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# REFINING RESEARCH TO IMPROVE THE LIVES OF LABORATORY MICE

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AGES: 11–12

Some scientific research includes experiments performed using animals. Many of the animals used in research are sentient, which means they have emotions or feelings that are probably similar to the positive and negative emotions that humans experience. Some experiments can cause animals to experience negative emotions like pain or fear. While animals can sometimes be replaced with other methods or used sparingly, in other situations there is no easy way to perform experiments without using animals. In these cases, scientists can protect animals by using refinement, which describes all efforts to improve the housing conditions, care, and scientific procedures that the animals experience. Refinement aims to avoid or lessen negative experiences or pain and to improve the animals' wellbeing. For example, scientists work hard to develop methods to give drugs to mice without using force, or to pick mice up more gently so the animals do not feel stress.

Thanks to the endeavors of the Swiss 3RCC, these articles have been translated into the three main Swiss languages of German, French, and Italian.

## ANIMAL EXPERIMENTS AND THE 3RS PRINCIPLE

Animals are used in research for many different reasons. For example, they are used to develop new medicines or to test potential medicines for safety and effectiveness before these drugs are tested on people. Animals are also used to check the safety of chemicals that we use in our daily lives, like cleaning products. Scientists also use animals to learn about diseases that affect both humans and animals. Many of the diseases scientists work on involve processes that can only be studied in living **organisms**—not in cells that scientists grow in the laboratory. For example, if scientists want to understand diseases of the brain, often only animal studies can help them do so. Several animal species are biologically similar to humans and suffer from some of the same diseases we do. It is often easier to perform experiments on animals than on humans, for two main reasons. First, scientists can control the environments that research animals live in, for example what the animals eat or how they are housed. This cannot be done with humans. Second, research on humans could expose those humans to health risks, which would be **unethical**.

Many people worry about the use of animals in research and would like to see animal research replaced with alternative methods. To protect animals as much as possible, scientists apply the **3Rs principle** to avoid or reduce animal use in research whenever possible. The 3Rs principle was formulated by two scientists, William Russel and Rex Burch, in 1959[1]. Their aim was to make animal research less harmful for the animals. The first R is **replacement**, which describes all efforts to completely avoid using animals in research, for example by using computers to simulate what happens in a human or animal brain. The principle of **reduction** deals with methods to reduce the number of animals used in research. Modern research methods that maximize the knowledge that scientists can get from each animal help to reduce the total number of animals needed. The third R is **refinement**, which describes changes in how scientists house and treat laboratory animals to reduce their suffering and increase their wellbeing.

Although the first and most important R is replacement, for some experiments it is impossible to use alternative methods like computer simulations or cells grown in the lab. Despite efforts to replace animal experimentation, around 12 million animals are still used every year in Europe for scientific experiments [1]. Because of this, refinement, the third R, is important. In most countries, the wellbeing of animals is protected by animal welfare laws that forbid cruel treatment of animals, which can include any treatments that let animals suffer unnecessarily. The laws also describe how animals should be housed and cared for. For example, these laws describe how much space a lab animal should have in its stable or cage. However, the refinement principle goes beyond the conditions that are set out by animal welfare laws—it strives to reduce negative impacts on research animals *as*

### ORGANISM

A living thing made up of one or more cells, for example a human, a fish, or a mouse.

### UNETHICAL

Actions or behaviors that do not follow the accepted rules of our society.

### 3RS PRINCIPLE

A principle formulated by two scientists in 1959, to make animal research less harmful for the animals. The 3Rs are replacement, reduction, and refinement.

[1] https://caat.jhsph.edu/principles/the-principles-of-humane-experimental-technique

### REPLACEMENT

Attempting to avoid the use of animals in research by replacing them with other methods.

### REDUCTION

Applying methods to minimize the number of animals used for research.

### REFINEMENT

Applying methods to minimize suffering and to improve welfare in animals used for research.

*much as possible*, and to make their lives better by continuously improving their living conditions.

