimes in freezing water; severance of the spinal cord; destruction of parts of the brain; burns or other fire-related injury; sleep deprivation; inescapable and severe electrical shock; fighting, sometimes to the death, to study aggression; survival surgery, sometimes multiple invasive procedures. The reader can do a search of the National Library of Medicine database, through PubMed (https://pubmed.ncbi.nlm.nih.gov/), to find literally thousands of contemporary examples of studies in which non-consenting beings – non-human animals – were subjected to manipulations such as these, in which pain and suffering were integral regardless whether there was any attempt to mitigate these pharmacologically. Pain relief is *not* mandatory and routinely is withheld because it would interfere with the results of the experiments or because it is claimed that we ‘cannot determine the animal is in pain’[16]. There is a growing body of evidence that demonstrates that our present perception on whether animals under certain conditions are in pain is limited because we have not been critical in our assessment[17].

The critical point to bear in mind is that, even with strict adherence to the law and guidelines, animals do suffer in biomedical research. It is true that certain funding agencies and institutions do not allow the types of studies I have mentioned to be done gratuitously. Nevertheless, if the painful procedure is considered unavoidable and if it is believed that pain relief drugs would interfere with the results, the studies are approved and done.

Although not all research using animals is as drastic as some of the examples I have given, there are other issues which make it problematical morally. As previously mentioned, almost all animals used in research eventually are killed, even if it is not necessary for the goals of the project. It simply is expedient to do so.

The animals in question usually are housed under conditions which are inconsistent with their natural inclinations and abilities or with their genetic makeup. They are not free to pursue whatever interests they might have. I have heard the housing of these animals compared with ‘palaces’ which are far better than what homeless people have. This is nonsense: homeless people are not removed from the streets and forced into research which results in their death. Regardless of how clean the animals’ quarters are, they still are, in effect, prisons; you cannot clean up what amounts to a concentration camp and expect that that corrects the underlying problem. For most animals, the quarters are sterile, barren enclosures which do little more than meet the animals’ immediate needs of food, water and shelter. These basic needs may not be provided, however, in experiments in which food or water deprivation either is part of the experiment or is part of the

14 Anon undated
15 Even though this falsehood may have been corrected after an indeterminate period, those making the original statement had to know it was false and apparently were trying to lull the public into thinking that animals used in research do not suffer.
16 It was not long ago that some surgeons did not even believe that human infants could feel pain (Rovner 1986).
17 Bradfield et al 1992

'training' process for the animals[18].

The animals' social, behavioural and psychological needs rarely are met, even though we have ample data on this subject. With most non-human primates, for example, the social structure and the opportunity for normal interactions with not only conspecifics (others of their kind) in general, but their family members in particular, is crucial for their physical and psychological well-being. When housed in breeding or research facilities, however, they are under conditions that cannot in any meaningful way meet their physical and psychological needs[19]. The standard and vast majority of the housing comprise small, barren, steel cages with no meaningful enrichment or opportunities for socialisation compared with what the individuals need as a species. With little opportunity for mental stimulation and physical exercise, these animals almost always develop abnormal and self-destructive behaviours that may include pacing, rocking, swaying, so-called floating limb syndrome, bar biting and self-mutilation. The self-injurious behaviour is often serious enough to require veterinary intervention and can lead to the death of the individual[20]. Most singly housed individuals develop one or, usually, more abnormal behaviours[21]. I discuss the issue of housing and other forms of restraint elsewhere[22].

Being deprived of the normal period of maternal relationship has an influence on this[23]. In breeding facilities, infant non-human primates who are to be used in or exported for research are removed from their mothers far sooner than is normal, sometimes immediately after birth. The normal relationship between mother and infant is often several years with respect to providing an opportunity for normal development. This means that these individuals are essentially mother-deprived and develop abnormally as a result. They may be raised in so-called nurseries and display more abnormal behaviour than mother-reared subjects and show differences in their chemical makeup[24]. These individuals also display a reduced capacity for dealing with stressors and develop and mature more slowly[25]. They also react differently to various medications[26]. The mothers themselves show substantial abnormal behaviour just by giving birth in captivity (cages)[27]. Although the cages for captive non-human primates may be within "legal limits" and are "approved" by breeders or researchers, they certainly are not conducive to the well-being of the individuals. This type of housing constitutes extreme privation for these highly intelligent, curious and social

18 Mathes et al 2012

19 One of my colleagues at the California National Primate Research Center tried to defend this type of housing by pointing out that the individuals could see and hear each other through the bars of the cages and thus could 'socialise' with one another. I pointed out that most human couples would find this a less than satisfactory living arrangement. The non-human primates in this case had no less demanding social needs than do human primates.

