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The Human Cost of Animal Experiments

First published in Nexus, Feb-March 2001

There is strong scientific that animal-based testing is grossly inaccurate in evaluating how a drug or product will affect humans and is a grave risk to the health and safety of people and animals alike, writes Katrina Fox.

Graphic pictures of cats with electrodes clamped to their heads, or monkeys strapped to chairs with their brains cut open, their eyes filled with pain and terror, are enough to upset momentarily even the most hardened person. But most of us put these images out of our mind and accept the situation, because we're told by the government and medical establishment that such experiments are for our own good. They insist that without these procedures there will never be cures for the world's diseases, and that those who oppose animal experiments are extremists holding back "progress".

Yet, despite the supposed stringency of animal tests on drugs deemed safe for human consumption and released onto the market, two million Americans become seriously ill and approximately 100,000 people die every year because of reactions to medicines they were prescribed.1 This figure exceeds the number of deaths from all illegal drugs combined, at an annual cost to the public of more than US$136 billion in health care expenses.2 In England, an estimated 70,000 deaths and cases of severe disability occur each year because of adverse reactions to prescription drugs, making this the third most common cause of death (after heart attack and stroke).3

The drug company Ciba-Geigy has estimated that only five per cent of chemicals found safe and effective in animal tests actually reach the market as prescription drugs.4 Even so, during 1976 to 1985 the US Food and Drug Administration (FDA) approved 209 new compounds-102 of which were either withdrawn or relabelled because of severe unpredicted side-effects including heart attacks, kidney failure, liver failure and stroke.5

The animal rights movement has lobbied for years against animal experimentation on moral and ethical grounds, but the scientific evidence against vivisection is far stronger. Researchers who put their careers on the line and publicly admit that animal-based models are inaccurate for evaluating the effects of drugs in humans are encouraged or forced to be silent in a billion-dollar industry.

Two such researchers are Dr Ray Greek, an American anaesthesiologist, and his wife, Jean Swingle Greek, a veterinary dermatologist. Both are ex-vivisectors who have studied medical and scientific literature which is largely unavailable and inscrutable to the public. Using the industry's own data, they expose in their new book, Sacred Cows and Golden Geese: The Human Cost of Animal Experimentation, how we are kept in the dark about the dangers to our health from animal experiments.

WHY ANIMAL MODELS ARE NOT PREDICTIVE

Open up a rat, a dog, a pig and a human and you will find much the same terrain, but with differences. But it is precisely these differences which have an impact when it comes to assimilating drugs. For example, rats, the species most commonly used in

vivisection, have no gall bladder and excrete bile very effectively. "Many drugs are excreted via bile, so this affects the half-life of the drug," explain Ray and Jean Greek. "Drugs bind to rat plasma much less efficiently. Rats always breathe through the nose. Because some chemicals are absorbed in the nose, some are filtered. So rats get a different mix of substances entering their systems. Also, they are nocturnal. Their gut flora are in a different location. Their skin has different absorptive properties than that of humans. Any one of these discrepancies will alter drug metabolism."

These differences are only on a gross level. Medications act on a microscopic level, initiating or interrupting chemical reactions that are far too small for the human eye to observe. "We differ on the cellular level and molecular level and, importantly, that is where disease occurs," the authors explain. "The cells of chimps are very similar to [the cells of] humans, but the spatial organisation of the cells is vastly different."

Even those who favour the animal model admit its unpredictability among their peers. Dr Ralph Heywood, director of Huntingdon Research Center in the United States, says: "The best guess for the correlation of adverse reactions in man and animal toxicity data is somewhere between five and 25 per cent."6
Dr Herbert Hensel, Director of the Institute of Physiology at Marburg University, goes further: "In the opinion of leading biostatisticians, it is not possible to transfer the probability predictions from animals to humansÉ At present, therefore, there exists no possibility at all of a scientifically based prediction. In this respect, the situation is even less favourable than a game of chance."7

Even the most widely respected textbook on animal experimentation states: "Uncritical reliance on the results of animal tests can be dangerously misleading and has cost the health and lives of tens of thousands of humans."8
The best-known example of this is thalidomide. Mothers who took this drug to ameliorate morning sickness gave birth to children with shocking deformities, with most lacking developed limbs. Animal tests had not predicted this. The first recorded case of side effects occurred on Christmas Day 1956, but in 1957 the drug was released anyway.9

UNSAFE FOR HUMANS

The following, taken from Dr Ray and Jean Greek's book, are just some examples of pharmaceutical drugs which have been deemed safe for human use after extensive animal testing, but which were later found to cause serious side effects.

