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Public perception of laboratory animal testing: Historical, philosophical, and ethical view

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Abstract

The use of laboratory animals in biomedical research is a matter of intense public debate. Recent statistics indicates that about half of the western population, sensitive to this discussion, would be in favor of animal testing while the other half would oppose it. Here, outlining scientific, historical, ethical, and philosophical aspects, we provide an integrated view explaining the reasons why biomedical research can hardly abandon laboratory animal testing. In this paper, we retrace the historical moments that mark the relationship between humans and other animal species. Then starting from Darwin's position on animal experimentation, we outline the steps that over time allowed the introduction of laws and rules that regulate animals' use in biomedical research. In our analysis, we present the perspectives of various authors, with the aim of delineating a theoretical framework within which to insert the ethical debate on laboratory animals research. Through the analysis of fundamental philosophical concepts and some practical examples, we propose a view according to which laboratory animals experimentation become ethically acceptable as far as it is guided by the goal of improving humans and other animal species (i.e., pets) life. Among the elements analyzed, there is the concept of *responsibility* that only active moral subjects (humans) have towards themselves and towards passive moral subjects (other animal species). We delineate the principle of *cruelty* that is useful to understand why research in laboratory animals should not be assimilated to a cruel act. Moreover, we touch upon the concepts of necessity and "good cause" to underline that, if biomedical research would have the possibility to avoid using animals, it would surely do that. To provide an example of the negative consequences occurring from not allowing laboratory animal research, we analyze the recent experience of Covid-19 epidemic. Finally, recalling the principle of "heuristics and biases" by Kahneman, we discuss why scientists should reconsider the way they are conveying information about their research to the general public.

KEYWORDS

3R principles, animal experimentation, animal rights, Covid-19, moral responsibility

1 | INTRODUCTION

In recent years, the use of laboratory animals in biomedical research has been a matter of intense public debate. The most recent statistics suggest that about half of the Western population, who generally are sensitive to this discussion, are in favor of animal testing, but the other half oppose it. Over the years, the European Union (EU), Canada, the United States, and several other countries have

introduced laws to regulate the use of laboratory animal testing. These laws are generally well balanced and have been promulgated after consulting the main stakeholders (i.e., researchers, patient associations, associations for the protection of animals, and so forth) who are sensitive to this matter. Unfortunately, despite these efforts, the public debate has often suffered from misleading information that is disseminated by individuals or groups who oppose animal testing. Researchers have neglected to respond to such aggressive media campaigns with adequately effective communication. A prototypical example is the widespread use of the term "vivisection" that is used in an effort to stigmatize laboratory animal testing, notwithstanding the fact that science abhors vivisection, which is an illegal behavior that was banned by law and abandoned decades ago. Something similar is also happening in the case of vaccination, against which false information campaigns have been launched by groups of people who are generically identified as "Anti-Vaxers." These groups deny the success of vaccination strategies to eradicate several serious infectious diseases, such as smallpox and poliomyelitis, although such opposition to vaccination carries an incalculable risk of severe public health damage.

The recent SARS-CoV2 pandemic and its social and political impact and dramatic consequences on public health systems are bringing new attention to the value of biomedical research. This situation provides an opportunity to replace disinformation with a constructive debate on the importance of animal testing and vaccination. In recent decades, much has been done to protect the rights of laboratory animals, but it is also clear that, based on present knowledge and available technologies, in specific research fields it is not possible to completely abandon in vivo animal testing by replacing it with alternative methods. The present work outlines historical, ethical, and philosophical aspects that stem from the recognition that animal testing is essential to advance biomedical research; it is required for the development of drugs and vaccines that meet both human and veterinary needs.

2 | ANIMALS AND HUMANS: AN HISTORICAL VIEW

From an evolutionary perspective, we as *Homo sapiens* started our journey through time much later than several other species. Since the moment we developed our fine-tuned biological structures and uniquely complex central nervous system, we became "transcendent" beings (Table 1). We started to *symbolize* (Table 1), develop complex abstract thinking, and act accordingly. This high cognitive abilities are unlikely so well developed in other animal species, and this is what makes us different from them.

We can use memories to attribute meanings, interpret the present, and think in perspective to anticipate the future. Through evolution, we also progressively acquired high cognitive faculties that are utilized to explore ways to improve our living conditions. We learned to use objects as tools and employ other animals to reach our aims, which is oftentimes linked to survival instincts but in some other cases independent from them, such as in the case of arts or companionship.