Although recent provisions of the Animal Welfare Act require that the social or psychological needs of non-human primates be considered, there is little agreement on what those needs may be. Furthermore, the decision on how these provisions are to be met is left to the conscience and willingness of the people using the animals, not someone without a vested interest in the situation. In all cases, the provisions fall substantially short of what these animals could have in a free-living situation. In most cases, the provisions result in only short-term relief or are so insubstantial as to be nonsensical. For example, simply placing toys in a cage, which is often done, has been shown to provide no meaningful diversion for these individuals (Bayne et al 1993).

20 Lutz et al 2007

21 Lutz et al 2003

22 Buyukmihci 2023-02-01

23 Lutz et al 2007; Suomi 1997

24 Bastian et al 2003; Bellanca & Crockett 2002; Boyce et al 1995; Champoux et al 2002; Clarke 1993; Higley et al 1992; Suomi 1991; Winslow et al 2003

25 Durham & Newell-Morris 2006; Fahlke et al 2000

26 Clarke et al 1999

27 Brent et al 2002

creatures[28].

As can be inferred by the biochemical, behavioural and structural differences between normal non-human primates and those reared or kept in laboratory cages, the privation endured by these individuals is not only detrimental to them, it also introduces tremendous confounding effects on data which come from them. The same is the case for other species. Even routine procedures such as catching and handling by humans, forced restraint, injections, or repeated blood sampling can cause great anxiety and stress for these animals[29]. The animals do not make good research subjects as a result. In addition to the studies cited concerning non-human primates, there are numerous other scientific publications showing how factors such as environment and socialisation have a profound effect on the results of a particular experiment[30].These findings cast considerable doubt on the validity of much of the published scientific reports in the world literature. Can we assume those data are reliable or are there major flaws caused by the methods of housing and handling the animal subjects[31]?

Those who defend the harming and killing of animals in research state that the individuals are treated “humanely”. This flies in the face of common sense. To be humane is to have sympathy for another, to have mercy, to be tender and kind. If you provide pain relief after you have destroyed part of the spinal cord in a macaque or squirrel monkey as part of an experimental study[32], how can this be considered humane? If it were not for you, there would have been no pain in the first place. If you think we are treating animals used in research humanely, I suggest you substitute the words “human child” in the place of “animal” for a particular experiment and see if you still consider such treatment “humane”, even if the study is intended to help other children.

When my colleagues admit that animals used in research suffer, they try to justify the suffering by pointing out that humans are suffering, too. They try to appeal to your emotions by showing you sick children and reducing the issue to a nonsensical “us or them” scenario. There is no proof that *not* using the animals would somehow lead to the death of the children. Perhaps more importantly, is it the fault of other animals that we, too, are subject to disease and death? Why do we believe that because *we* suffer, innocent others must pay a price? In that context, it appears that the harming and killing of animals in the name of science is merely an expression of unconscionable selfishness on our part, something which goes against all the best qualities of human nature.

Although my colleagues continually cite work which purportedly will “save or improve the lives of humans or other animals”, most of what is done to animals has no obvious or declared value in this regard, is poorly done[33], the results are heavily biased to conclude more relevance than warranted[34] or simply never is relevant to managing human patients[35]. There are many thousands, perhaps millions, of examples of work in which there were profound negative consequences for the animal subjects (in addition to being killed), but which could not logically be defended by appealing to a greater societal good which might have come from the work.