Amrinone: Use of this drug for treating heart failure led to 20 per cent of patients developing thrombocytopenia (a lack of blood cells needed for clotting), despite a comprehensive program of animal studies in mice, rats, hamsters, guinea pigs, dogs and rhesus monkeys. Some of these patients died.

Birth control pills: These are known to cause life-threatening blood clots in some women, yet scientists have still not been able to reproduce this finding in animals. In fact, dog testing predicted that the pill would decrease the likelihood of clotting.

Chloramphenicol: This antibiotic caused life-threatening anaemia in humans. Chloramphenicol is an example of a drug whose effects vary from species to species: dogs do well with it, cats die from it, cows tolerate it but horses do not. It is so toxic to susceptible humans that its use has been outlawed in animals used for food. The tiny amount consumed from ingesting a hamburger made from a treated cow will cause death in such a person unless they receive a bone marrow transplant.

Clioquinol: This anti-diarrhoeal passed tests in rats, cats, dogs and rabbits. It was pulled off the shelves all over the world in 1982 after it was found to cause blindness and paralysis in humans.

Diethylstilbestrol: This synthetic oestrogen was designed to prevent miscarriage, but it did just the opposite by increasing the rate of spontaneous abortions, premature births and neo-natal deaths. No human trials were done; all the safety data were collected from animals.

Eraldin: This heart drug was withdrawn in 1975 after causing serious side effects in an estimated 7,000 victims, 23 of whom died. It had been tested for six years in mice, rats, dogs and monkeys and when introduced on the market was "particularly notable for the thoroughness with which its toxicity was studied in animals, to the satisfaction of the authorities".10 Even long after the drug was withdrawn, scientists failed to reproduce these results in animals.

Floxin: This antibiotic progressed through animal testing, only to cause seizures and psychosis when used by humans.

Isuprel: A medication used to treat asthma, it proved devastatingly toxic to humans in the amounts recommended based on animal studies. In Great Britain alone, 3,500 asthmatics died from using the medication.

Manoplax: This heart drug, which had been tested on rats, mice, rabbits, cats and guinea-pigs, was withdrawn worldwide in 1993 after analysis of patients showed that those taking it were at increased risk of hospitalisation and/or death.

Methysergide: This treatment for migraine led to severe scarring of the heart, kidneys and blood vessels in the abdomen, although scientists have been unable to reproduce these effects in animals.

Opren: This treatment for rheumatism and arthritis killed 61 people and caused 3,500 adverse reactions. Withdrawn in 1982, the drug had been tested on monkeys and other animals for nine years with no adverse side effects.

Phenylpropanolamine (PPA): This drug, found in many common cold and flu remedies, was banned by the FDA in the US after it was linked to causing between 200 and 500 strokes in young women a year.

Primacor: This medication, given when the heart is not pumping enough blood, worked well in rats but increased deaths in humans by 30 per cent.¥ Ritodrine: This drug, prescribed to avert premature labour, induced pulmonary oedema (fluid in the lungs, causing breathing difficulties and possibly death).

Suprofen: This arthritis drug was withdrawn from the market when patients suffered kidney toxicity. Prior to its release, researchers said this about the animal tests: "...excellent safety profile. No cardiac, renal [kidney] or central nervous system [side effects] in any species."11

Tamoxifen: This drug, used to treat and prevent breast cancer in women, caused liver tumours in rats but not in mice or hamsters.12 The drug has been shown to be harmless to the developing foetus of rabbits and monkeys, but to cause bone abnormalities in rat foetuses.13 One of the side effects is nausea and vomiting, but this was not predicted in animal studies, even though high doses were tested in dogs - the species considered most predictive of vomiting in humans.14 The drug has also been implicated in uterine

cancer, blood clots, memory loss, absence of periods, and eye damage such as cataracts.15

Zomax: This arthritis drug killed 14 people and caused many more to suffer.