TABLE 1 Definition of the philosophical concepts as used

Term	Description
Transcendence	Human capability of "going beyond" what is material and concrete. For example, we can say that we "transcend" a perceptive stimulus, such as physical pain, when we elaborate it at a secondary level by analyzing it in terms of abstract concepts (e.g., "pity," "cruelty," or "injustice"). We are "transcendent" beings because we can think and act according to abstract concepts.
Symbolization	From the capability of transcendence comes the concept of symbolization, by which we assign an evocative value to what we find in our perceptive experience, both at a linguistic level (by nominating things or by speaking about what is absent) and at psychological, moral, philosophical, social levels (by explaining phenomena through some conceptual senses; e.g., the concept of God).
Utilitarianism	An ethical theory founded by the philosophers Jeremy Bentham and John Stewart Mill between the 18th and the 19th centuries. According to utilitarianism, a right action is the one that promotes happiness or prevent pain for every affected subject.
Speciesism	The practice of considering and treating members of a species as morally superior to members of the other species.
Deontology	An ethical theory according to which the morality of an action should be evaluated on the basis of its intrinsic rightfulness or wrongfulness and not on the basis of its consequences.
Moral status	A subject has his own moral status if he is considered, under certain general rules, worthy of having rights and a moral consideration among other moral subjects.
Moral agent or active moral subject	Differently from "moral patient" or "passive moral subject," a moral agent is a subject that has the capability of acting accordingly to his awareness and of recognizing that every action could have consequences on other subjects. A moral patient, instead, is a subject who has to be respected, on the basis of his rights or of another subject's duties, but without having his own duties.
Awareness	The capability of being conscious of what is perceived, sensed, felt, thought and so forth.
Responsibility	The capability of foreseeing the consequences of one's behavior and of changing it according to them.

Animal domestication and breeding have been fundamental to the development of cultural and social human structures. Through domestication and breeding, humans could become sedentary because it was possible to have food and help without the need to hunt or be nomadic. The first animal that was domesticated was the dog, which was "the culmination of a process that initiated with

European hunter-gatherers and the canids with whom they interacted."[1] After the dog, other animals were also domesticated, such cows, pigs, and sheep, which were bred for food, clothes, or help with strenuous work, mostly in agriculture. Later, horses and several other animals became important to guarantee the functioning of increasingly complex societies.

In parallel, humans have learned to use animals for less immediate and urgent purposes. Domestication has become a way to select some completely captive species to be used for other purposes, such as companionship, entertainment, and scientific research. To develop new knowledge and improve peoples' lives, particularly relevant has become the use of animals in the fields of medicine, pharmacology, biology, physiology, and cognitive psychology, among others.

In the age of Hippocrates,[2] the dissection of human corpses was prohibited, and animals were used to study human anatomy by analogy. "The parallels between human and animal physiology and pathology were noted long ago, and the practice that we today call 'animal research' is rooted back to the period of the ancient Egypt and Greece."[3] During the 17th century, modern science, still in its infancy, was influenced by ideas of one of the most prominent philosophers of the time, Renée Descartes. According to his thinking, animals resemble material machines that lack intellect or spiritual elements, which are possessed by humans only. As a consequence of this vision, beginning in the 17th century, the use of animals in science steadily increased. In the 19th century, Charles Darwin published his most fundamental work, *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*,[4] in which he showed profound similarities between human and nonhuman animals. In the 20th century, thanks to the irreplaceable contribution of laboratory animal experiments, new branches of science, such as pharmacology and immunology, were developed.

At the time of Hippocrates, Aristotle, and Galen and generally until the 18th century, animals were used for experiments without moral or legal restrictions because it was considered the only possible and legitimate way to avoid using humans. In the later 17th and 18th centuries, a moral debate began. Darwin himself was immersed in the public controversy about the use of live animals for scientific purposes. Opinions ranging from not allowing experimentation on animals to testing them if no pain was inflicted and finally to let the animal feel pain. Darwin, being an animal lover, although conflicted, found vivisection justifiable only for true physiological investigations but not simply for "mere damnable and detestable curiosity." In 1875, Darwin was one of 53 witnesses called by the Royal commission to testify on the practice of using live animal testing. In his statement, he emphasized that progress in physiology was possible only with the aid of experiments on living animals, but that the animals must be rendered insensible to pain.

