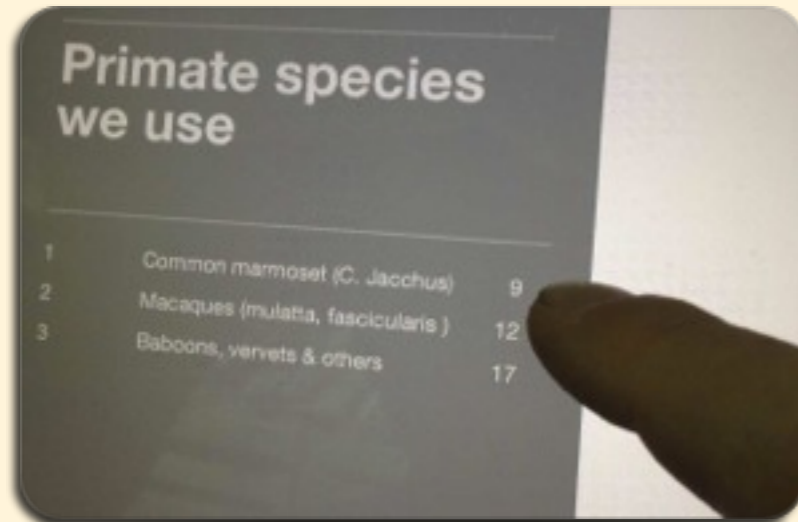


Primates in Medical Research



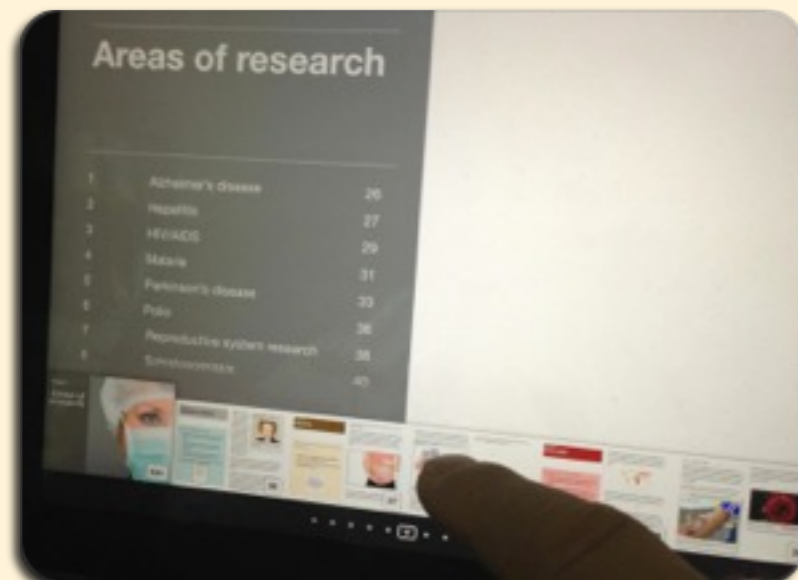
How to use this iBook



Touch **Section title** to go directly to the Section



Sweep right or left to view all photos in a gallery



Touch **Page** to go directly to the desired page



Pinch out any photo-gallery or video to watch it in bigger size or full screen. Pinch in to return

Chapter 1

Preamble



Why does medical research require monkeys?

How do researchers work with primates? And which species do researchers work with? In this book we will explain the role primates play in scientific research and show you how primates have played a vital role in medical advances for conditions as varied as malaria and HIV/Aids, Alzheimer's disease and polio.



Chapter 1

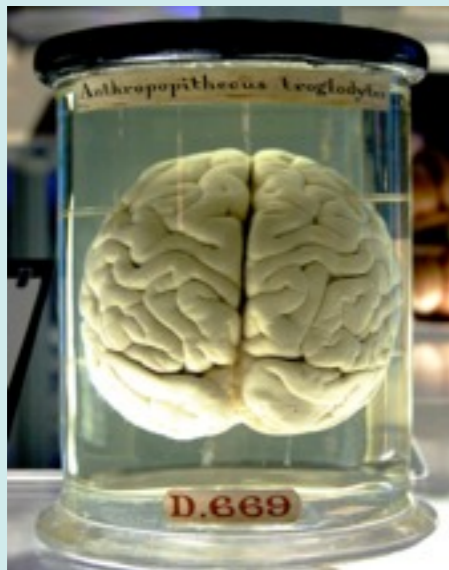
Why do we use primates in research?



All primates are similar

A SHARED BIOLOGY

1. Anatomical similarities - eyes and brain
2. Physiological similarities - immune and reproductive systems
3. We are similar because we share a common ancestor



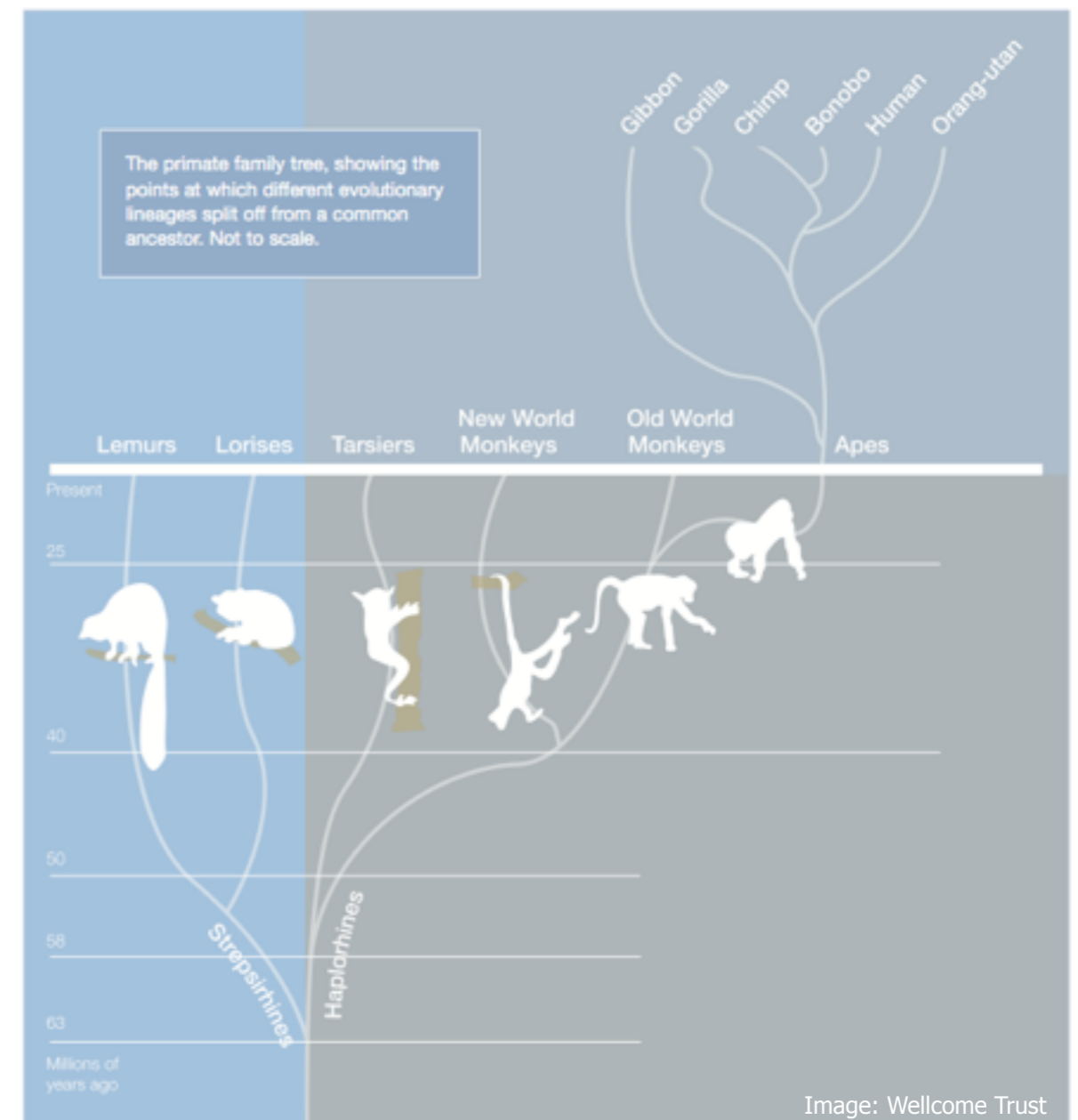
Chimpanzee brain



Human brain

Humans are primates so it is not surprising that studying non-human primates can tell us about ourselves. We share the majority of our genes, have similar anatomies, and very similar physiologies. But we also study primates to cure their diseases

THE PRIMATE FAMILY TREE



Anatomical similarities

Non-human primates are the closest species' to humans in terms of biological make-up, so they are thought to have a high degree of sentience. For this reason, they are rarely used in medical research. However some important areas cannot be studied in mice and rats.

Primates have forward-facing eyes on the front of the skull that give binocular vision, allowing accurate distance perception. The evolution of color vision in primates is unique among most mammals, so much research into vision has required primates.

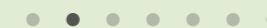
The brains, reproductive and immune systems of primates are more similar to our own; more so than those of other mammals. Research on primates is therefore highly relevant to people.

Many serious diseases affect the brain: Stroke, Alzheimer's disease, Parkinson's disease and other neurodegenerative disorders all involve damage to the brain.

Anatomical similarities - monkey and human



Human and ape anatomy (image science photo library)



Physiological similarities

Primates are sufficiently similar to humans to increase understanding of many reproductive problems – for example, miscarriage and premature birth, and endometriosis (abnormal growth of tissue lining the uterus).

The immune system is central to our defence against infectious organisms. Our immune systems differ from those of rodents in key ways, relating to the infection process and the immune response, making primates more suitable for studying some aspects of infectious disease in people.

Vaccines work by boosting our immune response to infections. Many vaccines are used to prevent disease around the world, but we still have no such defence

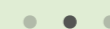
against diseases such as HIV/AIDS or malaria, which currently kill millions of people a year.

So medical researchers say that research on primates is justified when the potential benefits for health and science are great, and there are no realistic alternatives.

GALLERY 1.1 Physiological similarities between monkey and human



Human and primates both have similar pregnancy, birth and newborn care



Chapter 2

Primate species we use



Macaques (*Macaca*)

CYNOMOLGUS MACAQUE

1. Macaques in science
2. Rhesus factor
3. Monkeys in space
4. Cloned and transgenic monkeys

Macaque or Cynomolgus monkey (*Macaca fascicularis*)

In the wild macaques live in female dominated troops and occupy a variety of habitats ranging from grasslands to forests. They are not threatened species in the wild (IUCN category - least concern).

This species is the most common research primate, and accounts for around 80% of all macaques used. A native of S.E. Asia, the Cynomolgus macaque is smaller and less aggressive than the rhesus macaque (*Macaca mulatta*) which is also used in research.

The rhesus monkey is larger and more expensive to keep.

GALLERY 2.1 Macaque species



Lactating *Cynomolgus macaque* (*Macaca fascicularis*) mother with young baby (image Bushmitz BFC)

1 of 12

Macaques in science

Macaques are relatively easy to keep in captivity and because of their wide availability and closeness to humans anatomically and physiologically, they have been used extensively in medical and biological research on human and animal health-related topics.

The discoverers of the rhesus factor, one of the elements of a person's blood group, Karl Landsteiner and Alexander Wiener gave the rhesus macaque's

name to their discovery. Other medical breakthroughs from rhesus macaques include:

- development of the rabies, smallpox, polio vaccines
- creation of drugs to manage HIV/AIDS
- understanding of the female reproductive cycle and development of the embryo
- propagation of embryonic stem cells.

Cloned and transgenic monkeys

In January 2000, the rhesus macaque became the first cloned primate with the birth of Tetra. A year later in January 2001 the birth of ANDi saw the first transgenic primate.

ANDi carries foreign genes originally from a jellyfish.