QUESTIONABLE ACCURACY OF TOXICITY TESTS

One of the reasons why so many drugs cause adverse reactions in humans-reactions which were not predicted in animals-is because of the inaccuracy of the toxicity tests carried out. The most notorious of these is the LD50 Draize test ("LD50" stands for "Lethal Dose 50 per cent"), where animals-usually dogs and rats-are force-fed, forced to inhale or are injected with a chemical until 50 per cent of them die. That dosage is then designated as the LD50. Its unreliability is obvious when we consider the huge variables such as the age, weight and gender of the animals, not to mention the environmental conditions under which the test takes place. These variables render the results invalid even for the species tested, let alone for humans.

The LD50 test was still part of almost all regulatory guidelines for the safety assessment of chemicals worldwide until 10 years ago. In the United States, although the FDA no longer requires the test and will accept in vitro and other non-animal-based alternatives, it still accepts the LD50-so the testing continues.
In November 2000, the Organisation for Economic Co-Operation and Development (OECD), which comprises 29 member countries, agreed to abolish the LD50 test and phase it out during 2001.16 But the alternatives which will take its place are merely a refinement of the original; they still involve the use of animals and therefore are still wholly unreliable indicators for human health.

In the United States, the Voluntary Children's Health Chemical Testing Program is being developed by the Environmental Protection Agency (EPA), and it involves extensive animal testing to determine the "safe" amount of toxic poisons to which children can be exposed.

WHAT DOESN'T WORK FOR ANIMALS MAY WORK FOR HUMANS

As well as animal tests allowing unsafe drugs onto the market, the flip side is that human health is also compromised when drugs which may be beneficial to humans are prevented from being released. Most drugs have side effects, some of which are more acute than others, but many useful medications used to save lives would not have reached clinical trials if they had first been tested on animals.

We only have to look in our own medicine cabinets for examples. Today, around 29 billion aspirin per year are sold in the United States and twice that number worldwide, yet aspirin causes birth defects in mice and rats and results in such extensive blood abnormalities in cats that they can only take 20 per cent of the human dosage every third day.20 Another painkiller, ibuprofen, causes kidney failure in dogs, even at low doses.

Other prescription drugs were initially unavailable to people because animal studies predicted side effects not found in humans. They include:

Corticosteroids: These have been shown to cause cancer in some rodents, despite their being used safely by humans for years.

Depo-Provera: This contraceptive was barred from release in the US in 1973 because it caused cancer in dogs and baboons.

FK506: This anti-rejection drug was almost shelved before it proceeded to clinical trials. After experimenting on dogs, researchers said animal toxicity was too severe to proceed to the clinical trial stage.

Furosemide: Mice, rats and hamsters suffer liver damage from this diuretic, but humans do not. It is widely prescribed for the treatment of high blood pressure and heart disease.

Isoniazid: This medication, commonly used for treating tuberculosis, caused cancer in animals.

Penicillin: The release of penicillin was delayed when its discoverer, Alexander Fleming, put it to one side because it did not work in rabbits. This is because rabbits excrete penicillin in their urine. Only when Fleming had a sick human patient and nothing else to try, did he administer penicillin - with excellent results.

Prilosec: The release of this gastrointestinal medication was delayed for 12 years because of an effect in animals which did not occur in humans.

Streptomycin: This popular antibiotic caused birth defects such as limb malformations in the offspring of rats.

THE CANCER WAR

According to Dr Ray and Jean Swingle Greek, 40 per cent of us will have a diagnosis of cancer at some time in our lives. It is the one disease which most of us will have had some encounter with, whether personally or through contact with friends or family. But despite billions of dollars poured into "cancer research", the medical establishment is not winning its war against the Big C. Deaths from the disease are increasing; for example, from 1973 to 1992 they went up by 6.3 per cent in the United States.

The Greeks reveal in their book that despite thousands of substances being fed to, painted on and injected into hundreds of millions of animals, we are no closer to saving lives. "In many cases, it [animal experimentation] has actually led to more life loss and introduced new dangers," they argue.