Public awareness of the need to control the use of experimental animals progressively increased, leading to the promotion of specific legislation, such as "An Act Against Plowing by the Tayle, and Pulling the Wool Off Living Sheep," which was passed by the Parliament of Ireland in 1635 and was one of the first known laws on animal protection. In the 20th century, because of the explosion of biomedical sciences, the use of animals for laboratory testing increased enormously, creating conditions for the establishment of a new area of research, laboratory animal science. "This is a multidisciplinary branch of science aimed at contributing to the quality of experiments in which animals are used and at improving their welfare. It encompasses the biology of laboratory animals, their environmental requirements, genetic and microbiological standardization, prevention and treatment of disease, experimental techniques, anesthesia, analgesia and euthanasia, alternatives to their use, and ethics."[5]

3 | THE USE OF LABORATORY ANIMALS TODAY

Experiments on laboratory animals today are conducted at the global level for different scopes and in different fields of study. Laboratory animals are employed to model humans' and other animals' pathologies, develop new pharmaceutical products, produce vaccines, and perform toxicological studies. A recent report indicated that in 2015, 37 countries, for which statistics are available, reported the use of 41.8 million experimental procedures (defined according to the European Union Directive 2010/63/EU; article 3,1) performed on laboratory animals worldwide.[6] The most widespread use of experimental animals occurs in China, with an estimated number of 20,496,670 procedures, followed by Japan and the United States with an adjusted number of approximately 15,000,000 procedures each. By far, the most commonly used animals are mice and rats, followed by birds, fish, reptiles, amphibians, and cephalopods. Significantly fewer dogs and monkeys are used, mostly in China and the United States. In total, the number of dogs and monkeys used in the 36 countries that communicated the data was 112,265 and 92,431, respectively.[6] Another statistical report indicated that, between 2014 and 2016 in Europe, the total number of procedures conducted on laboratory animals has been rather stable ranging from 10,356,578 to 10,853,401.[7]

In all countries, animal experimentation is strictly controlled by specific laws and can only be conducted in compliance with them. A general principle that underlies these laws and that is also valorized by the internationally recognized and accepted guidelines of the *Guide for the Care and Use of Laboratory Animals*[8] is the "Replace, Reduce, Refine" (3R) principle,[9,10] which was first suggested by the English researchers William Russell and Rex Burch in 1959.[11] According to the 3Rs, experimental procedures must always respect the following three basic principles.

- According to "replace," any time possible, the use of animals should be replaced with in vitro or in silico tests[12,13] or with invertebrates[14–16]
- According to "reduce," the number of animals used should always be kept to the absolute minimum that is needed for a specific experiment. The information that is gathered per animal should always be maximized to reduce the number of animals used as much as possible.

- According to "refine," researchers must study and adopt a series of methods to improve laboratory animals' welfare, such as caring about their housing conditions and minimizing pain, suffering, and distress.

The 3R principles are currently considered the most efficient and morally acceptable way to guarantee animals' rights on the one hand and advance scientific progress on the other.

In the United States, animal testing procedures were for the first time regulated by the Animal Welfare Act (AWA) of 1966, which has been amended four times (1970, 1976, 1985, and 1991). The AWA is integrated in the Public Health Service (PHS) Policy on the Humane Care and Use of Laboratory Animals that was published in 1985 and is periodically updated. The PHS policy requires research institutions to establish and maintain appropriate measures to ensure the adequate care and use of animals that are involved in animal testing and research.

In Europe, the use of laboratory animals for research was first regulated by EU Directive 86/609EEC and more recently by Directive 2010/63/EU[17] that applies to all live nonhuman vertebrate animals, including independently feeding larval forms, fetal forms of mammals from the last third of gestation during normal development, and live cephalopods (Art. 1 [3]). The 3R principles are one of the main inspirational elements of 2010/63/EU. After the EU Directive was promoted, EU member states had to comply with it by establishing their own national laws to regulate the care and use of laboratory animals, authorize research protocols for animal experimentation, and supervise proper application of the norms. Proposed research projects, in addition to guaranteeing animal welfare, must use the lowest neurologically evolved species within the constraints of the experiment and the lowest number of subjects possible. 2010/63/EU is a well-balanced directive that was passed after years of discussion between various stakeholders, including researchers, patient associations, and animal protection associations.