Also at issue is the scientific appropriateness of using one species as a “model” for another[36]. Research involving the *induction* of diseases in healthy subjects is not scientifically valid. There are

28 Lutz et al 2014; Pereira 1991
29 Novak et al 2013
30 Beynen 1992; Chamove 1989; Fouts 1976; Gross & Siegel 1982; Kraemer et al 1984; McGrath et al 1984; Reinhardt 1997; Romero 1976; Shichinohe et al 1990; Solomon et al 1968; Vesell et al 1976
31 Pereira 1991
32 Barra et al 2022; Sengupta et al 2021
33 Pound et al 2004
34 Ledford 2013
35 Contopoulos-Ioannidis et al 2003
36 Akhtar et al 2009; Seok et al 2013

reasons why some people, for example, get certain diseases and others living under ostensibly the same conditions do not. When a disease is artificially induced, particularly by overwhelming the subject's natural defence mechanisms, this is not analogous to the situation where the disease is contracted spontaneously. When the disease is not even a natural one for the animal, this problem is compounded and confounded even further. The differences which allow for contraction of a particular disease by one person, but not by another, are not addressed, however these are the very aspects we should be investigating. The only scientifically credible manner of investigation would be through studying the two populations themselves. One such striking example is the finding of people naturally resistant to rabies in some communities in Peru[37].

Although there are fundamental similarities between, for example, various mammals, there also exist substantial differences. Even a cursory review of the scientific literature reveals that some of these differences would make extrapolation of findings in non-human to human mammals tenuous at best and very dangerous at worst[38]. Negative findings are even ignored when dealing with human patients[39], demonstrating that medical personnel do not necessarily place great credence on animal studies.

Although a great deal of money has been, and is being, spent to find so-called cures or treatments for various ailments, relatively little is spent to prevent these ailments even when this is possible. Even the so-called war on cancer has been criticised for its lack of focus on prevention and the poor results[40]. Most of the types of cancer which affect humans allegedly can be prevented[41], often simply by changes in diet from one which is based upon animal products to one which is plant based[42].

Lung cancer and other diseases due to tobacco products are still being studied by forcing animals to smoke or use nicotine[43]. Paradoxically, we annually spend *billions* of dollars to promote the use of tobacco products, *over half of the money coming from our taxes*[44].

Using animals as "models" of substance abuse for drugs such as alcohol (ethanol), cocaine, heroin, tetrahydrocannabinol and many others continues[45] despite the fact that substance abuse is a human disease with no known counterpart in other animals. It is far more complex than simply taking drugs. The combination of factors at play, such as genetics, emotional and personal experiences and socioeconomic aspects, can never be simulated or resolved through research using other animals. The millions of dollars or other funds spent every year on this research would be better used to directly help the millions of people who suffer from substance abuse. We know the essentials of the effects of these drugs and can prevent them, if the patient is willing. Researchers themselves are questioning the validity of using animals for this research[46].

Unless we are willing to take advantage of all available opportunities to prevent cancer or other

37 Gilbert et al 2012; Willoughby 2012
38 Anon 1991; Bechtol 1992; Berger & Dimhofer 1995; Bito 1990; Bosshard 1985; Bruner et al 1993; Chapin et al 1993; D'Mello 1993; Dorman et al 1993; Eastwood et al 2010; Felsche et al 2022; Garin et al 2022; Headon et al 1985; Herrera et al 2022; Jacobs & Harwerth 1989; Jenden 1991; Neergaard 1993; Oksenberg et al 1992; Packwood & Gordon 1975; Rea et al 1988; Smith et al 1984; Spearow et al 1999; Tolbert et al 2022; Van Heijst 1991; Wen et al 2022; Wiebers et al 1990; Zbinden & Flury-Roversi 1981; Zhan et al 1992
39 Newell & Malnick 2017
40 Bailar & Smith 1986; Cairns 1985; Cohen & Diamond 1986
41 Esselstyn 1991; Weisburger 1991
42 Lee et al 1991; Schatzkin et al 1989; Willett 1989
43 Holtyn et al 2020; Le Foll et al 2007; Nader et al 2022
44 Cohen & Diamond 1986
45 Ding et al 2023; Gerak & France 2022; Pareek et al 2023; Rahimi et al 2023
46 Magliaro & Ahluwalia 2022

diseases in ourselves, we behave in a morally reprehensible manner if we continue to harm other animals in a search for a "cure". What kind of a moral statement are we making as the US government cuts funds for mental health and drug addiction programs and then spends millions of dollars for drug addiction studies on animals? What are we saying to people who *presently* are afflicted with these conditions and cannot obtain treatment because of lack of financial support?

I do not think there is any question that subjecting other animals to the types of things we do in the name of science is fundamentally unethical and immoral. Biomedical research using animals is not *necessary* for human health and safety. Instead, it is a choice we make, just like our choice of food or clothing. Will the human species wither and die if we stop harming or killing other animals in the name of science? Although this is what some would have you believe, the idea is absurd. The human species has prospered and increased in numbers dramatically over the millennia despite the fact that biomedical research of any substance has been in effect for only little more than a century. Although the use of other animals has been associated with our understanding of certain phenomena, it does not follow that this use was necessary or must continue. There is no proof that the advances associated with the use of these animals could not have come about without them. We simply do not know.