There are more than 200 different forms of human cancer. Some of these have counterparts in animals, although even these differ greatly from those in humans in terms of cause, effect, treatment and prognosis. An histiocytoma is fatal in humans but benign in dogs, as all cancers have species-specific effects.

Ironically, in the 1950s the only known carcinogens were those found by studying humans epidemiologically, the authors explain. "A study of dyeworkers showed a high incidence of bladder cancer," they write. "Droves of dyed lab animals failed to prove the rule. Chromium was found to be carcinogenic in humans but not in animals. The link between radiation and cancer was also reported from clinical studies by that time. In 1956, British doctors warned of carcinogenic effects of X-rays given during pregnancy, resulting in childhood cancers. But no amount of irradiated pregnant quadrupeds necessarily produced the same effect.
"In these instances and many others, the inability to validate carcinogenicity in animals kept cancer-causing agents legal for a much longer time."

Asbestos is another example. The link between cancer and asbestos was made as long ago as 1907; but, after scientists failed to induce the disease in animals, it took more than 30 years before the human-model evidence became irrefutable.

Ray and Jean Greek point out that, between 1970 and 1985, researchers subjected an estimated 300 to 400 million animals to more than half a million compounds to check for anticancer effects. Based on these animal experiments, only 80 compounds progressed to clinical trials. Just 24 proved to have any anticancer activity in humans, and, of these, 12 went on to have a substantial role in chemotherapy. But, all 12 of these compounds were chemical variations of previously known chemotherapeutic agents. The fact that these chemicals could be used to fight cancer had already been predicted by their chemical structure.21 In other words, for 15 years, billions of dollars of investment money was ploughed into subjecting millions of animals to the most painful, cruel and barbaric procedures and then killing them, all of which proved nothing new.

Even the US National Cancer Institute (NCI) has admitted its failures. In the Los Angeles Times of 6 May 1998, NCI Director Dr Richard Klausner was quoted as saying: "The history of cancer research has been a history of curing cancer in the mouse. We have cured mice of cancer for decades and it simply didn't work in humans."

In the United States in the 1990s, scientists came up with the idea of genetically engineering rats to accept human cancers. But in 63 per cent of cases, according to the Greeks, the human tumours in the rats did not respond to chemotherapies which are "currently and effectively" used in humans, because the way cancers grow in animals is different from how they grow in humans. It begs the question as to how many anticancer drugs which could be successful in treating human cancers have been missed because they did not work in mice or rats. Chemotherapeutic agents which have been successful in humans have all come from non-animal means, according to the Greeks.

The next time any of us is tempted to put money into a tin shaken by cancer research charities which fund research using animal models, we would do well to remember the words of Dr Irwin Bross, formerly of the Roswell Park Memorial Institute for Cancer Research, in testimony before the US Congress in 1981: "While conflicting animal results have often delayed and hampered advances in the war on cancer, they have never produced a single substantial advance in either the prevention or treatment of human cancer."

WHY ANIMAL-BASED RESEARCH CONTINUES, DESPITE THE EVIDENCE

If even the proponents of the vivisection lobby admit that animal studies are inaccurate and produce little reliable data for human extrapolation, why on earth do they continue to employ these methods?

Dr Werner Hartinger, a German surgeon, surmised in 1989: "There are, in fact, only two categories of doctors and scientists who are not opposed to vivisection: those who don't know enough about it, and those who make money from it."

The latter in particular, according to Ray and Jean Greek, is the main reason. "Scientists are just like the rest of us, materialistic and opportunistic. They, too, struggle to survive and excel in a competitive world," they argue.

Dr Irwin Bross agrees. In 1986 he was quoted in Cancer Research on Animals as saying: "They [scientists] may claim to love truth; but when it is a matter of truth versus dollars, they love the dollars more." To get grants for research and stay employed, you must churn out papers with the utmost regularity. And the fastest and easiest way to get papers published is to use animal experimentation.

"Animal experimentation is tidy," the Greeks explain. "The lovely thing about rats is that you can go home on Friday night and rest assured that they will still be in their cages when you get back on Monday. On the other hand, clinical research on humans can be

tricky. Clinicians have no control over patients who may not return for follow-up appointments. Human subjects may even be dishonest about their lifestyles. You can addict monkeys to crack cocaine or heroin in your nice, clean lab. If you want to study human crack or heroin addicts, you may have to interact with potentially nasty people."