## SENTIENT ANIMALS CAN EXPERIENCE NEGATIVE EMOTIONS

Why do we care that lab animals are treated well and that their living conditions are good? Some animals, including many of those used in science, are sentient. Being sentient means these animals have emotions that are probably similar to the positive and negative emotions that humans experience. Some experiments can cause sentient animals to experience negative emotions, like pain or fear. When sentient animals, including humans, experience very strong negative emotions, or even mild negative emotions for a long time, they may suffer.

Which animals are sentient and can therefore experience suffering? This is not an easy question to answer, and there are many differing opinions on the issue. In the future, research on animal **sentience** may change our minds, but currently all vertebrates (animals with backbones) are believed to be sentient, including mammals, birds, fish, reptiles, and amphibians. Invertebrates (animals without backbones) like insects and worms are not currently thought to experience positive and negative emotions the same way humans and vertebrates do [2]. Therefore, at this point in time, most invertebrates are not considered sentient by most scientists (Figure 1). However, there are certain invertebrates—like the lobster and the octopus—that *do* react similarly to vertebrates when they experience painful situations. So, some scientists include these animals in the group of sentient animals and ask for their strict protection. Switzerland, for example, includes octopi in its animal welfare laws.

**SENTIENCE**

Being sentient means to have (positive and negative) emotions.

**Figure 1**

Sentient animals are believed to experience positive and negative emotions similar to those experienced by humans. At this time, non-sentient animals are not currently thought to experience positive and negative emotions the same way humans and vertebrates do.

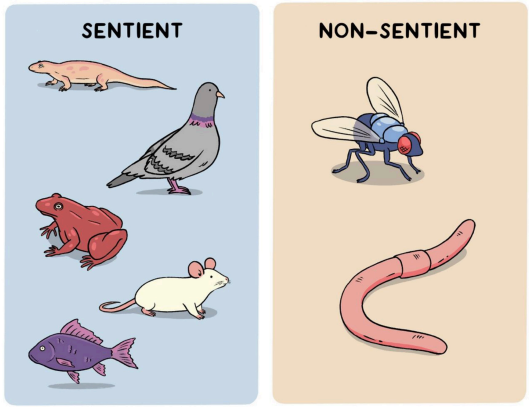


Figure 1

## IMPROVING THE LIVES OF LABORATORY MICE

To describe how refinement efforts can improve animal welfare, we will concentrate on mice because mice are the most widely used research animals around the globe. Depending on the country, mice make up 50–75% of all animals used in research, mainly because mice reproduce or breed quickly and can be easily housed in the laboratory. Mice are tiny mammals that have many things in common with humans, including much of their genetic information and many bodily processes. The genetic information of the mouse is also easy for scientists to change, which makes mice good for many experiments. Research using **genetically modified** mice allows scientists to imitate and study human diseases in mice, as well as to find new medicines to treat these diseases.

**GENETIC MODIFICATION**

Changing the characteristics of an organism by changing its DNA. DNA is the material that carries all the information about how an organism looks and functions.

**FREQUENCIES**

Here, audio frequency. Frequency is how many sound waves are produced by the animal per second.

The welfare of mice is important because they are sentient animals that interact with each other socially. For example, did you know that male mice sing love songs for female mice, in **frequencies** that are beyond the level of human hearing [3]? Or that mice can tell if another mouse is feeling unwell and change their behavior accordingly—for example, by reacting more strongly to negative experiences like pain [4]? In humans we call this empathy—the ability to understand or feel what others are feeling.

Mice need certain conditions to live healthy, happy lives. Good conditions for mice include having material to build cozy nests to keep themselves warm, living in groups with other mice, and being cared for by humans who understand their needs. There are also many ways that experiments can be improved to reduce the negative emotions mice experience, like pain or fear. Examples include helping mice to get used to being around humans before the experiments start or giving mice pain killers when painful experiments are performed.

## A SPOONFUL OF SUGAR HELPS THE MEDICINE GO DOWN

When mice are used in experiments in which they must take medicines—to prove that a new drug helps to treat a disease, for example—these medicines must sometimes be swallowed by the mice. Mice do not swallow all medicines willingly, especially if the drugs taste bitter. To get around this, scientists sometimes give the medicines through a tube inserted into the mouse's mouth directly into its stomach. This is unpleasant for the mouse, so even though the procedure is allowed by law when it is scientifically necessary, scientists try to use the refinement principle to make giving drugs more pleasant for mice. For example, scientists from the University of Zurich, Switzerland [5], use this easy solution: mice like fatty, sweet food, so they mix the drug with a tasty substance like sweetened condensed

milk. Mice will happily lick up all the medicated condensed milk from a measuring device called a pipette (Figure 2).