Monkeys in space

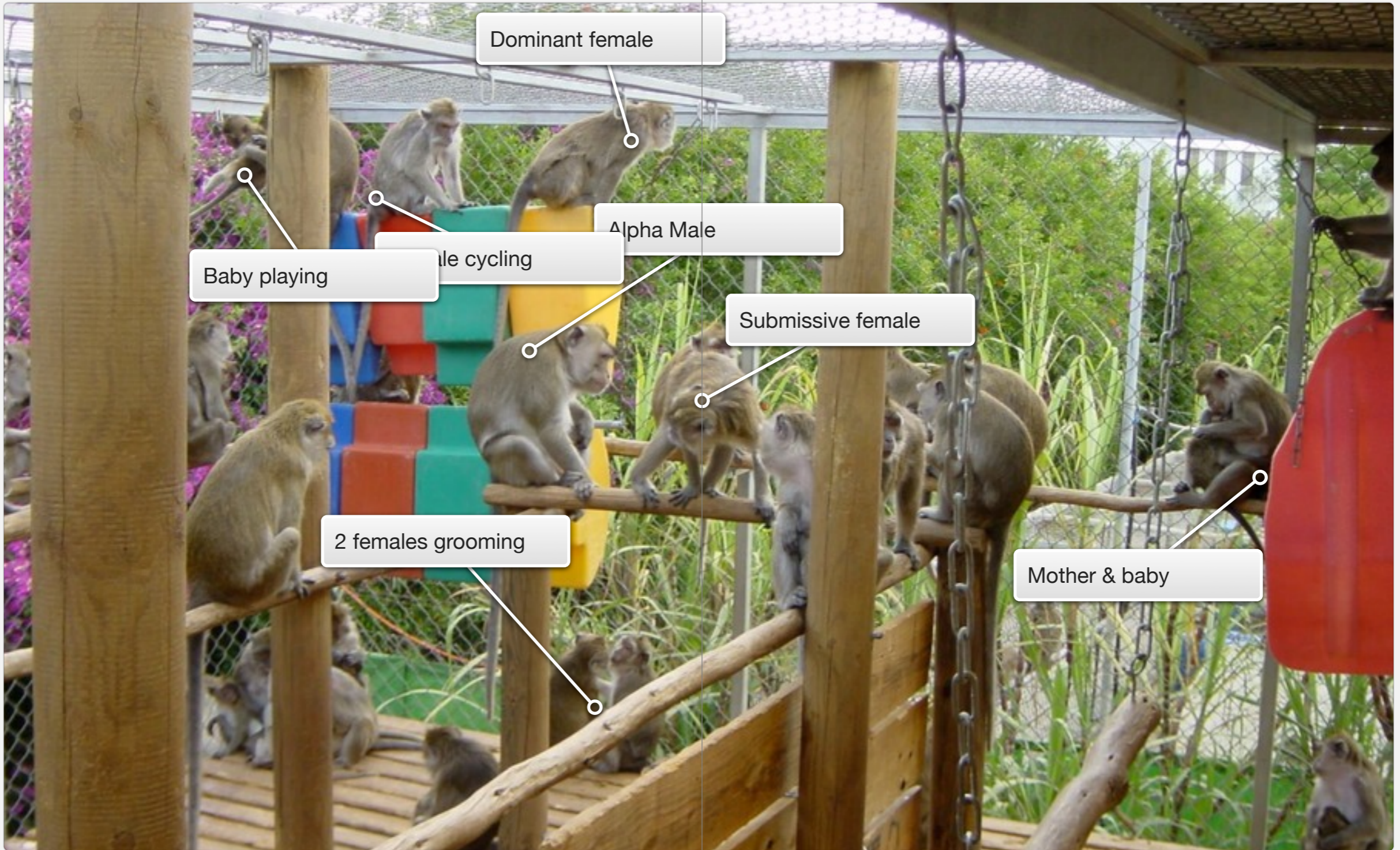
The U.S. Army, the U.S. Air Force, and NASA launched rhesus macaques into outer space during the 1950s and 1960s, and the Soviet/Russian space program launched them into space as recently as 1997 on the Bion missions.

One of these primates ("Able"), which was launched on a suborbital spaceflight in 1959, was one of the two first living beings (along with "Miss Baker" on the same mission) to travel in space and return alive.

MOVIE 2.1 Animals in Space (extract) US Air Force 1947



INTERACTIVE 2.1 *Cynomolgus macaque* social group



Marmosets (*Callithrix*)

COMMON MARMOSET (*CALLITHRIX JACCHUS*)

1. Marmosets in the wild
2. Marmosets in science

Common marmosets originated in the Atlantic Coastal Forest in Northeast Brazil but have now also been introduced to some parts of South East Brazil, including some urban areas. They are light, arboreal monkeys and weigh less than a can of baked beans.

Their claw-like nails allow them to cling to trees. In the wild they live in small family groups of 3-15 individuals. Their day is spent socialising, and finding and feeding on gum, insects, lizards, snails, fruit, flowers and nectar.

Females flick their tongues at males to solicit mating. The gestation period lasts for five months, and marmosets commonly give birth to two non-identical twins.

GALLERY 2.2 Marmosets and tamarins in research



Marmosets in medical research (image UAR)

1 of 14

Common marmosets employ a number of vocal and visual communications. To signal alarm, aggression, and submission, marmosets use the "partial open mouth stare," "frown," and "slit-stare", respectively. To display fear or submission, marmosets flatten their ear-tufts close to their heads.

Marmosets will use scent gland on their chests and anogenital regions to mark objects. These are meant to communicate social and reproductive status.

Marmosets in Science

Marmosets are used as an animal model to investigate Parkinson's disease. To create a model of Parkinson's a chemical called MPTP is injected into the marmosets. This destroys the *substantia nigra*, the part of the brain that is associated with the fine control of movement. It is damage to the *substantia nigra* that cause the symptoms of Parkinson's disease.

After the marmosets have been given MPTP they develop a lasting tremor, much like the human disease and can be treated with potential medication. This has been a successful way of finding new treatments for Parkinson's disease.

The discovery of MPTP was an accident. Drug-users in the US took contaminated material and developed parkinsonian-like symptoms. When one of these unfortunates committed suicide an examination of his brain revealed parkinsonian-like damage. This led to the unravelling of a medical mystery described very well in *The Case of The Frozen Addicts*.

MOVIE 2.2 Marmosets



Looped video

AUDIO 2.1 Marmoset calls



Baboons, vervets and other primates

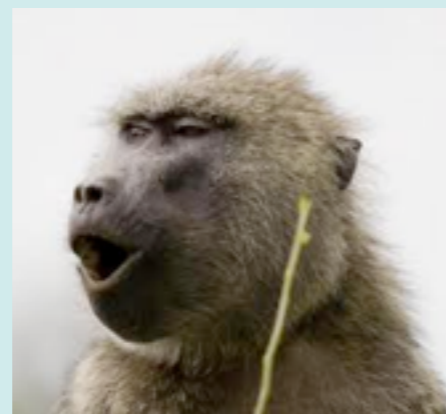
BABOONS AND SQUIRREL MONKEYS

1. Squirrel monkeys and colour vision
2. Baboons (*Simia hamadryas*)
3. Baboons in science: Schistosomiasis, vaccines and artificial blood vessels
4. Gorillas in Science: Ebola vaccines

AUDIO 2.3
Vervet calling



AUDIO 2.2
Baboon calling



Squirrel Monkey (*Saimiri spp*)

Squirrel monkeys live in the tropical forests of Central and South America in the canopy layer.

GALLERY 2.3 Vervet squirrel monkey



Vervet monkey playing (image shutterstock)



Color vision in squirrel monkeys has been extensively studied to understand human problems with vision. In 2009 gene therapy gave the human OPN1LW gene to adult male squirrel monkeys, producing fully human-like trichromatic color vision.

Baboons (*Simia hamadryas*)

Baboons are ground dwelling and are found in open savannah, open woodland and hills across Africa. Their diets are omnivorous. Baboons in captivity have been known to live up to 45 years, while in the wild their life expectancy is about 30 years. Most baboons live in hierarchical troops of five to 250 animals.

GALLERY 2.4 Baboons and other species



Baboon resting



Baboons in Science: *Schistosomiasis*

Baboons are being used to develop a vaccine against Schistosomiasis (also known as bilharzia). The disease is caused by different species of the flatworm Schistosoma. *S. mansoni* and *S. haematobium* are mainly human parasites. *S. japonicum* infects a wide range of domestic livestock as well as humans.

It causes a chronic disease with symptoms including abdominal pain, fever, fatigue and eventually organ damage, especially to the liver.

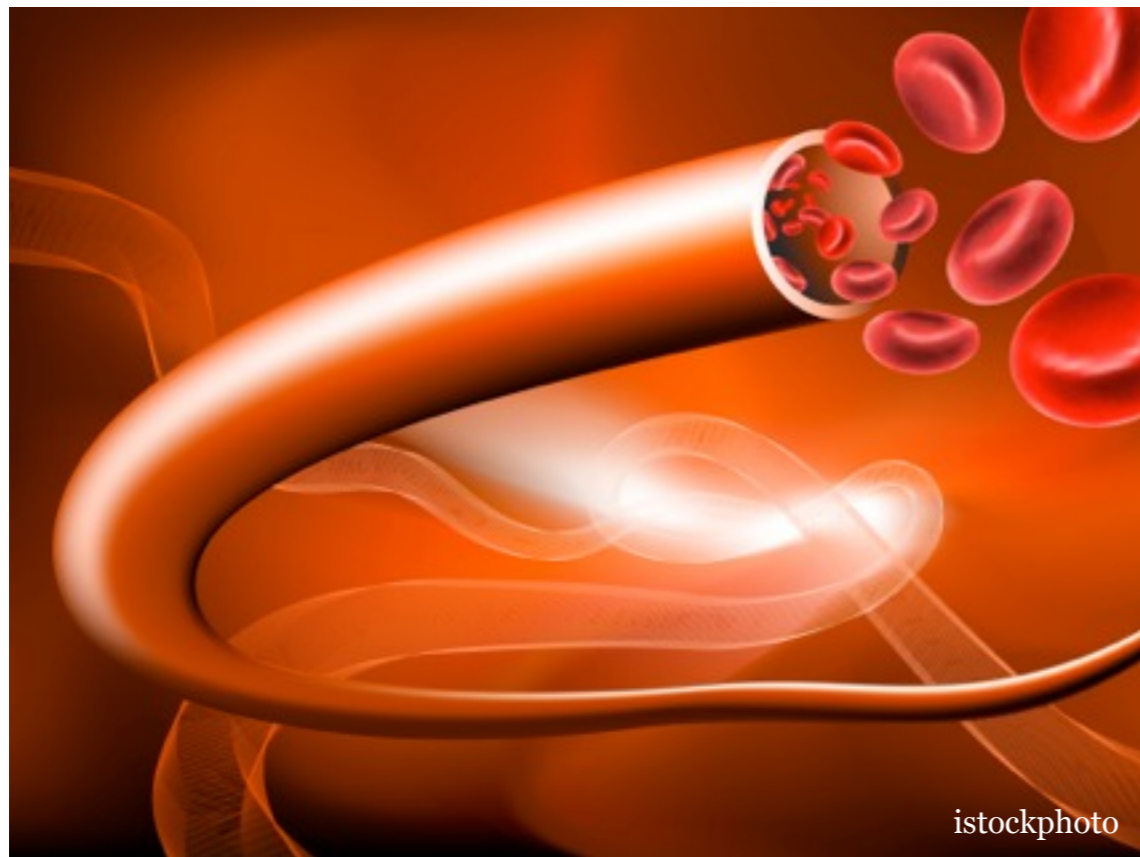
It is estimated that 780 million people are at risk of contracting the disease, with more than 200 million actual cases. Schistosomiasis is concentrated in sub-Saharan Africa with the highest infection intensities usually found in school-age children and young adults. Mortality in this region due to *Schistosomiasis* is estimated at 280,000 deaths a year.

Artificial blood vessels

Artificial blood vessels for use in heart bypass surgery have been successfully tested in baboons and dogs.

The artificial vessels were made using smooth muscle cells grown on tubular scaffolding. As the smooth muscle cells grow they secrete collagen, an important structural protein found in the walls of blood vessels.

The artificial vessels can be stored for up to a year, making them readily available, and can be used by any patient. Researchers can already grow blood vessels using a patient's own cells, but the process takes several months and so this is usually too long to wait before surgery.



The number of heart bypass operations in the UK is more than 28,000 per year. Surgery is needed to 'bypass' the blocked arteries which bring oxygen to the heart muscle. Coronary heart disease is the UK's biggest killer. The situation is similar for other parts of the world.

Chimpanzees, orang-utans and gorillas are no longer used in the EU because of their close resemblance to humans. Their use is banned unless the research is for the benefit of the animals themselves. An example of this is research into the ebola virus.

Gorillas in Science: Ebola vaccines

An Ebola epidemic has had a devastating impact on humans, chimps and gorillas in central Africa over the last decade.