Unfortunately, the translation of this EU Directive into national laws has generated some differences between EU member states. Italy, for example, introduced its "D.Lgs.vo 26/14" in 2014, which consists of an unprecedented restrictive interpretation of 2010/63/EU. Additionally, contrary to EU legislation, the use of laboratory animals for xenotransplantation experiments or studying substances of abuse is prohibited, thus creating a significant negative bias in the biomedical research potential of Italy compared with other EU member states. It is worth mentioning also the example of Germany that, in addition to translating the EU Directive into a national law, similarly to Switzerland has implemented the principle of animal protection in its constitution.

4 | ANIMAL RIGHT ACTIVISM

Undoubtedly, animal right movements have contributed to important progresses towards the establishment of a balanced relationship between humans and other animal species. For example, they have contributed to enhance the awareness of the scientific community to the use of laboratory animals in biomedical research. They provided a significant contribution to the promulgation of laws that balancing between the different views allow an adequate protection of laboratory animals without hampering biomedical research. Moreover, they have had a critical role in promoting the recognition of equality between humans and other animal species, so that in some cases, the principle of protection of animal rights has been introduced in national constitutional laws.

On the other hand, it should be condemned when animal right activism leads to inappropriate initiatives, often by single or small groups of individuals, that acting against the law strikes research centers and hospitals or attempt to discredit science. There are examples of scientists that due to alleged accuses by animal right activists have been illegally hindered in their research or have been removed from some of their responsibilities and then found innocent by the court. Occasionally, assaults on research centers, universities, and hospitals have been organized to free the laboratory animals. These actions have detrimental consequences not only for the institutions but also for the animals that bred in captivity and are not able to survive in natural environments.

Beyond these considerations, it is clear that the use of laboratory animals in science is a matter of intense public debate that is based on legal, moral, and ethical evaluations. To adequately address this issue, it is important to structure the discussion within a well-defined theoretical framework.

5 | THEORETICAL VIEWS

It is not easy to find concordance between opinions in ethical debates. General scientific data that unquestionably support any one of the different positions may not be sufficient. Consequently, a particular empathy-based position is perceived as a universally valid philosophical position. As Immanuel Kant pointed out, however, the only universally relevant moral statement is one that, under the same conditions, can be recognized as valid by anyone who is endowed with reason.[18]

The ethical debate about animal rights is one example in which a universally valid moral statement is difficult to imagine—multiple diverse positions are worthy of consideration.[19] For example, such authors as Peter Singer and Tom Regan, although starting from different points of view, have provided arguments that support the thesis that it is wrong to use animals. Other authors, such as the utilitarian Raymond G. Frey and Peter Carruthers, embrace contractualism and stand for the practice of laboratory animal testing.

In *Animal Liberation*,[20] Singer applies the "Principle of Equal Consideration of Interests." According to this principle, humans and other animal species must have the same interests and rights. Singer criticizes what he calls "speciesism" (Table 1), a morally wrong practice of treating one animal species as morally more important than others. Singer anchors this equality principle between members of different species to the experience of suffering, which is common to people and animals. According to this utilitarian perspective (Table 1),

everyone who feels pain and suffering naturally wants to avoid them; consequently, provoking pain is cruel and disrespectful of others' rights.

Regan instead bases his defense of animal rights on a deontological argument (Table 1), according to which the concept of the "intrinsic value" of a subject-of-a-life, a definition that cannot only be applied to humans but also to animals. In fact, animals are living beings, and this is sufficient to assert that, like humans, animals should never be considered objects. These two different but convergent theoretical approaches support a common position according to which the use of animals for food or testing has to be avoided as a morally unacceptable practice.

Like Singers, Frey[21,22] supports the principle of utilitarianism, but he comes to an opposite conclusion. According to him, animals, in contrast to humans, are not aware of "interests," beliefs, or desires; therefore, it is wrong to attribute the same value to humans and other living species.