It is appalling that my scientist colleagues, who normally have high standards and insist upon solid evidence before accepting something as fact, appear to lose all perspective when it comes to this issue by making sweeping and unsubstantiated statements with respect to the importance of animal research. They often state that virtually every medical discovery has depended upon the use of these animals or could not have been discovered without their use. This is pure speculation on their part. A conscientious scientist would ask if there had been a controlled study comparing advances with and without the use of animals. Such a study is virtually impossible retrospectively. There is no question that the use of animals did play a part, but so did studies on humans and studies in the physical sciences. No one really knows which aspect had the deciding role or could have been eliminated.

Perhaps the most ignorant and unscientific statement made by many is that discontinuing the use of animals in research would cause science to come to a halt and that we would never find cures for such things as AIDS, cancer or heart disease. How can anyone know that this would be true? Besides, this ignores or denies the numerous discoveries which were based purely on clinical observations of human and veterinary patients or human volunteers – and which continue today. Even people heavily involved in and unrelentingly supportive of experimental research using animals at my university have pointed out the critical importance of clinical observations:

> *"A great deal of our knowledge about disease in general and specifically animal diseases has resulted from studies on naturally occurring diseases in animals under clinical as contrasted to controlled conditions. Major contributions to our understanding of the epidemiology, etiology, processes or mechanism of disease and control and treatment of a wide variety of animal diseases has resulted from proper clinical observations. It is largely through quality clinical research that the veterinary profession acquires new and more effective ways to provide improved veterinary services to society."*[47]

Moreover, Elias A. Zerhouni, M.D., Director of the National Institutes of Health (2002-2008), has been critical of the use of animals as "models" for people:

> *"'We have moved away from studying human disease in humans,' he lamented. 'We all drank the Kool-Aid on that one, me included.' With the ability to knock in or knock out any gene in a mouse—which 'can't sue us,' Zerhouni quipped—researchers have over-relied on animal data. 'The problem is that it hasn't worked, and it's time we stopped dancing around the problem...We*

47 Academic Senate 1981

need to refocus and adapt new methodologies for use in humans to understand disease biology in humans.'"[48]

To get some historical perspective on the nature of biomedical research, people should read the book *Who Goes First?*[49]. This book was written by Lawrence Altman who was a physician on the faculty at New York University at the time of preparing this manuscript. He is not an animal rights activist, but is someone who has been very interested in the history behind various medical advances. What Dr Altman points out, with careful documentation, is that many advances in medicine have not depended upon the use of animals, but primarily have come about through experimentation on humans, often the scientists themselves. His book had been acclaimed by people such as Daniel C. Tosteson, who had been dean of the faculty of medicine at Harvard University and Dr Michael E. DeBakey, who was a famous heart surgeon and chancellor of Baylor College of Medicine. Dr Altman did not write this book to defend or criticise animal research and perhaps that is why it is an unbiased look at how medical discoveries we take for granted today really came to be.

Furthermore, most advances, in terms of increasing the longevity and quality of our lives, have not come about through the use of animals, or even from the discipline of medicine[50]. The greatest benefits have come from adequate nourishment and proper sanitation. In addition, many of the great medical advances such as penicillin, the X-ray and numerous others came from work which did not initially involve animals.

Researchers state and appear to believe that experimental research allows variables to be precisely controlled, as opposed to the situation seen in studies on human subjects. This is illusory for many reasons, including substantial differences in how animals are housed, what food is provided, the background and genetic aspects of the animals, how the animals are treated and so forth. Furthermore, the notion that standardisation is always a good thing may be fallacious in nature:

"A popular notion about experiments is that it is beneficial to reduce subjects' biological and environmental variability to mitigate the influence of confounding factors on the response. The argument is that by keeping the levels of such factors fixed — a process called standardization — we increase precision by limiting the component of response variance that is not due to the experimental treatment. Unfortunately, although standardization increases power, it can also induce such unrealistically low variability that the results do not generalize to the population of interest and may thus be irreproducible — the so-called 'standardization fallacy'"[51]