Several vaccines have protected laboratory monkeys from Ebola and they are likely to also be effective in chimpanzees and gorillas. It is hoped that as well as saving western gorillas from extinction, these will also help pave the way for a human Ebola vaccine. The vaccines are now being

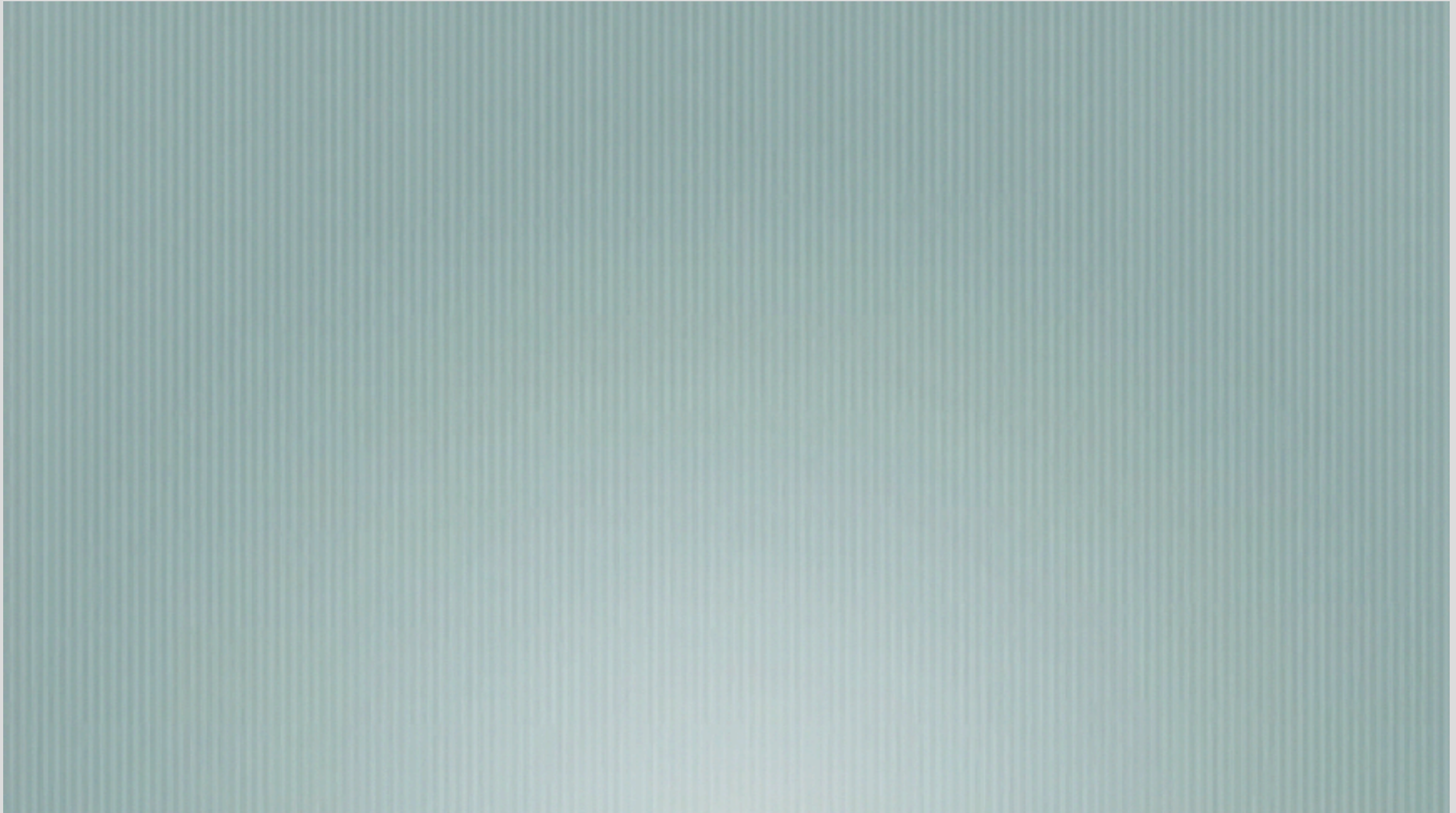
developed by a collaborative task force, whose objective is to tackle the ape Ebola crisis. Captive and field studies are being used to determine the best delivery methods for the vaccine.



History of medical advances with



MOVIE 3.1 Timeline of medical discoveries made with primate models



Touch to play or stop movie

Chapter 4

Areas of research

Primates have played a vital role in medical research over the last century and continue to be essential today.



Alzheimer's disease

WHAT IS ALZHEIMER'S DISEASE?

1. Alzheimer's disease is the most common cause of dementia. It is a physical disease affecting the brain.
2. Protein 'plaques' and 'tangles' develop in the structure of the brain, leading to the death of brain cells.
3. The disease affects around **496,000** people in the UK and **5.4 million** people in the US.
4. Dementia affects one in 14 people over the age of 65 and one in six over the age of 80.

Alzheimer's disease affects more than 18 million people worldwide. It is a chronic debilitating disease that leads to irreversible memory loss, due to selective neuronal cell death. Accurate diagnosis, by autopsy, has revealed that the clinical features of Alzheimer's are the presence of beta-amyloid plaques and tau protein tangles in specific parts of the brain.

Studies in macaque monkeys in the early 1990s led to the identification of the critical regions of the brain that are essential for cognition and memory and, like humans, ageing monkeys may show evidence of beta-amyloid plaques and lose neurones as they age.

Partial models of Alzheimer's may also be created by priming monkeys with small amounts of human amyloid – they will develop plaques later whilst still reasonably young. As primates can be trained to perform memory-related tasks that permit the evaluation of changes in cognitive memory and emotional behaviour during ageing, they can be used to evaluate various treatment and prevention strategies.

GALLERY 4.1 Alzheimer victims



UK Prime Minister Baroness Margaret Thatcher (image Chris Collins, Margaret Thatcher Foundation)



Anxiety and self-doubt

MACAQUES MODEL MENTAL STATES



The prefrontal cortex is one of the key areas in the brain that malfunctions in anxiety disorders and other psychiatric illnesses. The human brain, like that of other primates, has a complex prefrontal cortex, which continues to develop into adulthood.

Research on rhesus monkeys has shown that having an anxious temperament at an early age is linked to

higher activity in the amygdala, a part of the brain that regulates emotion and triggers reactions to anxiety. In adulthood, these monkeys were still observed to be more anxious than their peers. The overactive amygdala has since been linked to decreased activity of a gene known as *NTRK3*, making this a potential target for developing treatments.

macaques can also model subtle mental states such as self-doubt and uncertainty when making decisions. Scientists taught the macaques to play a 'fuzzy logic' game in which they had to decide whether the pixel density on a screen was sparse or dense, moving a joystick to either the letter S or D. They received a treat each time they got the right answer, but the game paused for a few seconds for each wrong answer.

However, a third option was possible. The macaques could select a question mark, moving them onto the next round without the pause. The macaques would select this when they were apparently unsure of the correct choice. This behaviour is similar to how humans behave when faced with the task. It seems the macaques are self-aware of when they are likely to make an error. The results do not apply to all species of monkey: capuchin monkeys trained to play the same game never selected the question mark.

Colour blindness

SQUIRREL MONKEYS MODEL COLOUR BLINDNESS



Gene therapy has been used to correct red-green colour blindness in squirrel monkeys

Red-green colour blindness, by far the most common form of colour blindness, affects approximately 6% of men worldwide. This occurs in the absence of either the long-wavelength (red) or middle-wavelength (green) pigments in the cone cells of the eye.

As primates have very similar visual systems, research can be applied across species. However, non-human primates are unable to tell us what colours they can see. This means that researchers must train the monkeys in their care to complete tasks and puzzles that require differentiating colours in exchange for a treat (such as grape juice). These monkeys can be used as models for treatments for colour blindness.

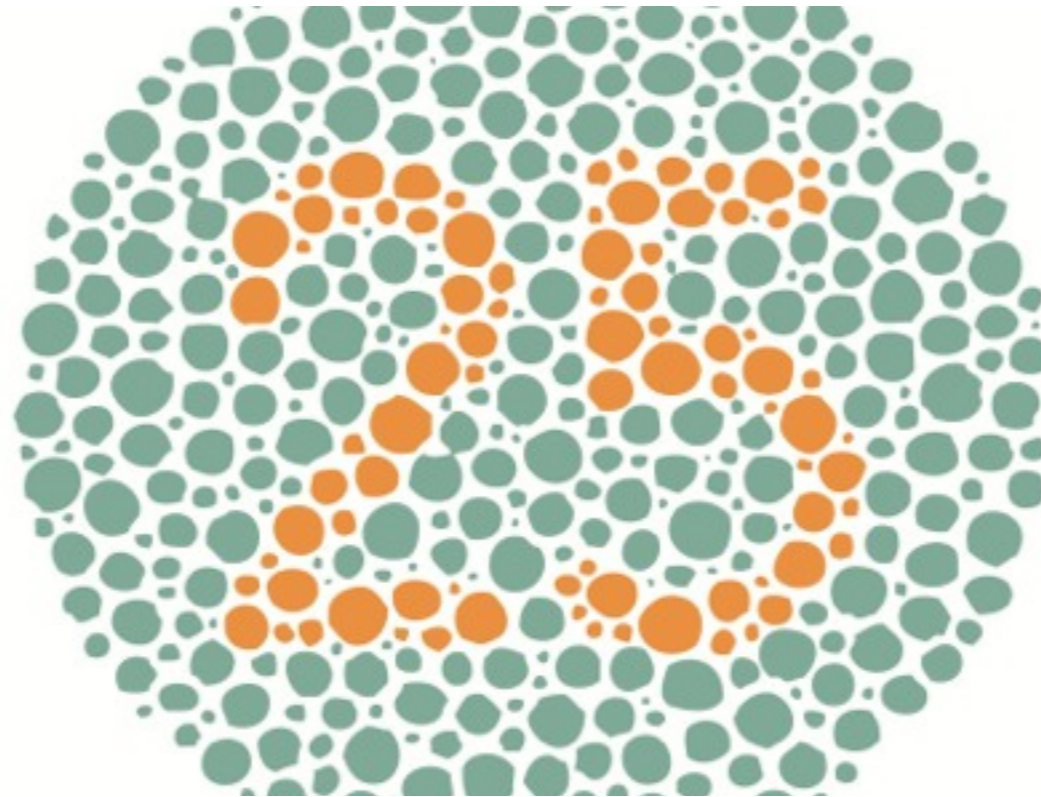
Colour blind adult squirrel monkeys were treated with gene therapy, which introduced a gene to produce a protein called long-wavelength opsin that makes the pigments required to differentiate between red and green.

After 20 weeks, the monkeys' colour vision had improved dramatically and they were able to distinguish between colours as normal. This overturned the idea that the brain would only be able to process a new input at an early stage in development. This could therefore lead to treatments for colour blindness in adult humans.

Are you colour blind?

Question 1 of 5

What number you see ?



- A.** 25
- B.** 45
- C.** 40
- D.** 18



Check Answer



Hepatitis E (HEV)

RHESUS MACAQUES IN DEVELOPMENT OF HEPATITIS E VACCINE

1. Hepatitis E virus (HEV) infects **20 million** people a year and kills **70,000**
2. Rhesus macaque monkeys were used to design the first HEV vaccine.



Wikimedia

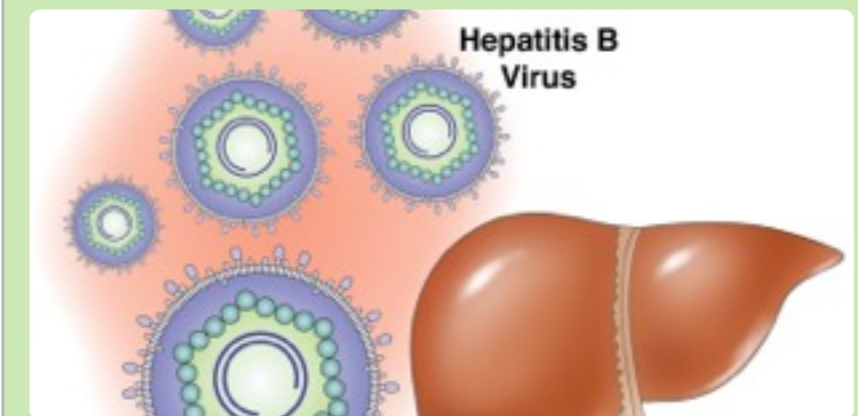
The world's first hepatitis E vaccine was Hecolin. It took 14 year to develop. Hepatitis E virus (HEV) infects 20 million people a year and kills 70,000. It dramatically increases the incidence of mortality in pregnant women, particularly those in their second and third trimesters, and those who have chronic liver disease. The mortality rate for heavily pregnant women is a shocking 20%.

HEV occurs worldwide but is especially prevalent in Asia. Transmission occurs through the faecal-oral route, producing higher rates of transmission in areas of poor sanitation.

Rhesus macaque monkeys were used in the preclinical stage to design the vaccine and to establish optimum dosage levels. Researchers found in later tests on rhesus macaques that when an initial high dose and a later low dose of HEV 239 were administered,

the vaccination was almost 100% efficacious against HEV.