Another opponent of the equalitarian vision is Carruthers,[23] who justifies the use of animals based on the fact that they do not have the same mental capacity as humans. According to Carruthers, animals can have beliefs and desires and engage in practical reasoning in response to them. Animals can feel pain and fear and can suffer, but they are not "rational agents" because they are not able to govern their behavior in accordance with universal moral rules that are obeyed by most members of a community. Hence, no animal has the "moral standing" that only humans have. According to Carruthers' conclusion, because animals do not have the same moral status (Table 1) as humans, they cannot have the same rights. In other words, he states that moral agents (Table 1) like humans (i.e., subjects who have moral responsibilities) must postpone responsibilities toward animals to promote their interests. Carruthers further pushes his position to the extreme by asserting that "a duty not to slaughter your neighbor's dog might be an instance of a duty not to damage others' property."[19]

As can be seen, general discussions about whether it is right or wrong to use animals in scientific research can lead to many disagreements and unsatisfactory conclusions for anyone. The fundamental question is why we should care about human rights more than animal rights. There is likely no unique or universal answer to this question, and there are equally sustainable and even opposing ethical positions on this matter. When engaging in this debate, it would be useful to concentrate as much as possible on a few elements.

6 | ACTIVE AND PASSIVE MORAL SUBJECT AND RESPONSIBILITY

The first element to consider is that the moral sense is a human characteristic that makes individuals of our species "active moral subjects." Conversely, the behavior of nonhuman animals is to a large extent instinctual. Hence, animals should be viewed as "passive moral subjects." They are unable to recognize their own moral status and their own rights. Thus, being human an "active moral subject," he also has the prerogative to recognize rights to other living subjects. The human being is thus the only "responsible" agent (Table 1). He has the responsibility to respect animals' rights but without neglecting his own and those of his species. Moreover, from a slightly different point of view, according to Hans Jonas,[24] human responsibility requires that the respect of nature and other species is a human duty more than other species' rights.

7 | ANIMAL TESTING IS NOT CRUELTY

Another element to consider is the concept of cruelty because, in most cases, animal experimentation is perceived as a cruel practice by the general public. Of course, for humans, it is a moral imperative to abhor cruelty. We should not harm animals by using them for experimentation if this means to be cruel. However, is the use of laboratory animals cruel when they are used for the "right purpose"? Are we performing acts of cruelty, or are we fulfilling a necessity? Cruelty must be condemned as a wrong behavior; to do so, however, we must first clearly define it.

We think that the first element that makes an act cruel is awareness (Table 1). To be considered cruel, a person must be aware of the fact that he is harming someone or something else by provoking unnecessary pain or suffering. Without awareness, there is no cruelty. So, for example, a person who does not have the mental faculties to recognize others' suffering should not be judged as cruel. The second element that we consider important is the ability to "symbolize" the act, which we already described as the capacity to attribute to it a specific meaning and value.

The third condition for an act to be considered cruel is that it must be done *freely*, without a reason, scope, or need, and only with an inner intention of satisfying some personal pleasure, such as the pleasure of inflicting harm only for the sake of it. The difference between a non-cruel act and a cruel act resides in the intention behind it. If the intention is informed by a very strong *need* that requires that act and that act only, with no other possible alternatives, then the act could be considered non-cruel even if it is harmful to others. Instead, if the intention that motivates an act that causes harm to another individual is based on a personal interest or satisfying unnecessary pleasure, then the act can be judged as cruel. One of the arguments against animal research is that it is freely enacted cruel behavior. Based on the elements delineated above, animal testing can be considered cruel only if a scientist acts in the absence of a necessity and if he uses an animal to satisfy a personal desire to harm or experience pleasure from harming. On the contrary, it cannot be considered cruel if the work of a scientist reflects the necessity of improving humans' and other species' lives.

8 | ANIMAL EXPERIMENTATION IS A NECESSITY AND A "GOOD CAUSE"

Of course, we must also reflect on the concept of "necessity," which directly derives from the concept of "need." A need is opposite to the

desire for an unnecessary pleasure. Ethical and bioethical norms recommend the avoidance of unnecessary pleasure if it harms others' rights, but they cannot suppress a natural need. If animal testing is the only way (or the most appropriate way) to improve the condition of people and their pets who suffer or save their lives, then this can be viewed as a legitimate need.

Another element to consider is the principle of "good cause." As animal rights' supporters contend, a cause that is good for humans may not be good for other animal species that are employed for that purpose. Conversely, what is not a good cause is not necessarily a bad cause either. Under ethically controlled circumstances, even if the cause could not be good for the animals that are used because, for example, they do not themselves benefit from being used, it is not necessarily bad in absolute terms. Testing drugs on laboratory animals is also useful for developing medications to ameliorate or save the lives of our pets and other nonhuman animals in general.