Unfortunately, regardless of one's beliefs about the use of animals in research, the reality is that it will continue for the foreseeable future. Therefore, although abolition should be the goal of every compassionate and ethically minded person, the situation must be approached in as practical a manner as is possible. Although regulation of exploitation tends to perpetuate that exploitation, it is of little use to the individuals already suffering, and to those slated for use in the future, to take an all or none stance. There are numerous areas on which progress could be made in reducing animal use and suffering without creating the illusion that human progress will be adversely affected. There is no reason why we cannot, as a society, come to a consensus that the use of certain species such as non-human primates simply is not permissible, regardless of what we think might be the potential value of the research, because the ethical costs are too great. I realise that this can be justly criticised as a "speciesist" view. The complex behaviour and cognition of most non-human primate species, however, means that these animals likely suffer more profoundly than

48 McManus 2013
49 Altman 1987
50 Holzman 1989; McKinlay & McKinlay 1977
51 Voelkl et al 2021

other species when used in invasive research[52].

Some research using animals should be summarily banned while we grapple with the larger issue of whether any use is permissible. Examples include: 1) those involving unalleviated pain; 2) those involving the use neuromuscular blocking agents; 3) psychological research; 4) brain function studies; 5) drug addiction studies; and 6) the induction of trauma. There is no justification to subject any animal to unalleviated pain. Neuromuscular blocking agents afford no anaesthesia, but render the animal incapable of moving. There always is the risk, even if an anaesthetic is used concurrently, that the animal may be conscious and in pain without our knowing it. Animals are inappropriate in the study of human behaviour because they are not humans, and because they are not even themselves when they are locked up in cages and forced to live a life not consistent with who they are as beings[53]. The same is true for brain function, which can best be studied in people. There are numerous human drug addicts and victims of trauma who can be studied in order to learn how to manage afflicted humans.

We need to place greater emphasis on the study of humans and what I term nature's "experiments"[54]. For example, suppose one wants to learn more about how myopia (nearsightedness) develops. This could be induced artificially in macaques by depriving them of vision after birth. Different species of macaques, however, have markedly different reactions to the same experimental procedure[55]. Which, then, is the situation which mimics the human condition? *One cannot know from the animal studies*. A different approach could use people who have had natural afflictions which fit the design of the experiment, such as people born with cataracts or other opacities of their ocular media[56].

To determine the connections of the retina to various parts of the brain, one could study a person who has had an eye removed at some point in their life. Sophisticated electrophysiological and biochemical studies can be conducted throughout the person's lifetime. Later, after the person dies, the brain could be studied, comparing the anatomy and biochemistry with that of a person who had not lost an eye. The same principle can be applied to any situation[57].

The level of sophistication for human studies necessary to understand and treat various diseases is considerable[58]. For example, Kiyosawa and coworkers[59], using human volunteers and positron emission tomography, demonstrated a regional reduction in cerebral glucose metabolism in patients with optic neuropathy. Similar technology was used to study cerebral glucose metabolism in patients with depression[60]. Others[61] have studied patients with refractory seizure disorders who were undergoing evaluation for therapeutic brain surgery. These patients had had subdural electrode grids implanted. Cortical mapping was done by electrical stimulation of the

52 Padrell et al 2021
53 Bannister 1981; Pereira 1991; Petticrew & Smith 2012; Sapolsky 1993
54 There are many tragedies which befall humans. Where these are unavoidable, we should learn what we can from them (Cowey & Alexander 2012; Janerich et al 1990; Koren & Graham 1992). For example, cocaine addiction and its impact on the unborn fetus has given clues to the sudden infant death syndrome (Gingras et al 1990). Children born to alcoholic mothers have been studied to learn the effects of this condition on them (Day et al 1991).
55 Raviola & Wiesel 1985
56 Hoyt et al 1981; Twomey et al 1990
57 Palca 1990; von Noorden et al 1983; Weiskrantz et al 1974
58 Breveglieri et al 2022; Charvet et al 2022; Dreyer & Rieger 2021; Hsu et al 2022; Larsson et al 2010; Lawwill 1978; Nunez et al 2022; Pan et al 2023; Ramirez et al 2022; Reeders et al 2023; Sugiyama et al 2022; Toker et al 2022; Warrington et al 2022; Wesselink et al 2022; Westerberg et al 2022; Wong & Sharpe 1999; Yurt et al 2022
59 Kiyosawa et al 1989
60 Baxter et al 1989
61 Uematsu et al 1992

cerebral cortex in order to learn important neuroanatomical details of the human motor cortex, information virtually impossible to derive from other animals.