GALLERY 4.2 Hepatitis



Hepatitis B virus (shutterstock)

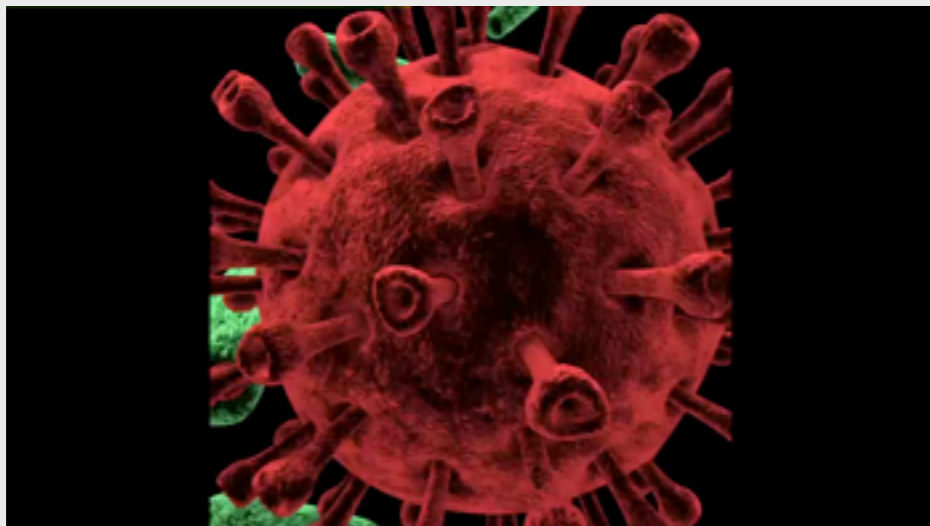


HIV/AIDS

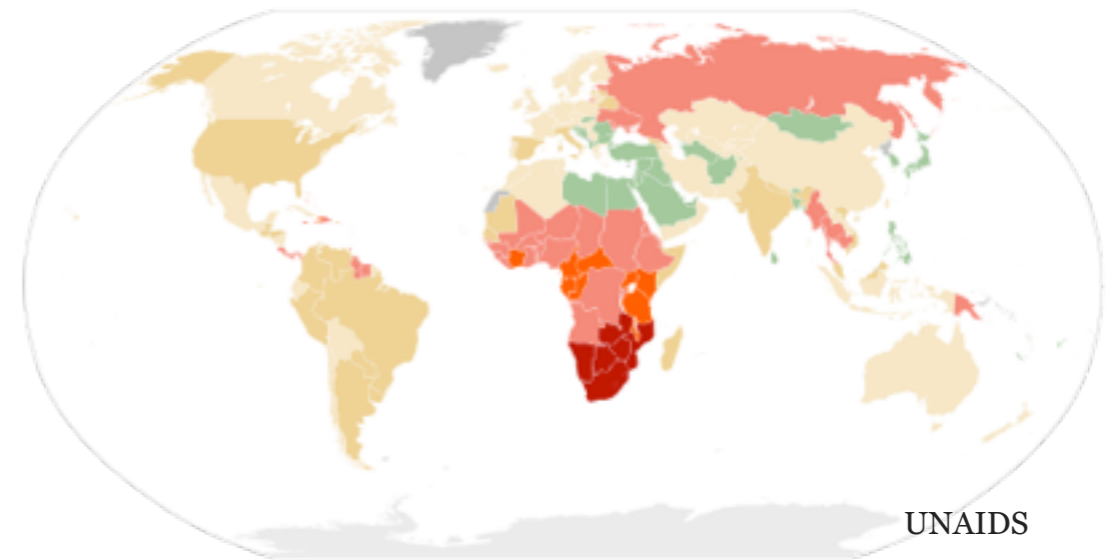
PRIMATES' ROLE IN TREATMENTS

1. **34 million** people have HIV worldwide
2. HIV/AIDS caused about **1.8 million** deaths in 2010.

MOVIE 4.1 HIV virus - 3D view



HIV/AIDS is a global pandemic. As of 2010, approximately 34 million people have HIV worldwide. Of these approximately 16.8 million are women and 3.4 million are less than 15 years old. HIV/AIDS caused about 1.8 million deaths in 2010.



The most frequent mode of transmission of HIV is through sexual contact with an infected person. Worldwide, the majority of cases of transmission occur through heterosexual contacts. Chimpanzees and now macaques were used to understand how infection with HIV led to AIDS.

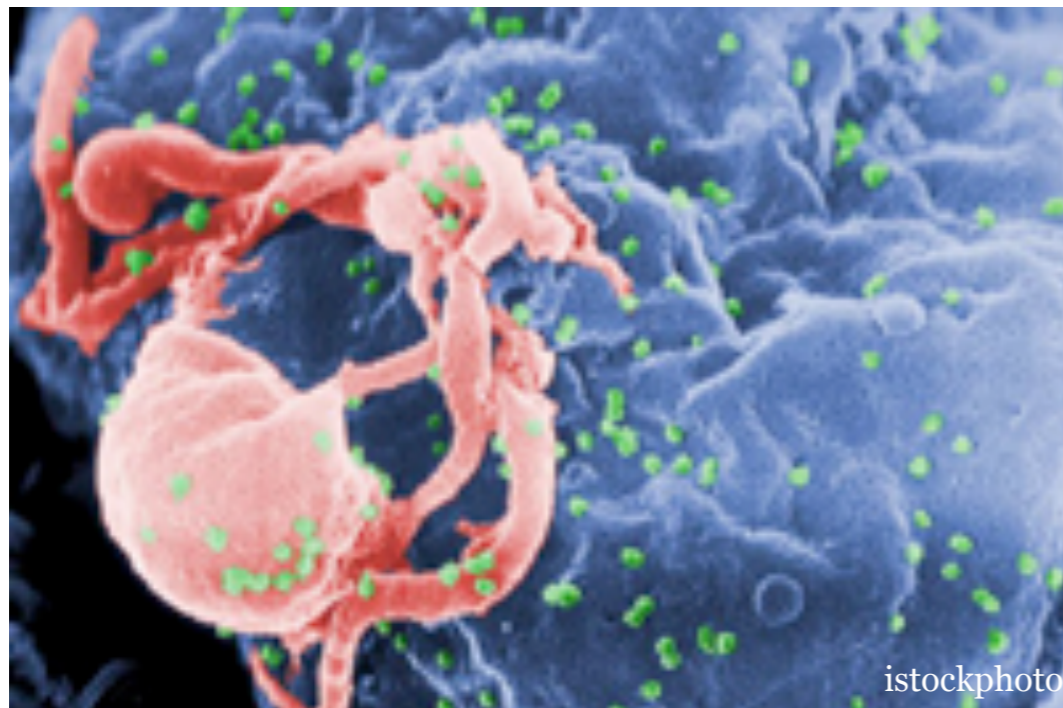
Vaccines

Hopes that primates could be used in the development of a Human Immunodeficiency Virus (HIV) vaccine were dashed when it was found that the virus did not cause disease in chimpanzees. However, primates do have their own species-

specific immunodeficiency virus, Simian Immunodeficiency Virus (SIV), and they develop an AIDS-like condition when infected with SIV. This is not surprising as HIV and SIV have similar genes and properties, and both attack T helper (CD4) immune system cells.

SIV as a model of HIV

Simian Immunodeficiency Virus (SIV) is similar to HIV and animals infected with SIV are used as a model to understand HIV infection and treatment. Macaques are susceptible to SIV, and the virus goes on to cause a fatal immunodeficiency syndrome in this species. Researchers have also found that SIV is sensitive to similar drugs to HIV and they have exploited these similarities to develop and test many antiviral medications, particularly those used in prophylaxis.



A disadvantage with SIV is that the sequence of its genes and proteins differ in places to that of HIV, which means that some HIV vaccines cannot be tested directly against SIV.

To overcome that difficulty in the mid 1990s scientists developed SHIVs, genetically engineered viruses consisting of a combination of SIV and HIV genes which did produce AIDS-like symptoms in macaques.

GALLERY 4.3 HIV/AIDS



Condom use dramatically reduces transmission of the virus (shutterstock)



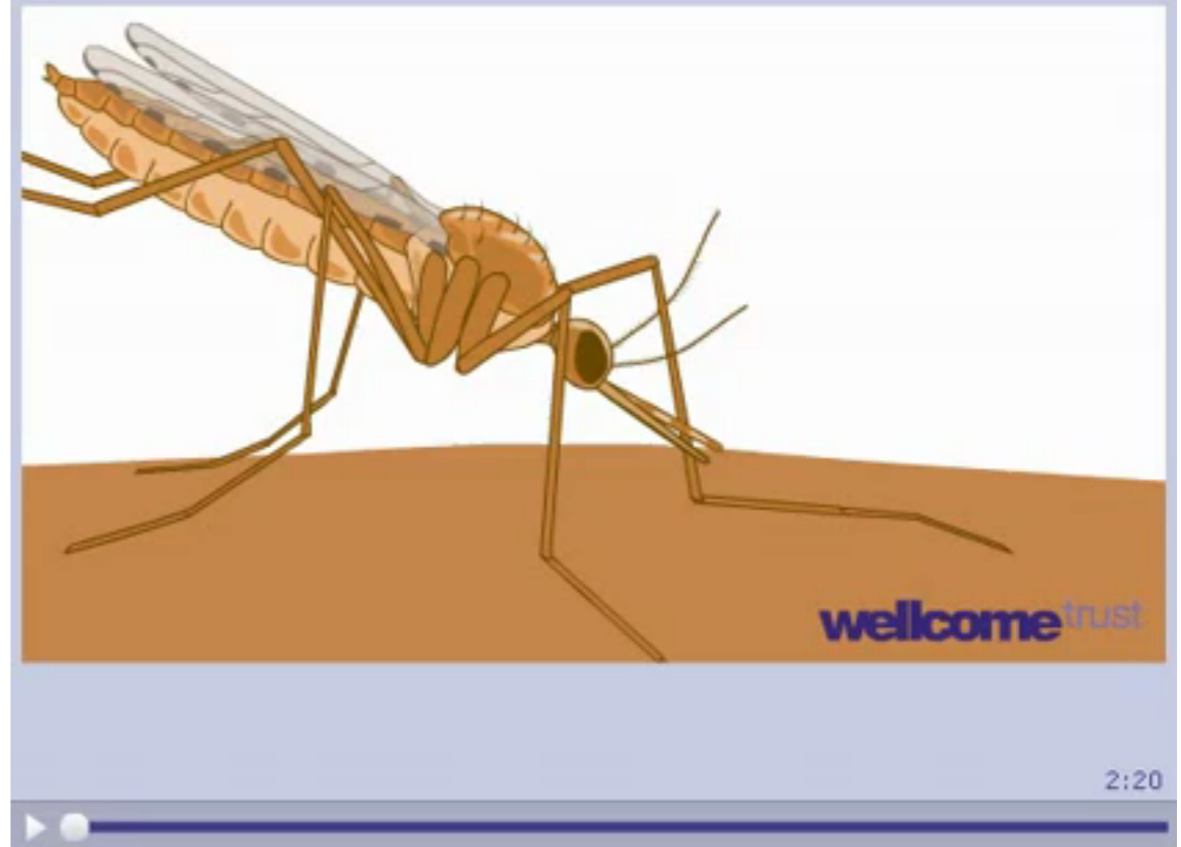
Malaria

AOTUS MONKEYS AND MALARIA

1. Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected mosquitoes.
2. In 2010, malaria caused an estimated **660 000** deaths, mostly among African children.
3. Non-immune travellers from malaria-free areas are very vulnerable to the disease when they get infected.



Malaria Life Cycle - Human Stages



Malaria is caused by a parasite called ***Plasmodium***, which is transmitted via the bites of infected mosquitoes. In the human body, the parasites multiply in the liver, and then infect red blood cells.

Symptoms of malaria include fever, headache, and vomiting, and usually appear between 10 and 15 days after the mosquito bite. If not treated, malaria can quickly become life-threatening by disrupting the blood supply to vital organs.

In many parts of the world, the parasites have developed resistance to a number of malaria medicines.

Primate models

Aotus monkeys are a primate that are extremely valuable models for understanding malaria, screening anti-malarial drugs and vaccine development.

The monkeys do not die from malaria although they may harbour the parasite. The reason why primates resist disease when infected, whereas humans do not, is an important question for researchers to answer. Additionally, the fact that primates can harbour an infection without becoming seriously ill makes them ideal for research into vaccine and drug development.

A cheap vaccine purified from the milk of genetically modified mice has protected monkeys against the disease. Only one of five immunised animals contracted the disease, compared with six out of seven unvaccinated monkeys. The mice were engineered to carry the gene for a surface protein from *Plasmodium falciparum*.