This argument should be carefully considered by those who believe that ethics cannot be speciesist, and it cannot consider only what is best for humans because, as explained above, laboratory animals are also used to protect and improve the lives of other animal species.

9 | CAN BIOMEDICAL RESEARCH AVOID USING LABORATORY ANIMALS?

In addition to the ethical and theoretical perspectives that are discussed above, in which we sought to clarify that experimental research is a necessity and not cruel, we should also consider the practical reasons why biomedical research cannot avoid the use of animal testing.

As mentioned previously, the use of laboratory animals adheres to the principle of "good cause," and it is conducted in compliance with laws that are promoted to guarantee animals' rights. The 3R principles are the basic principles that have inspired current laws that regulate the use of laboratory animals. Consistent with the 3Rs is a commitment to engage in animal testing only when valid alternatives are unavailable. The main possible alternatives to in vivo tests are in vitro cell and tissue cultures or in silico computer-assisted experiments.[25] These alternative methods are indeed largely practiced in biomedical research, and their use has greatly contributed to the *reduction* of laboratory animals. Nonetheless, the complexity of various organs (e.g., the brain) and difficulty mimicking the function of a human organism in vitro or in silico make it impossible to fully replace in vivo laboratory animal testing. In fact, in most cases, the only way to study pathologies that afflict both humans and other species is by replicating them in animal models. The efficacy and toxicity of new drugs and vaccines, at some point in their development, can only be studied in living animals.[26] Testing a drug on a single cell or using an in silico approach (or both) would certainly help identify important characteristics of molecules that make them viable or not for further development. However, verification of their efficacy and safety profile is possible only if animal testing is performed. The alternative to this is an unsustainable risk (and thus unethical) to develop treatments without proven safety and efficacy. To prevent these risks, drug regulatory agencies stipulate that any new medication, vaccine, or cure in general must be tested in laboratory animals prior to entering the clinical stage.

The history of thalidomide offers the most famous example of what can happen if drugs are developed in the absence of adequate preclinical testing. In 1957, this drug was commercialized to treat insomnia, headaches, and nausea after having been tested only in rodents, but never during pregnancy. Unfortunately, it was extensively used by women to treat nausea and vomiting during pregnancy.[27] During that period, an unprecedented number of cases of phocomelia and other birth defects occurred in all 46 countries where the drug was marketed. Years later, thalidomide was identified as the cause of this disaster and subsequently withdrawn from the market. This led to some controversies about the predictive ability of animal experimentation.[28]

The dramatic experience with thalidomide is often recalled to support positions against the use of laboratory animals in biomedical research. However, two facts need to be considered. The first is the logical fallacy and hasty generalization of the assertion that animal testing on thalidomide was not predictive and therefore any animal testing is not predictive. In fact, there are several other cases in which the use of laboratory animals has been very important for the early detection of drug toxicity. The second and most important fact, when the story of thalidomide is viewed from a different perspective, demonstrates the importance of using laboratory animals in preclinical research. The problem with this drug arose from the insufficient evaluation of its toxicity in laboratory animals, from the fact that all of the experiments were conducted in rodents (which were shown to be less sensitive to thalidomide compared with other species, including humans) and from the lack of tests during pregnancy. Hence, what caused the problem was not the poor predictive validity of animal testing but rather the inappropriate animal model that was used and insufficient preclinical investigations of the drug.

This dramatic experience led to the establishment of new guidelines and laws to regulate the preclinical testing of drugs. For example, these new guidelines stipulated that any new molecule or vaccine must be tested on at least two different animal species before moving to the clinical stage. Thanks to advances in the optimal use of laboratory animals, the risks for humans can be minimized by detecting the toxicity of new drugs very early during development. Recent data indicate that approximately 80% of compounds that are under development fail to enter the clinical stage, and approximately 40% of them are stopped after a lack of tolerability or signs of toxicity are found in laboratory animals.[29]

10 | CONCLUSIONS

Although the moral debate about using animals for scientific research is far from providing universally acceptable answers, we tried to

address it from different points of view, both theoretical and practical ones. To go even deeper into the matter, we think that it is also important to explore some practical examples. For instance, let us consider the recent experience with the SARS-Cov2 pandemic that began around December 2019 in Wuhan, China, and spread worldwide in less than 3 months. We rapidly learned how dangerous this virus is. In the absence of effective medications or specific vaccines, several countries implemented what they viewed as necessary measures to control further spread of the disease. Such measures included lockdowns and social isolation to protect their populations and give biomedical researchers sufficient time to develop effective treatments.