Others[62] have used positron emission tomography or magnetic resonance imaging to learn about human brain structure and function, including measuring activity-related changes in regional cerebral blood flow to identify brain regions which are active in humans during reading or playing the piano. This combination of cognitive and neurobiological approaches has provided information about the functional anatomy of perception, attention, motor control, and language in the human being, again, something not likely to be possible with non-human subjects.

Hewitt and co-workers[63] at the Robert Wood Johnson Medical School are using cultured human skin to study the effects of burns. Kaufman and co-workers[64] at the Brain Imaging Center of McLean Hospital, using magnetic resonance imaging, demonstrated in human volunteers that even low-dose cocaine constricts brain blood vessels, sometimes severely, supporting concerns that it can cause either acute or gradual loss of brain cells.

Other techniques that can be used on humans include transcranial magnetic stimulation to study the functionality of the circuitry and connectivity of the brain[65], diffusion tensor imaging for evaluation of nerve dysfunction[66], magnetoencephalography to study intricate brain function[67] or single photon emission computed tomography to evaluate treatment effects[68]. These are just a few of the numerous techniques that are available for getting useful information from and for humans.

These types of studies provide us with information about *human* structure, *human* function and *human* disease which will be invaluable in understanding and treating *human* disorders. As pointed out earlier in this manuscript, even a previous director of the NIH acknowledged that we were relying too heavily on animal research and that we needed to focus on research using humans. These human studies also demonstrate that claims that animals are absolutely necessary are not true[69]. These and other methods can be used in numerous other disciplines. They can even lead to substantial savings in health care costs to society[70]. I mention these not just to point out specific examples of alternatives to animals[71]. More importantly, I am emphasising what could be done if there was a change in attitude, a change from one which views other animals as mere “tools” to one which considers them to be deserving of the same respect as humans. If we did this, then we could concentrate our efforts and resources on improving available alternatives and developing new ones[72]. Necessity would become the mother of invention. We could begin the journey out of the Dark Ages of violence and destruction perpetrated without consent and against the will of individuals in the name of science.

The issue of the use of animals in research is complex. The individual concerned about the injustice and lack of scientific credibility of the situation can easily become overwhelmed. You can,

62 Petersen et al 1988,1990; Posner et al 1988; Sallet et al 2013; Sergent et al 1992
63 Ragland 1998
64 Kaufman et al 1998
65 Koch et al 2009
66 Sugiyama et al 2009
67 Vartiainen et al 2009
68 Akar et al 2009
69 There even are alternatives to such problematical situations as assessing the neurotoxicity of batches of polio vaccine (Chumakov et al 1992).
70 Goldberg 1988
71 Some have argued that animals probably were used in the development of some of these methods. As I mentioned earlier, even where this is true, it is unknown whether their use was pivotal. Furthermore, what has happened in the past should be put in perspective. It seems unreasonable to discontinue using something if morally unacceptable behaviour no longer is an integral part of it.
72 Benam et al 2016; Blackwell 2013; Ma et al 2015

however, personally do several things to help reduce animal use and suffering. You can strive to buy products which were not tested on animals and which do not contain materials made from them; adopting a vegan lifestyle. This can be done with little to no inconvenience on your part. These ethical alternatives are numerous, easily available and growing in number. Even if you do not embrace the concept of animal rights or equal consideration for all animals, there is no legitimate reason why you should not choose a product which does what you want it to do, but which is not associated with animal suffering.

You can urge government entities to stop providing funds for research which has little to no relevance for human health or which is associated with considerable suffering. The major institutions providing funds for research in the US, for example, are the NIH and National Science Foundation. Both receive their funds through appropriations from Congress. If Congress would put some stipulations on what categories of research could not be done using public funds, this could go a long way in reducing frivolous animal use and suffering.

We have polluted the earth's land, air and water. We have destroyed – and continue to destroy – millions of hectares of habitat such as rainforests, which destruction will have serious negative effects on *us*, as well as others. We are responsible for the extermination of billions of animals on a yearly basis. We have caused the extinction of hundreds of species. We have placed the spectre of nuclear holocaust on the world. A human being dies every two seconds of every day of every week due to malnourishment related conditions, including outright starvation. The importance of biomedical research with respect to human health and the health of the planet, as it is being done today, pales in comparison.