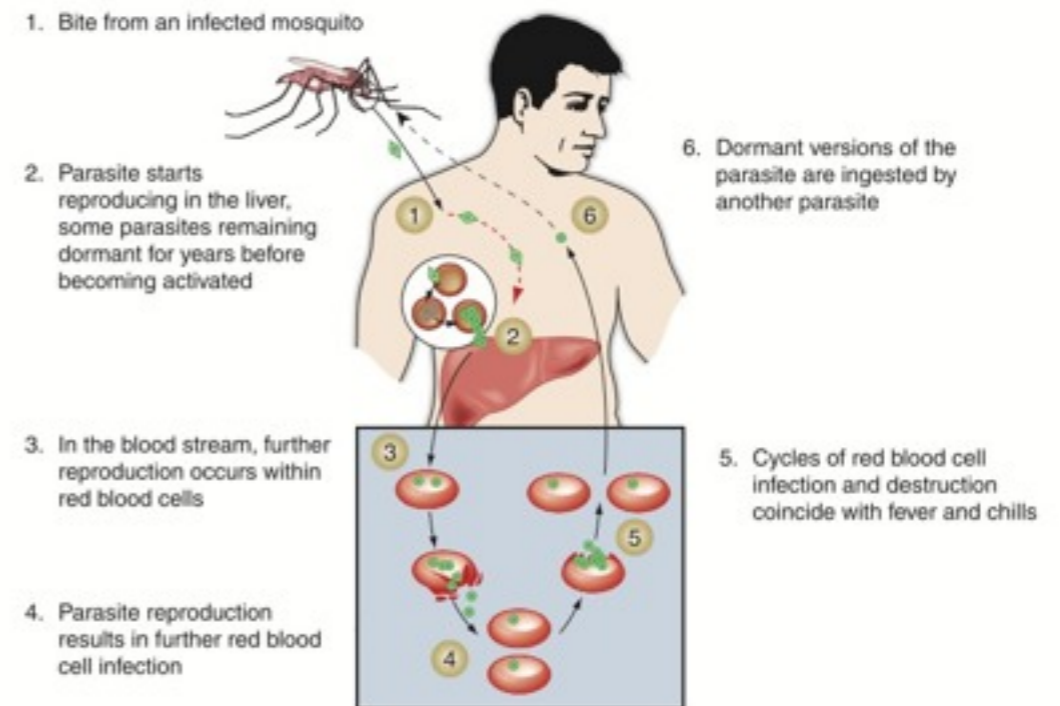
The same team also modified goats to produce the protein in their milk, raising the prospect that one herd

of goats could produce enough vaccine for the whole of Africa. The next step will be to find out whether the vaccine produced in goats' milk also protects monkeys.

Owl Monkey - the primate model for Malaria research



GALLERY 4.4 Malaria



Malaria infection cycle (shutterstock)



Parkinson's disease

MARMOSETS AND PARKINSON'S DISEASE

1. Parkinson's is a progressive neurological condition.
2. People with Parkinson's don't have enough of a chemical called dopamine because some nerve cells in their brain have died.
3. Without dopamine people can find that their movements become slower so it takes longer to do things.
4. One person in every 500 has Parkinson's. That's about 127,000 people in the UK.
5. There's currently no cure for Parkinson's disease

The current treatments for Parkinson's disease (PD) would not have been possible without fundamental research on monkeys.

The cause of Parkinson's disease was found by chance when Californian drug addicts injected a home-made compound containing MPTP and developed Parkinson's-like symptoms.

The suicide and subsequent post-mortem of one of the addicts revealed that the changes in the brain were identical to that of true PD patients. Shortly after, scientists showed that they could model the disease by giving MPTP to large primates. In the primates with Parkinson's-like symptoms there is overactivity in a part of the brain that controls movement – namely the subthalamic nucleus – and that the overactivity is due to the loss of neurones in the substantia nigra that manufacture the chemical messenger dopamine.

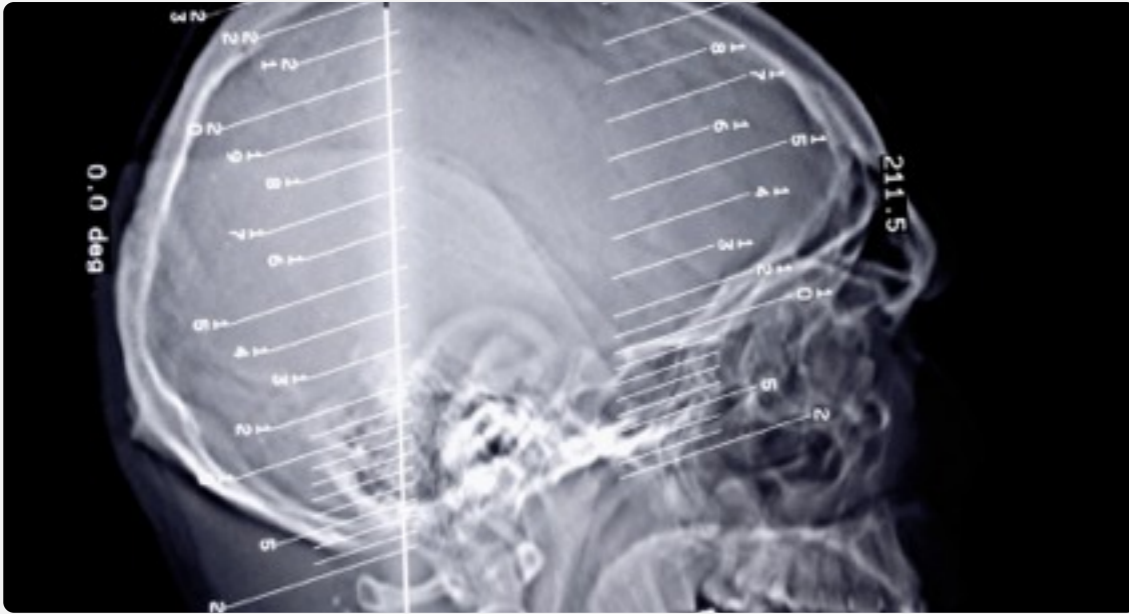
This explained why giving L-dopa, a precursor of dopamine, was an effective treatment. So far, all the

MOVIE 4.2 Parkinson's disease controlled by brain implant



Mike Robbins suffers from Parkinson's Disease. He demonstrates how a pacemaker implanted in his brain controls his symptoms.

GALLERY 4.5 Parkinson's Disease



Brain scan (shutterstock)



dopamine based therapies that have been tested in the MPTP-treated primate have proven to be highly predictive of their clinical action in people. However, L-dopa and related anti-parkinsonian medicines have side effects and their effectiveness wears off over long-term treatment.

One side-effect of PD can be tremors and shaking. These can be extreme for some sufferers of PD.

Alim Benabid and colleagues in Grenoble, France were the first to find that by implanting an electrode into the

brain tremors could be controlled and normal movement restored.

This surgical technique, known as Deep Brain Stimulation (DBS), has been approved in Canada, Europe and Australia since 1998 for the treatment of PD. The procedure involves implanting electrodes into the patient's skull whilst they are awake. A battery-operated pacemaker that sends continuous electrical pulses to the brain is placed under the skin.

The patient can turn off the pacemaker, eg at night, with the use of a special magnet. The high frequency stimulation 'paralyses' the overactive nerve cells giving a significant reduction in their tremor. So far, worldwide, around 40,000 patients have been treated with this technique which often reduces or eliminates the need for anti-tremor medication.

Polio

MONKEYS USED TO DEVELOP POLIO VACCINE

1. Polio can cause paralysis
2. How Polio was discovered
3. How a vaccine was developed



Countries with polio

Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. The virus is transmitted through contaminated food and water, and multiplies in the intestine, from where it can invade the nervous system. Many infected people have no symptoms, but do excrete the virus in their faeces, transmitting infection to others.

Initial symptoms of polio include fever, fatigue, headache, vomiting, stiffness in the neck, and pain in the limbs. In a small proportion of cases, the disease causes paralysis, which is often permanent. Polio can only be prevented by immunization.



Discovery of polio

Proof that polio was an infectious disease came in 1908, when Dr Karl Landsteiner and Dr Erwin Popper managed to induce polio in monkeys by injecting them with extracts of the spinal cord of a boy who had died from polio. The disease could then be transmitted from monkey to monkey, providing an invaluable model of the disease.

Development of the polio vaccine

Dr John Enders and his colleagues in the 1940s showed that polio virus could be grown in human tissue, and this breakthrough was awarded the Nobel Prize in 1954. In the 1940s, the virus was too small to be seen with any available technique. The one way Dr Enders could check that he had in fact extracted the virus from mouse brain tissue and

grown it in culture was by injecting the culture fluid into mice and monkeys, where it produced paralysis typical of polio.

About 40 years of research using monkeys, rats and mice led directly to the introduction of the Salk and Sabin polio vaccines in the 1950s. Professor Albert Sabin's 1956 paper in the *Journal of the American Medical Association* stated:

"Approximately 9,000 monkeys, 150 chimpanzees and 133 human volunteers have been used thus far in the quantitative studies of various characteristics of different strains of polio virus. [These studies] were necessary to solve many problems before an oral polio vaccine could become a reality."

Until recently, each lot of vaccines had to be tested on monkeys to ensure that they were safe. However, in the last couple of years the WHO has approved and recommended that a transgenic mouse test for polio be used instead. Interestingly, the polio vaccine has been used to protect a wild colony of East African colony of chimpanzees from a potential epidemic.

Polio now survives only among the world's poorest and most marginalized communities. The World Health Organisation's goal is to reach every last child with polio vaccine and ensure a polio-free world for future generations.

GALLERY 4.6 Polio vaccine discovery

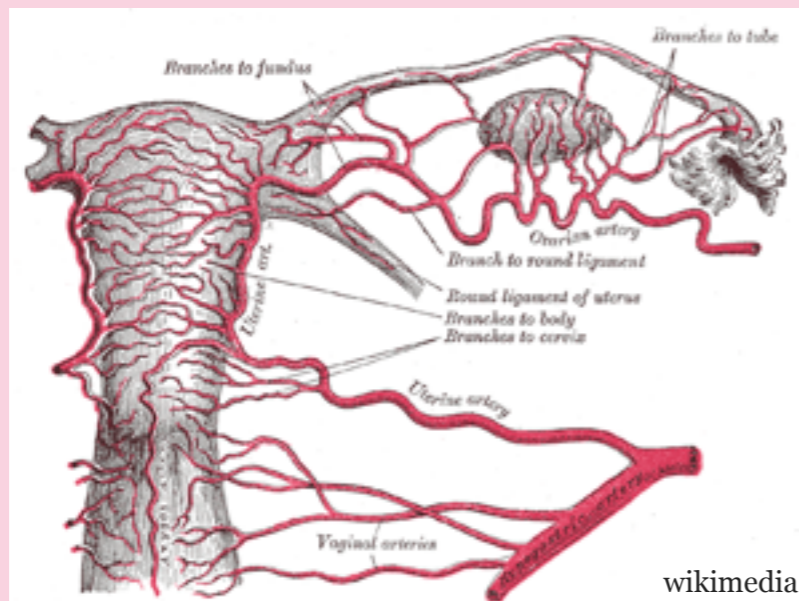


An Egyptian stele thought to represent a polio victim, 18th Dynasty (1403–1365 BC) (shutterstock)

Reproductive system research

FEMALE MACAQUES AND MARMOSETS USED FOR FEMALE HUMANS

1. Women and other female primates are the only mammals that ovulate and menstruate every month.
2. The hormones produced by monkey and human pituitary glands are very similar.



GALLERY 4.7 Macaques in reproductive system research



Female macaque have the same reproductive system and menstrual cycle as women and that is the reason they are the best model for reproductive research (shutterstock)



Although reproduction in primates and other mammals may seem similar, there are fundamental differences, particularly in the way that hormones react to the release of eggs by the ovaries, and the processes involved in pregnancy, birth and lactation.

While rodents are suitable for some studies, only primates are sufficiently similar to humans to increase understanding of many reproductive problems – for

example, miscarriage and premature birth and endometriosis (abnormal growth of tissue lining the uterus).

Work in this area is focusing on increasing our understanding of blood vessel formation, angiogenesis. In adults, angiogenesis occurs in the female reproductive system – for example, to build up blood vessels to nourish the womb during the menstrual cycle and early pregnancy, and to supply nutrients to the egg-containing follicles of the ovaries as they grow before ovulation.

Scientists think that many disorders affecting women – such as early miscarriage, endometriosis, polycystic ovary syndrome and problems with menstrual bleeding – occur when angiogenesis is not regulated properly by the body.

The hormones produced by a monkey's pituitary gland, which are essential to the production of sex hormones, are very similar to those of humans. Women and other female primates are the only mammals that ovulate and menstruate every month.

This gives monkeys a uniquely important role in research into human reproduction. Female macaques or marmoset monkeys are injected with compounds

designed to inhibit or stimulate the growth factor molecules that scientists believe are involved in angiogenesis.