As "active moral subjects," we can decide whether to use or not use laboratory animal testing to advance research on SARS-Cov2. A hypothetical scenario can be constructed in which we choose not to practice laboratory animal testing for biomedical research. Our knowledge of the disease would progress much slower. Based on current scientific knowledge, new drugs or vaccines could not be developed. To reduce the risk of infections, we would likely be forced to live in social isolation for very long periods of time, from months to years.

One alternative might be to simply ignore or disregard the epidemic and maintain our usual lifestyles. In such a scenario, the disease would rapidly spread, many people would become infected, and many casualties would arise, especially in less developed countries where healthcare systems are relatively poorly developed and insufficiently organized to face this infectious disease. History has taught us that this indeed happened several times in the past during plague, smallpox, and cholera epidemics. These catastrophic events were followed by even more dramatic experiences, including long-lasting famines and wars, that impoverished entire populations and killed millions of people. One such example was the so-called "Black Death," a fatal pandemic of bubonic plague that devastated whole populations in Europe, Africa, and Asia between 1346 and 1353 and resulted in 75–200 million deaths.

Thanks to advances in science, however, today medications and vaccines can be developed in relatively short periods of time, thus mitigating the impact of SARS-Cov2 that otherwise could be catastrophic. Acting rapidly and efficiently in biomedical research means that we need to use laboratory animals. In addition, existing medications that we are using to mitigate the consequences of SARS-Cov2 infection, such as drugs or vaccines that are approved for humans or other animals, were developed after extensive testing in laboratory animals. Is it an acceptable moral decision not to use them because they were initially tested in animals?

For ethical reasons, an individual with full cognitive capacity can decide not to use drugs that were developed from animal testing. This is an acceptable position because individuals possess full cognitive capacity. More complex is when such a choice is made by people who suffer from cognitive impairments, psychological instability, or other cases of compromised judgment.

Moreover, an unacceptable position would be when an individual's conscientious objection is imposed on other people to limit their access to drugs or other medical treatments. For example, the "no-vax" position is not ethically acceptable because reducing the number of people who are vaccinated consequently heightens the risk of spreading an infectious disease in the whole population, with severe consequences especially for those who, because of specific circumstances (i.e., immunodepression), cannot be vaccinated.

Unfortunately, unfair or misleading information, characterized by high emotional loads, that depict laboratory animals as victims of human progress has a tremendous impact on this ethical debate, and public opinion can be easily swayed by it. As Daniel Kahneman[30,31] pointed out in his theory of heuristics and bias, particularly in complex situations, when it is difficult to provide an exhaustive answer (i.e., in ethical debates), humans engage in cognitive processes that "substitute" the original question with an alternative one that is easier to answer. For example, if the question is, "How many laboratory animals are you willing to sacrifice to advance human knowledge about a certain disease and develop a new medication?" then the alternative question is, "How much emotion do I feel when I save the life of animals that are otherwise used for laboratory testing?" The answer to this latter question does not respond to the original one but provides a rapid solution to the ethical dilemma.

If this is the cognitive process that contributes to biasing public opinion toward the protection of animal rights to the detriment of societal progress and human health, then scientists should probably reconsider the way they are the vehicles of information about their own research work. To communicate rational information and statistical data on how many human lives biomedical research can save by developing a new medication will probably not work. But if the ethical question is posed differently, such as, "How many people who suffer from untreatable disease are you willing to save by allowing laboratory animal testing?" then the heuristic questions will be, "How much emotion do I feel when I save human beings who suffer from a disease that threatens their lives?" At the margin between these two views is the fundamental role of responsibility, which links the needs of being responsible for the rights of both humans and other animals to create a liminal space we call ethics. In this space, every action must be pondered, and appropriate questions need to be asked to find the right balance when engaging in open and healthy debate. The example of SARS-Cov2 is both real and recent and tells us that our responsibility is to act consciously to find an optimal balance between protecting animal rights and the obligation to act in an attempt to advance human society and improve the quality of life of our own species. So we believe that it is an opportunity for science to pose the right questions to raise public awareness about the importance of animal testing in biomedical research.

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