When contemplating or discussing the issue of animals used in research, the most important point to consider is that these animals are not "things", they are living beings who share with us the drive to live freely. They are not here *for* us. They are not our tasters, we are not their kings. Their value does not depend upon their utility to us. Humans are not the only ones deserving of freedom and the pursuit of their interests. Other animals have just as much right to share the experience we call life. Harming or killing these individuals in the name of science does not make it noble or right. We do to these individuals what we do because we are capable of doing so, operating under the morally reprehensible 'principle' of "might makes right". Our own sense of morality demands that our treatment of them be fair and just.

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    "...it is apparent that cholelithiasis is part of the price of achieving the Western way of life."
    "Nations that consume greater amounts of dietary fat per person have the highest mortality rates from breast cancer...When persons migrate from a nation of low incidence of breast cancer to a nation of higher frequency, these immigrants will have the same high rate of breast cancer as their new nation by the second and third generation..."
    "...carcinoma of the prostate gland, which closely correlates with the epidemiologic factors of breast cancer in terms of fat consumption..."
    "...association of fat with an increased incidence of carcinoma of the colon. ... Women who consume red meat daily had a 2.5 times risk of colon cancer compared to those who ate red meat less than once a month. No associated increased risk was noted with vegetable fat. ... Possible mechanisms include the observation that diets high in fat increase the excretion of bile acids... which have been noted in persons with higher rates of colon cancer and polyps...Bile acids act as a tumor promoter... ...bile acid modification by intestinal flora is decreased in vegetarians and those who reduce their beef fat intake..."
    "...osteoporosis, a disease of protein excess. ... The women of Bantu who are over 60 years of age do not have osteoporosis. They have a huge calcium drain, having an average of 10 children and nursing each child for 14 months. Their diet includes 440 mg of calcium per day, half of our recommended daily allowance... They are protected because they eat only 50 gm of protein daily. When they move to civilization their protein intake increases and they develop osteoporosis... The Eskimo consumes a diet that is high in protein (250 to 400 gm per day) and a diet high in calcium (2000 mg per day); yet, despite much physical activity, they have one of the highest rates of osteoporosis... Millions of Americans have osteoporosis, accounting for 190,000 hip fractures annually... Fifteen thousand women die each year as a result of hip fractures. Despite such data, osteoporosis is unknown in many countries around the world except in Western civilization, which consumes two to three times more protein than required."
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...systematic efforts have not been made as yet to reveal the biological dysfunctions caused in hardier primates such as macaques by standard laboratory conditions. Life-long solitary occupation of caging not much larger than subjects' bodies is one such condition that is disquieting."
"Because primates are born with an evolutionary legacy of profound and complex gregariousness, it is an inescapable, primary hypothesis for all research on captive primates that documented results substantially reflect idiomorphic responses to housing conditions. It is impossible for scientists working with individually-caged beings to interpret any experimental paradigm before identifying the underlying effects of such housing regimes on the systems that they study."
"Our studies document that indoor-outdoor housing for social groups produces demonstrably

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    "Primatologists themselves have warned repeatedly about over-generalising from primate data to human societies... Indeed the data may not even be generalisable between similar species of monkey, as comparative research and field studies suggest that there are striking differences in group composition, social spacing, dominance and aggression between species... The social and hierarchical behaviour of Macaca fascicularis, the species used in many of these studies, may not therefore even be representative of all of its own genus, which raises doubt about extrapolation to higher primates."
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As far as the results of all the experimental work done so far, "Among compounds subjected to clinical trials [in humans], none has proven efficacious, nor have any of these agents come into general clinical use."
They also state: "We would like to offer...some reasons why an over-reliance upon such models may impede rather than advance scientific progress in the treatment of this disease."
They then provide evidence on why the experimental situation is simply not analogous to the real situation, and state "...that the discrepancies between animal research observations and those in humans will not disappear by developing ways of improving clinical research."
With respect to how we will learn information to help human patients with stroke, "Ultimately, however, the answers to many of our questions regarding the underlying pathophysiology and treatment of stroke do not lie with continued attempts to model the human situation perfectly in animals, but rather with the development of techniques to enable the study of more basic metabolism, pathophysiology, and anatomical imaging detail in living humans."

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