Time is also of the essence. "A rat's generation time is weeks, not decades. By the time a clinician publishes one good paper, an animal experimenter can publish at least five. The easiest way to publish is to take a concept already published and change something, the type of animal used, the dose of the drug, the method of assessing the results or some other variable." It is the number, as opposed to the value of research, that is important to those wishing to get on in their scientific career.

Acceptance of the status quo, not rocking the boat, is also a key factor. The pressure on students and young doctors to publish should not be underestimated. It has led to a proliferation of scientific journals which are often edited by researchers using animal experiments. This means that vivisectionists are able to put forward their work, but those who are against animal studies can find no place to publish-despite there being an estimated 100,000 scientific journals in print today. Many of these journals rely on advertising revenue from pharmaceutical companies and others who make products for animal experimenters.

Mainstream media also collude to keep anti-vivisectionists' work out of the public eye. At the UK press conference of the Greeks' new book, not one journalist from a national newspaper attended, despite novelist Jilly Cooper being there to promote it. Reporters and editors soon realise that if they want to hang onto their jobs and maintain a steady flow of breaking news, they must keep their contacts happy. Most of these scientific contacts will be part of the animal experimentation lobby who will not take too kindly to the prospect of having their industry exposed as a money-making fraud.

This money, by the way, is yours. The US Government spends around $10 billion of taxpayers' money each year on animal-based research, according to the Greeks. The largest single provider of funds to medical research institutions in the United States is the National Institutes of Health (NIH). But only one-third of NIH competing research grant applications includes human subjects.22 So it is not hard to see why animal studies are the preferred option of researchers with career ambitions and mortgages to pay.

Then there is the grip of corporations to contend with. The animal experimentation industry grosses between an estimated 100 billion and one trillion dollars a year worldwide. This figure includes the employment of hundreds of thousands of people, including those who manufacture and sell jackets for immobilising animals and pumps for force-feeding them, needles, cages, scalpels and equipment used to kill animals in a specific way, not to mention the sales of animals themselves. Take Cedar River Laboratories, for example, which specialises in selling cats; its price is usually $225 for animals less than 16 weeks old.

Pharmaceutical firms benefit from the industry, too. According to its 1999 annual report, Merck's sales for the year came in at $32,714 million. Animal experimentation is the quickest way of getting a new drug onto the market. Researchers given grant money by pharmaceutical companies are far more likely to come out with a positive review of the drug than those who are not receiving financial support. The Journal of the American Medical Association reported that 43 per cent of more than 2,000 researchers surveyed at the top 50 research universities said they had received gifts, including cash, even when the giver required prior approval of the results of the research being conducted.23

Even charities are not exempt from the profit-making loop. Many of them - such as the American Institute for Cancer Research, the American Diabetes Association and the American Heart Association, and the Imperial Cancer Research Fund and the British Heart Foundation (BHF) in the UK - fund or carry out animal-based research. Out of a total income of £56 million in 1998, the BHF spent £34.9 million on research, with only £5.1 million going into educational programs. In one test, dogs' chests were cut open and their blood was circulated out of their bodies and back again in order to allow blood pressure to change quickly in the neck arteries. The experimenters then came to the conclusion that a person bending down and suddenly standing up could experience dizziness and fainting.24

Animal testing also provides pharmaceutical firms with a weapon to protect themselves from being sued by people who have been damaged by their products. In Europe, all medications when they reach the final product stage are legally required to be tested on animals for carcinogenicity and birth defects. But, explains Wendy Higgins, campaigns director of the British Union for the Abolition of Vivisection, this is not the case in the developmental stages of a drug, which is where most animal testing goes on.

The situation in the United States is similar. According to Dr Ray Greek: "Most pharmaceutical firms do more testing than the government requires, so they can say in court that they saw no effects like the one that killed the plaintiff's wife. Officials will tell you off the record that they rely on animal testing and think that it is a big factor in protection from lawsuits." Or, the companies can turn around and dismiss the animal tests as being unreliable in humans. Either way, it is extremely hard for victims to take legal action against them.