**Figure 2**

Feeding a drug mixed with sweetened condensed milk to a mouse. Mice like to eat sweet and fatty substances, so they will easily lick up drugs that are mixed with foods like Nutella, peanut butter, or raspberry jam.


Figure 2

Other good ways of getting mice to swallow drugs without using any kind of force include mixing the medicine with Nutella, peanut butter, or raspberry jam. These methods avoid unpleasant experiences for the mice and also make scientists' lives easier because the mice will willingly eat these substances—so the scientists know that their mice have swallowed the full dose of the drug they are investigating.

## A PLEASANT RIDE: USING PLASTIC TUNNELS TO GENTLY PICK UP MICE

For many years, scientists picked up lab mice by their tails to move them from place to place (Figure 3A). It was easy for scientists to catch the mice this way without being bitten, but some scientists thought it might be unpleasant for mice and did research on better ways to pick them up. In the wild, mice live in burrows with tunnels. A researcher in Liverpool, England named Jane Hurst therefore checked whether mice prefer to be transported in a tunnel—and they do! Mice transported in tunnels are tamer and more relaxed than those picked up by their tails [6]. This is good for the wellbeing of the mice, and it makes the mice easier for scientists to work with. More and more scientists are training their mice to enter little plastic tunnels[2], which the scientists use to transport the mice (Figure 3B).

[2] https://www.nc3rs.org.uk/3rs-resources/mouse-handling

## OUTLOOK

In most countries, these and many other refinement techniques are not yet required by law, meaning scientists do not *have to* use them—but even though they are not required, these techniques are still being increasingly used these days. Use of refinement techniques is important because it helps to reduce animal suffering and improves animal welfare whenever we cannot fully replace animals in research.

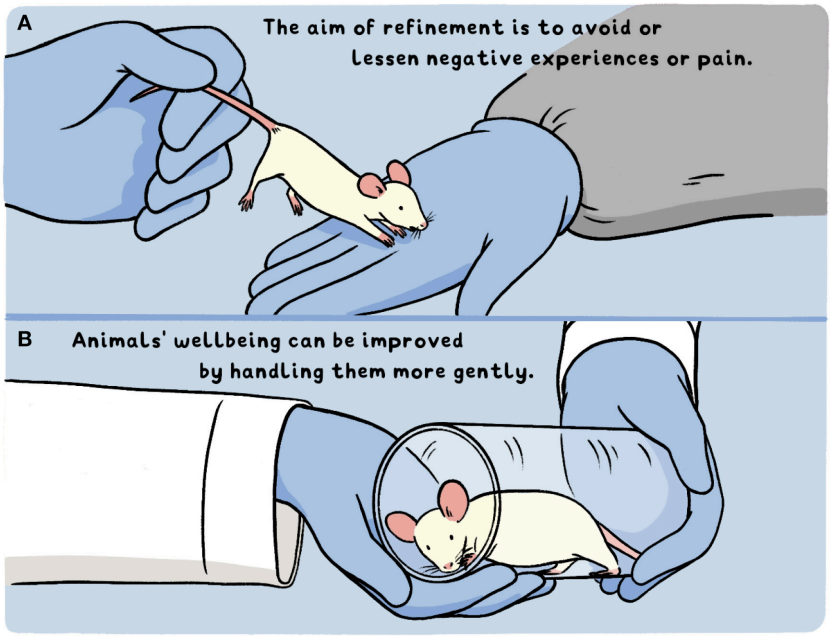


**Figure 3**

**(A)** In the past, most scientists caught mice by the tail to transport them. **(B)** Using plastic tunnels to transport mice keeps the mice more relaxed, which is both good for the mice and helpful for the scientists who work with them.

All around the globe, scientists are trying to convince their colleagues to implement more refinement into their animal experiments. How do *you* think we could increase the happiness and reduce the suffering of lab animals, and how could we best convince others to follow these practices?

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