IVF - In vitro fertilization

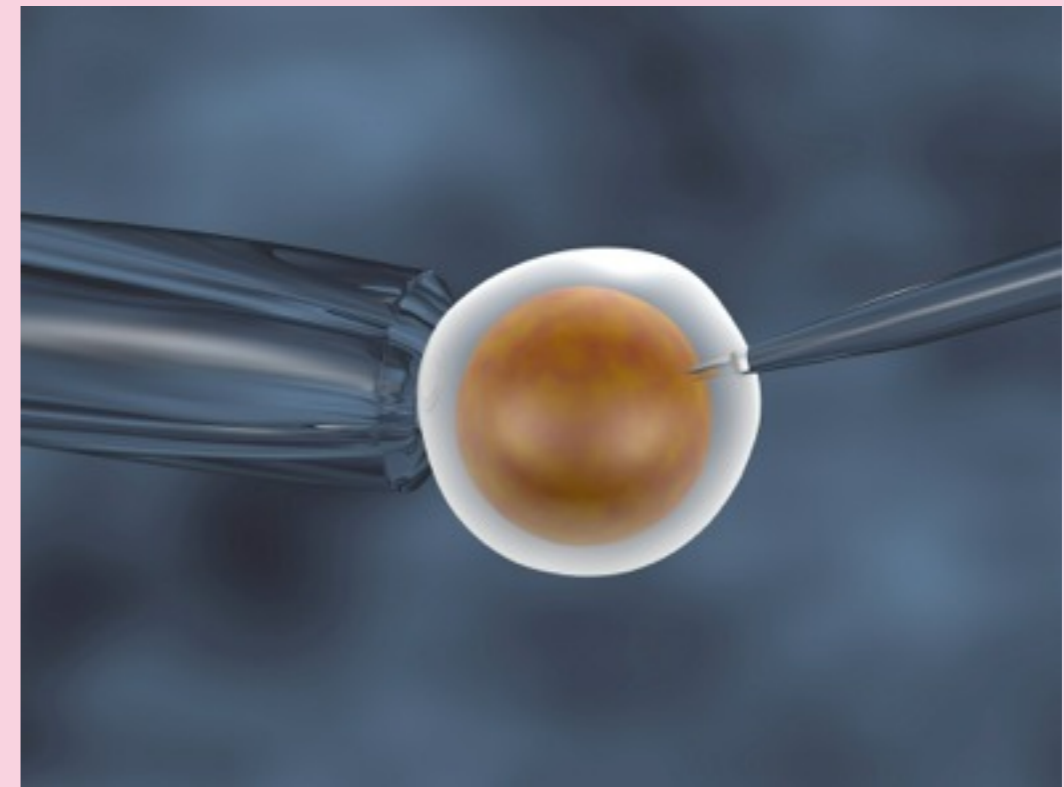


Image: shuttlestock

Schistosomiasis

SCHISTOSOMA INFECT HUMANS AND LIVESTOCK

1. **780 million** people are at risk of contracting the *Schistosomiasis* (also known as bilharzia)
2. **243 million** actual cases (WHO 2011)



Schistosomiasis

Schistosomiasis (also known as bilharzia) is caused by different species of the flatworm *Schistosoma*. It is estimated that 780 million people are at risk of contracting the disease, with more than 200 million actual cases. Numbers continue to rise, despite the implementation of control programmes, due in part to the introduction of wide-scale irrigation schemes which help the snail host disperse.

Schistosomiasis is the second most socioeconomically devastating parasitic disease after malaria.

Schistosomiasis is concentrated in sub-Saharan Africa with the highest prevalence and infection intensities usually found in school-age children and young adults; mortality in this region due to *S. mansoni* and *S. haematobium* is estimated at 280,000 deaths a year.

Primate models

Mice and primate models have proved invaluable in aiding our understanding of the progression of the disease that results from the host's immune response to accumulating tissue-trapped eggs.

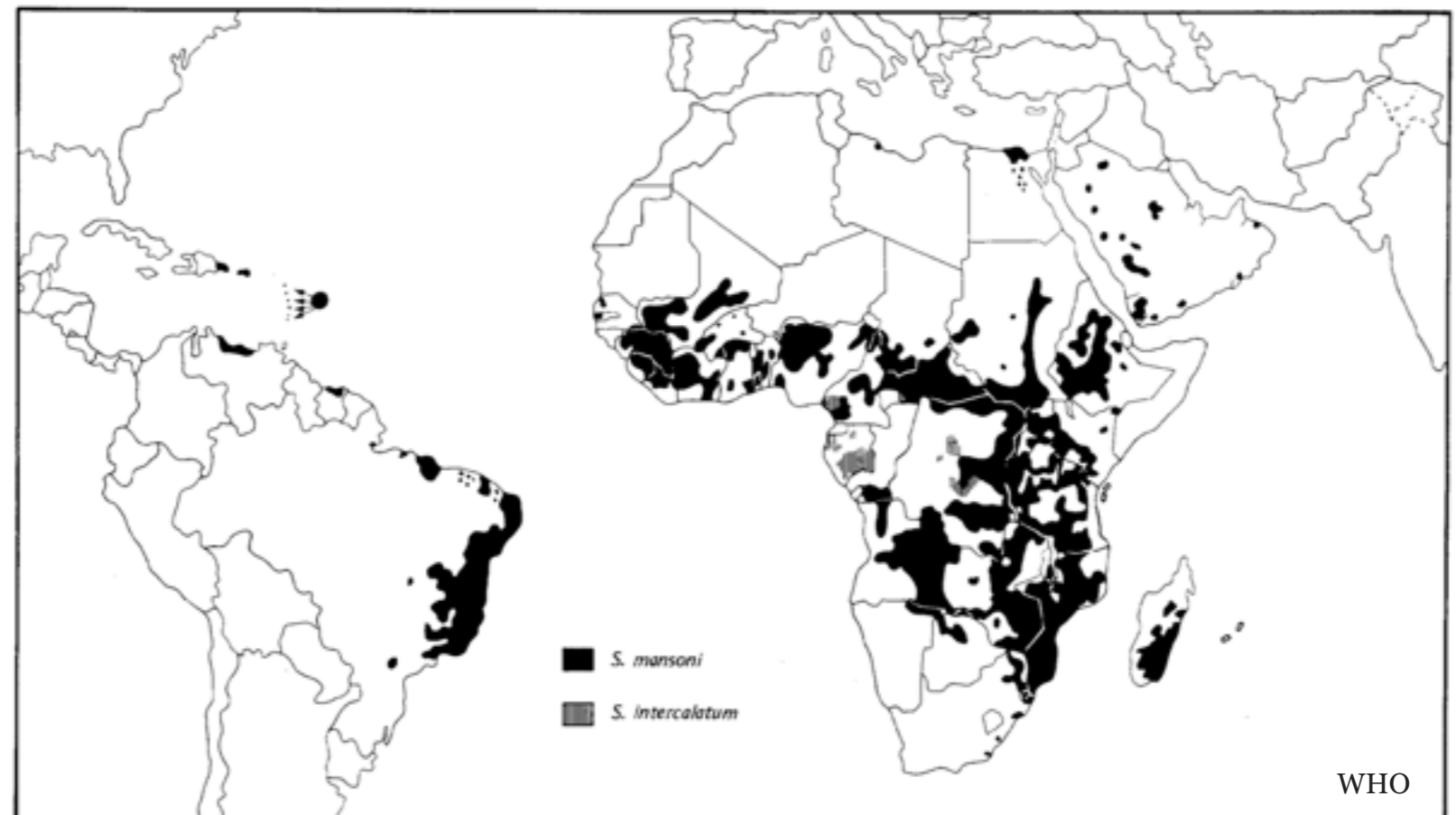
Secretions from these schistosome eggs cause a vigorous inflammatory response that is supposed to

protect the tissues against damage from the egg toxins. Unfortunately, the nodule of inflammatory cells (granuloma) that accumulates around each egg ultimately leads to tissue damage due to tissue scarring and excessive pathology.

As well as improving our understanding of how Schistosomiasis causes damage primates are currently being used to test potential vaccines.

Nonhuman primates have the advantage of having a long lifespan, which enables the development of extensive pathology. Nonhuman primate models may be particularly useful for vaccine research. Recent data based on the baboon indicate that infection in this non-human primate might mirror the human situation.

Baboons provide an excellent non-human primate model that produces pathology and disease closely resembling that observed in humans, and can provide insights into mechanisms regulating schistosomiasis pathology and immunity.



Stroke

STROKE - A LEADING CAUSE OF DEATH

1. Stroke causes 6 million deaths per year
2. Research with monkeys improved rehabilitation techniques

Stroke is the second leading cause of death worldwide with about 6 million deaths per year. It is caused by a blood clot blocking an artery and preventing blood from reaching areas of the brain.

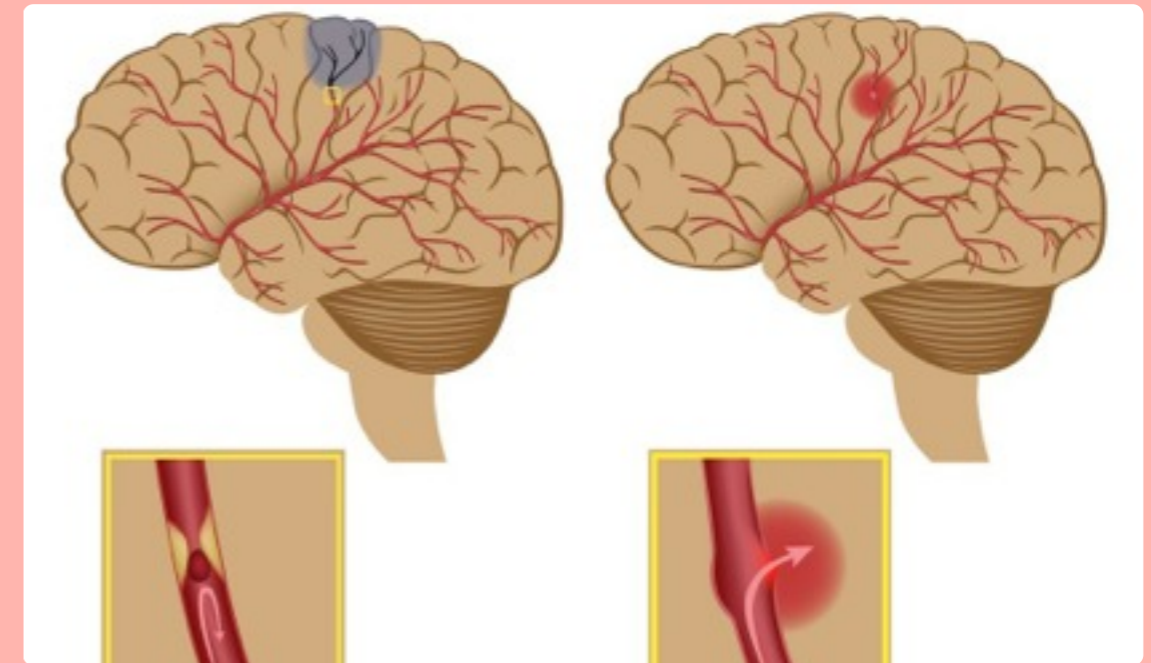
The complicated nature of this condition, particularly because it often occurs in combination with old age, high blood pressure and cardio-vascular disease, makes it difficult to produce reliable models in animals and this has hampered research into developing better treatments.

Research using monkeys have led to the development of our current understanding, therapies and rehabilitation techniques. Strokes can lead to loss of limb function, often along one side of the body.

Strokes can lead to loss of limb function, often along one side of the body. As far back as 1918, Robert Oden discovered that preventing monkeys from using their stronger side promoted their recovery following an induced stroke.

These monkeys were able to use their weaker arm within two weeks of this therapy, while monkeys without this intervention could not, even after six months. This technique is now known as constraint-induced movement therapy and is used in stroke patients today.

GALLERY 4.8 Stroke



Types of stroke (shutterstock)



Tuberculosis

TB INFECTS MONKEYS

1. One in three people have TB
2. Third of monkeys in Asia have TB
3. *Cynomolgus* macaques are a test species because of their human-like TB symptoms

Tuberculosis (TB) is a highly infectious disease that we have little power to stop so 1 in 3 people have the condition. Even though most infections are latent, they can reactivate and spread. The only current vaccine, known as BCG, can limit disease spread in children but cannot prevent infection.