ALTERNATIVES TO ANIMAL-BASED RESEARCH

Real developments always arise from a human-modelled foundation, Ray and Jean Greek assert. The potent painkiller morphine, for example, is extracted from poppy flowers. Quinine, used to treat malaria, comes from cinchona bark. Aspirin, the most widely used medication in the world, was first prescribed by Hippocrates in the form of willow bark. None of these owes anything to animal experiments.

Clinical studies of patients and good old-fashioned observation have led to the successful treatment of childhood leukaemia and thyroid disease. Our present HIV and AIDS therapies and a number of heart drugs have also been developed in this way.

In vitro or test-tube study has revolutionised medical research. Cell and tissue preservation technology is now so advanced that many different types of cells can be kept alive almost indefinitely, giving far more accurate results when studying disease on the microscopic level at which it occurs.

Autopsies and epidemiology are other key areas of research, with technology today allowing thousands of patients at multiple institutions to be tracked. Ray and Jean Greek point out that epidemiological studies discovered the link between folic acid deficiency and spina bifida. Epidemiological studies also showed the cause/effect relationship between smoking and cancer, cancer and diet, heart disease and cholesterol, coal dust and black lung disease, smoking and heart disease, among many other diseases. It was epidemiology that proved the link between smoking and lung disease, despite the tobacco industry arguing for years that this was not the case because animal-based models said so. Experimenters had tried unsuccessfully for more than half a century to give animals cancer with tobacco smoke. They reasoned that since animals do not get cancer from tobacco, there is no proof that it causes cancer. The tobacco industry even paid doctors in the 1950s and 1960s to advertise cigarettes.

Breast cancer is an area that has benefited from mathematical modelling where computers simulate parts of the human body. This is a relatively new area of research, as is computer-assisted research where molecules can be studied on screen using computer graphics which mimic the body's systems.

The Dr Hadwen Trust is a UK-based charity established to come up with alternative research techniques. It funded the development of a new brain-scanning technique for studying vision, which replaced the need for invasive experiments on cats and led to a revolution in the understanding of the human brain with untold potential. The Trust also funded a pioneering 3D computer model of human teeth which is used to predict the results of corrective dental procedures such as braces. These alternatives are not prohibitively expensive, either. Many are in fact cheaper than using animals. An initial cost of implementing new procedures would have to be incurred, but the long-term savings would justify the investment.

MORAL, ETHICAL AND SCIENTIFIC CONCERNS

The moral and ethical objections to vivisection will continue to rage on. If you are not interested in "animal rights", the use of animals in experiments will probably not bother you. But the scientific evidence against this practice should worry every single one of us who cares about our health.

Anyone who is yet to be convinced should take note of the section in Ray and Jean Greeks' book which outlines the results of a 1998 survey conducted by the Public Citizens' Health Research Group (PCHRG) in the United States. In the survey, 19 medical officers at the FDA said that 27 new drugs approved by the agency in the past three years should not have been. "Dr Sidney Wolfe, Director of the PCHRG, said that standards are going down because the agency has been under pressure from Congress to approve products more quickly. Of 172 officers interviewed, eight said there were 14 instances in the past three years where they had been told not to present their opinion to an advisory committee if it would reduce the likelihood of a drug's approval."25, 26

So, contrary to the propaganda put forward by the medical establishment to justify its work, animal experimentation does not save human lives. As the industry's **own** evidence proves, it does just the opposite.

Author's Note

This article is based on information contained in **Sacred Cows and Golden Geese: The Human Cost of Animal Experimentation**, by C. Ray Greek, MD, and Jean Swingle Greek (Continuum Publishing, London and New York, 2000, www.continuumbooks.com).

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Resources

Americans for Medical Advancement (website of Ray and Jean Greek): www.curedisease.com.

British Union for the Abolition of Vivisection: www.buav.org.

Dr Hadwen Trust for Humane Research: www.drhadwentrust.org.uk.

For more information on the EU's chemical testing program, see www.stopeuchemicaltests. com.

People for the Ethical Treatment of Animals (PETA): www.peta-online.org, for a full list of charities which fund and do not fund animal-based research and for more information on chemicals testing programs in the US.