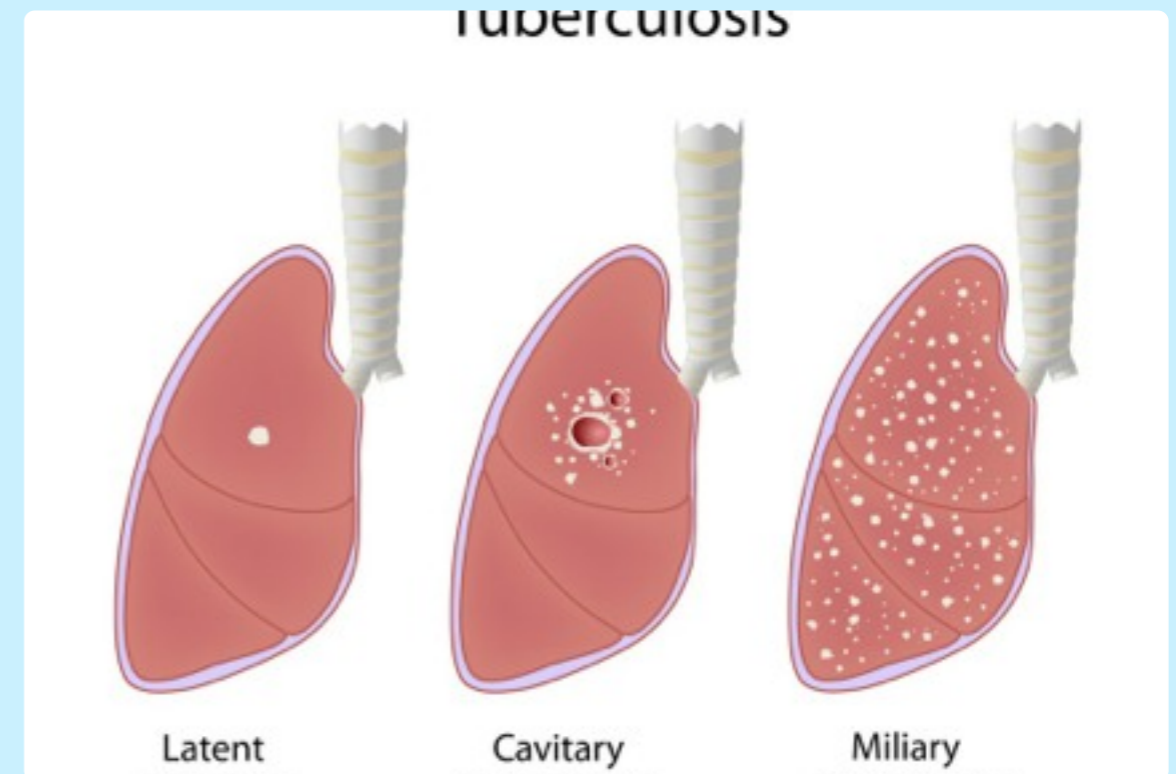
This disease also affects other primates with about a third of monkeys in Asia, where human tuberculosis is endemic, infected. This makes them an especially good model for the human disease.

Cynomolgus macaques are the main test species because of their human-like TB symptoms.

Research on these macaques has led to the H56 vaccine that acts as a booster for the BCG vaccine. This is able to reduce the effects of the disease and prevent reactivation of latent infection in macaques.

The vaccine is currently in human trials but it is likely to take several years before it can get approval because of the slow progress of the disease.

GALLERY 4.9 Tuberculosis



Tuberculosis damages the lung (shutterstock)

Chapter 6

Primate welfare





Primates are highly intelligent, sociable and energetic animals.

They need a stimulating, varied environment that reflects aspects of their natural habitat.

Typically they are housed in pairs or groups, with plenty of vertical space and perches for climbing and swinging and access to areas where they can play or find privacy when resting.

They are allowed to forage for their food, rather than receiving it passively, as this is an important daily activity in the wild.

Accommodation and housing

SOCIAL HOUSING

1. Accommodation should provide primates with sufficient space to carry out their normal behavioural repertoire.
2. Enclosures should allow animals to move up to where they feel more secure.

Accommodation should provide primates with sufficient space to carry out their normal behavioural repertoire such as resting, running, climbing, leaping, foraging and social interactions.

The volume and height of the cage (or enclosure) are particularly important for primates, which flee upwards when alarmed.

Cages and enclosures should be floor to ceiling high wherever possible, with adequate perching to allow all animals to move up to heights where they feel more secure.



Wisconsin National
Primate Research Centre

Marmosets

- Marmosets are tropical monkeys and require a temperature of 23-28 °C and humidity level of 40-70%.
- Enclosures should not be cleaned thoroughly more than every month or so because marmosets use scent marking.
- The enclosures should allow marmosets to remain above human head height and allow leaping and jumping.
- Access to outdoor enclosures improves welfare but must be restricted when the temperature falls below 5 °C.
- Access to living plants (and insects), and sources of wood for biting off resin, all add interest.
- Space and climbing structures in the vertical dimension are critical.

GALLERY 5.1 Marmoset housing



Marmoset in a well enriched cage (image UAR)



MOVIE 5.1 Marmosets in good quality housing



There is no sound on this video (UAR)

Macaques

- Macaques need to be housed in stable, compatible groups with enough space for exercise. They need a solid floor covered with a substrate such as straw and wood-shavings to conceal food and allow foraging.
- There should be sufficient enclosure height to allow vertical flight if alarmed with climbing structures such as perches, platforms, swings, ropes, ladders to increase useable space sufficient for all the animals in the unit to be occupy simultaneously.
- Macaques are sub-tropical mammals so require adequate light levels and a temperature above 15 °C.
- Access to outdoors should be provided wherever possible and toys, chews, tactile materials, and destructible materials provided to give a degree of control over the environment.

GALLERY 5.2 Macaque group cages



Macaques (UAR)



MOVIE 5.2 Macaques climbing on rings



Environmental Enrichment

ENRICHMENT AIMS TO IMPROVE WELFARE IN CAPTIVE ANIMALS

1. Encouraging natural behaviour
2. Social enrichment
3. Giving the animal control over their environment
4. Creating complexity in the environment



Encourage natural behaviour

In the wild, macaques spend a great deal of their days searching for, retrieving and processing food.

Therefore, it is not surprising that the easiest way to provide enrichment for the captive animals involves food.

Making it more difficult for them to access their food promotes foraging behavior, by hiding seeds in the straw on the floor of the pens for example.

Young macaques foraging naturally at BFC Israel



Different facilities have come up with ingenious methods of making feeding interesting such as Frozen Frisbee Salads.

Plastic frisbees are layered with fruit and vegetables, covered in water or juice, and frozen overnight. These can be handed directly to the primates or hung outside of the cages. The animals seem to have a great time picking up the treats as they gradually thaw.

GALLERY 5.3 Enriching macaque enclosures



Macaques are fond of water (image Bushmitz BFC)

Social enrichment

It is vital to keep primates in pairs or groups so that they can groom one another, resting, playing and huddle together.

Giving the animal control over their environment

One nice example is the use of mirrors controlled by the animal. Turning a handle changes the position of a mirror so the animal can see what or who is coming down the servicing corridors beside the pens.

MOVIE 5.4 Macaque family group (Medical Research Council, UK)



MOVIE 5.3 Macaque moves mirror (Medical Research Council, UK)



Creating complex environment

Complexity provides choice and choice allows a degree of control and reduces the likelihood of boredom

Complexity can be introduced through 'enrichment' in a variety of ways but typically it includes providing an appropriate variety of food in ways that present a challenge to reach or find it and by providing an interesting physical environment.

Ropes and swings to move and play on, loose objects like feathers to play with, live insects to chase, views

Well enriched group cage in Bioculture Mauritius



GALLERY 5.4 Complex primate environments



Macaques like to manipulate objects (image Bushmitz BFC)



through windows of live birds and humans all provide novelty and reduce boredom.

Frequent changes made to the enrichment can sustain attention and interaction and typically a facility will have a 'timetable' so that different options are made available in turn.

Handling and training

READY FOR RESEARCH

1. Primates can be trained in the breeding facility ready for their use in research.
2. This makes the transition between facilities easier on animal and handler.
3. The scientist receives animals that understand what is required of them.

Appropriate handling and training in the breeding facility makes it easier for the primate and scientist when the animal leaves for the research facility.

Methods of capture, handling, restraint and training seek to minimise any stress to the animals. Positive reinforcement techniques are used to train primates to cooperate with capture, handling, restraint and research procedures.

Gaining the trust of the nonhuman primate through socialization with people leads to cooperation with biomedical studies and avoids the need for restraint. In order to get to a point where the animal can be trained,

GALLERY 5.5 Trained primates



Monkey trained to take dosed drug from a syringe (Bioculture Mauritius)



trust must be conditioned by spending time in positive interactions.

Biomedical and quarantine facilities can get the animals used to people. There is often only a short amount of time between the acclimation period and the start of the experimental study, and this it is not enough time in it self to prevent anxiety.

This is why it is critical that human interaction begin at the time of infancy and continue during its youth in the breeding facility.

The expense of early training is more than paid back by animals remaining calm during their work.

MOVIE 5.5 Keeper interacting with macaque (Bioculture)



MOVIE 5.6 Carabiner training (MRC / University of Newcastle)



MOVIE 5.7 Presenting a leg for blood sampling (UAR)



Veterinary care

HIGH STANDARDS - EXTERNALLY INSPECTED

Research protocols reviewed annually

Primate research facilities either have their own veterinary staff or external staff who are available on call. Veterinary staff have appropriate training and experience in primate health and well-being, and this includes continuing professional development.

Research protocols

Research protocols such as anaesthesia, analgesia and humane endpoints are regularly reviewed. Vets also confirm that the facilities are suitably equipped for the procedures undertaken.

As well as checking to see the animals are in good health vets contribute to the design and routines that ensure primates have an enriched environment.

The UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) holds regular primate welfare meetings to share best practice. These meetings are free and open to laboratory personnel working directly with non-human primates.

In the UK Government inspectors who on the whole are also vets regularly make unannounced inspections of facilities.

GALLERY 5.6 Veterinary care of primates



Young macaque being inspected (UAR)



Law and regulation

The law regulating research with animals is strong and this is particularly so for primates. This chapter discusses the law in the EU, US and UK.



UK law

HOW RESEARCH WITH ANIMALS IS REGULATED

1. The law safeguards laboratory animal welfare.
2. Three separate types of licence are required for animal research or testing.
3. Research can only take place in research institutes or companies which have veterinary facilities and appropriate animal accommodation.
4. Research must be part of an approved research programme which has been given a project licence.
5. Research must be carried out by people with sufficient training, skills and experience as shown in their personal licence.
6. Primates are only used when other species are not suitable.

Regulation



There have been special controls on the use of laboratory animals in the UK since 1876. These were revised and extended in

1986 as the Animals (Scientific Procedures) Act (ASPA).

ASPA has recently been revised to transpose European Directive 2010/63/EU on the protection of animals used for scientific purposes. The revised legislation came into force on 1 January 2013.

This law safeguards laboratory animal welfare while allowing important medical research to continue. Central to ASPA is a harm-benefit assessment which must be applied before any research project involving animals can go ahead. Thus the costs, in terms of potential animal suffering, must be weighed against the potential benefits of the research.

Licences

Three separate types of licence are required for animal research or testing. Animal procedures can only:

- take place in research institutes or companies which have appropriate animal accommodation and veterinary facilities, and have been granted an Establishment Licence
- be part of an approved research or testing programme which has been given a project licence
- be carried out by people with sufficient training, skills and experience as shown in their personal licence

Licences are only granted if:

- the potential results are important enough to justify the use of animals (the cost benefit analysis)
- the research cannot be done using non-animal methods
- the minimum number of animals will be used
- dogs, cats or primates are only used when other species are not suitable

- any discomfort or suffering is kept to a minimum by appropriate use of anaesthetics or pain killers
- researchers and technicians conducting procedures have the necessary training, skills and experience
- research premises have the necessary facilities to look after the animals properly (as laid down in a Home Office Code of Practice).

In addition, a whole new level of regulation took effect in April 1999, with the introduction of local ethical review, now under the local Animal Welfare and Ethical Review Body (AWERB).

The [Home Office website](#) has more detailed information.



EU law

EUROPEAN COMMISSION

1. The European Commission has produced a directive that lays out a framework for animal welfare legislation (2010/63/EU).
2. 2010/63/EU came into force on 1 January 2013.



The European Commission recognises that animals are sentient beings. The general aim of EU legislation is to ensure that animals do not endure avoidable pain or suffering, and obliges the owner/keeper of animals to respect minimum welfare requirements.

European Directive 2010/63/EU

In November 2008, it was decided that the European Directive concerning the use of animals in research should be revised.

The final text of the Directive was finalised and signed on 22nd September 2010. It was formally published in the Official Journal of the European Union on the 20th October 2010 and was given its final name: 2010/63/EU. The directive then entered into force on the 9th November 2010. The Directive formally applied across Europe as of 1st January 2013.

History

In 1986 the European Council of Ministers adopted Directive 86/609/EEC on 'the protection of animals used for experimental and other scientific purposes'. The Directive sought to improve the controls on the use

of laboratory animals, set minimum standards for housing and for the training of those handling animals and supervising the experiments. The Directive also aimed to reduce the numbers of animals used for experiments by requiring that an animal experiment should not be performed when an alternative method exists, and by encouraging the development and validation of alternative methods to replace animal methods.

This legislation is largely a framework, and laws governing animal experiments in the UK, for example, were very much stricter. A few years ago, it became clear that officials within the European Commission wished to revise the Directive to promote improvements in the welfare of laboratory animals and to further encourage the development of alternative methods.

Since 1986 important progress has been made in science and new techniques have become available, such as use of transgenic animals, xenotransplantation, and cloning. According to the Commission, these require specific attention, which the old Directive does not provide.

Amongst other points the EU directive provides greater clarity over the use (and restrictions of the use) of non-human primates.

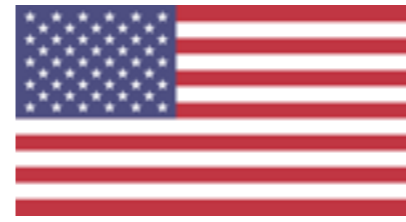
Not all EU states have adopted the directive into their domestic legislation (as of April 2013).



US law

RESEARCH WITH ANIMALS IN THE US

1. **Regulatory Requirements**
2. **The Institutional Official**
3. **Institutional Animal Care and Use Committee (IACUC)**
4. **The Attending Veterinarian**



Research with animals is guided by a complex set of federal and state laws, regulations, and guidelines, and by additional institutional policies implemented to systematically address federal requirements and as the result of a voluntary accreditation process. In addition to these laws and regulations, researchers and animal care technicians are guided by ethical considerations for the proper care and use of animals.

The **Public Health Service Policy on Humane Care and Use of Animals** (PHS Policy) and **USDA Animal Welfare Regulations** (AWRs) provide the primary regulatory basis for the existence and function of the Institutional Animal Care and Use Committee (IACUC), which must be established at any institution that receives PHS funding for vertebrate animal-based research, and/or which conducts animal-based research involving vertebrate animal species regulated by the USDA AWRs.

PHS Policy requires that all institutions base their animal care and use programs on the **Guide for the Care and Use of Laboratory Animals** (the Guide), and that euthanasia be consistent with the most current American Veterinary Medical Association (AVMA)

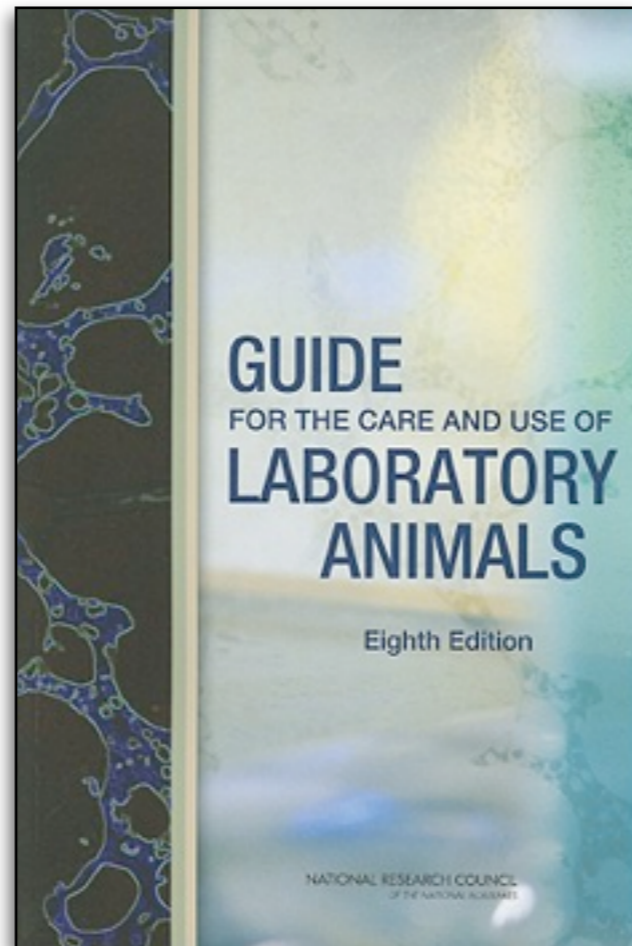
Guidelines on Euthanasia[5]. The PHS Policy also endorses the US Government Principles for the Utilization and Care of Vertebrate Animals Use in Testing, Research and Training, which form the foundation for ethical and humane care and use of laboratory animals in the United States.

Many institutions are also subject to additional standards that go above and beyond the regulatory requirements by maintaining accreditation through the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International.

Though accreditation is voluntary, many institutions choose to become AAALAC accredited as a way of demonstrating their high standards of animal care.

The Institutional Official

Each institution must identify an Institutional Official (IO) who is legally authorized to



commit, on behalf of the institution, that the requirements of the PHS Policy and USDA AWRs will be met. The IO is appointed by the Chief Executive Officer of each institution and must be assigned institutional responsibility to commit the financial and other resources to ensure compliance with the governing regulations, as well as to initiate and/or codify institutional policies and procedures to promote high-quality science and animal well-being. The IO does not need to be a scientist or work with animals, but must be someone who will accept responsibility for the wellbeing of the animals.”

The IO is responsible for providing general oversight and direction of the institutional animal care and use program. This includes taking the lead in creating a dynamic, compliant, and responsible institutional culture, and establishing an expectation of quality scientific research while promoting the humane use and well-being of animals used in research. To accomplish these goals, the IO must appoint and empower key personnel to provide day-to-day oversight of the program as well as the resources required to ensure quality science and promote animal well-being. The IO is additionally designated the responsibility to appoint members to the IACUC.

The Institutional Animal Care and Use Committee (IACUC)

The IACUC reports to the Institutional Official, as required by federal regulations. The Committee's specific responsibilities are spelled out in PHS Policy IV.B and USDA AWRs section 2.31(c):

1. The IACUC must review the institution's program for humane care and use of animals at least once every six months, using the Guide and USDA AWRs as the basis for evaluation.
2. The IACUC must inspect all of the institution's animal facilities at least once every six months, using the Guide and USDA AWRs as the basis for evaluation.
3. The IACUC is responsible for reviewing and, if warranted, investigating concerns involving the care and use of animals at the institution.
4. The IACUC is authorized to make recommendations to the Institutional Official regarding any aspect of the institution's animal program, facilities or personnel, to ensure regulatory compliance.

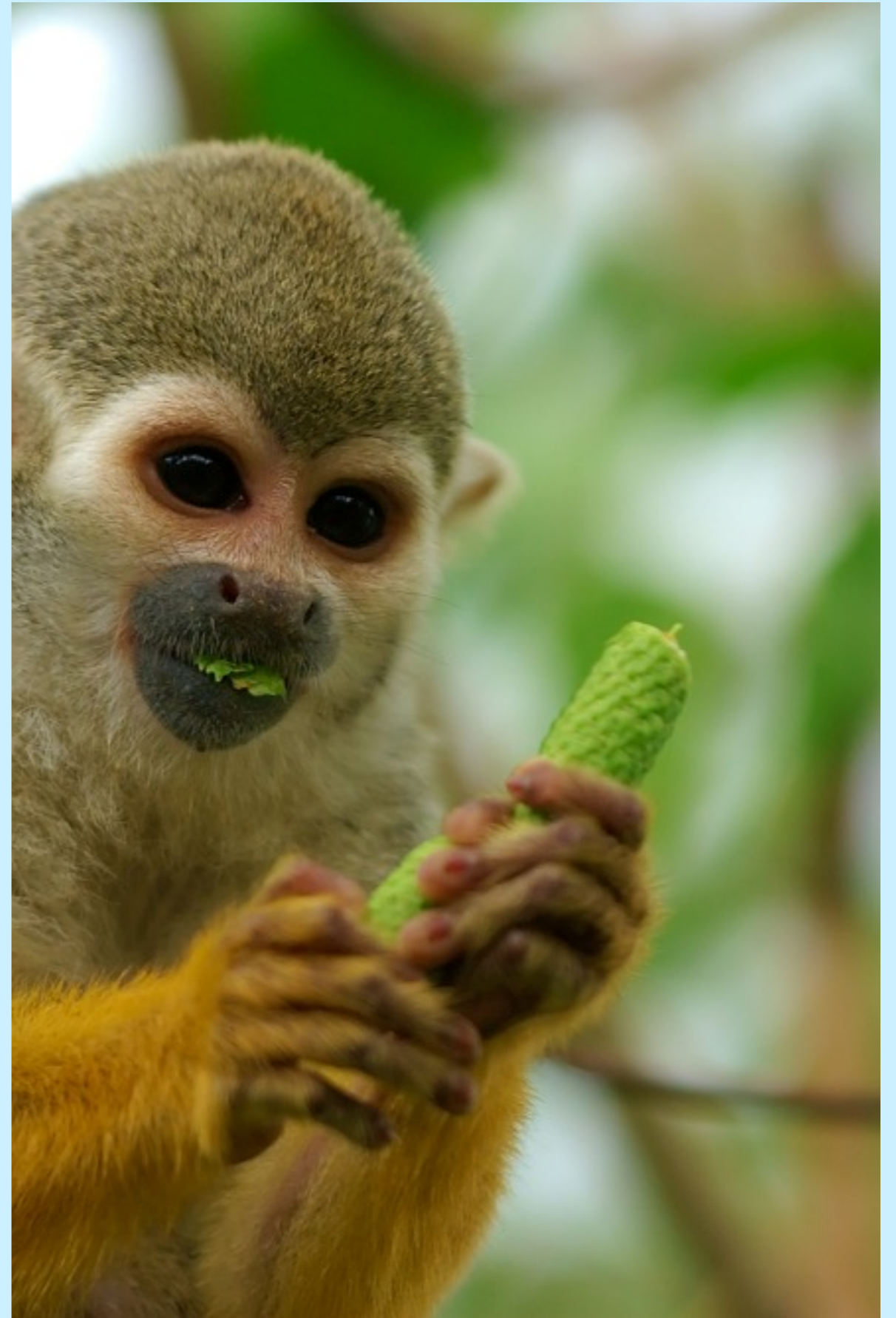
5. The IACUC must review and approve, require modifications in (to secure approval), or withhold approval of proposed activities related to the care and use of animals.
6. Similarly, the IACUC is required to review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities.
7. Finally, the IACUC must be authorized to suspend an activity involving animals if the IACUC determines the activity is not being conducted in accordance with the approved research protocol or with other applicable provisions of the USDA AWRs, the Guide, the institution's Assurance, or PHS Policy.

The Attending Veterinarian

Adequate veterinary medical care is an essential component of any research program and is mandated by both the PHS Policy and USDA AWRs. The Attending Veterinarian (AV) is the individual with legal responsibility for the health and welfare of animals at the research facility.

Resources

Within this section we provide links for downloading many of the images and videos in this ebook. We have also listed references for the majority of our content as well as links to organisations concerned with primate biology and welfare.



Monkeys photo galleries



Macaque social life (image shutterstock)



Marmoset (image UAR)



Video Gallery

MOVIE 7.1 Macaques at Oregon Health & Science University



MOVIE 7.3 Macaques in water



MOVIE 7.2 Marmosets and Parkinson's disease



MOVIE 7.4 Young macaque eating



Documents

Use of primates



<http://www.primate.wisc.edu/pin/nprcbrochure.pdf>



Primate welfare



<http://www.understandinganimalresearch.org.uk/media-library/download/document/16/>



Importance of research



<http://www.understandinganimalresearch.org.uk/media-library/download/document/2/>



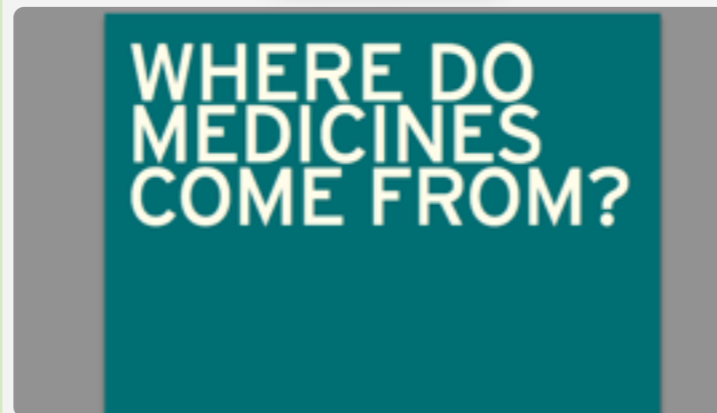
Regulations & guidelines



<http://www.understandinganimalresearch.org.uk/media-library/download/document/17/>



Education



<http://www.understandinganimalresearch.org.uk/media-library/download/document/4/>



Primate health and care



http://pasaprimates.org/wp-content/uploads/2007/05/PASA-vet-manual-2nd-edition_reduced.pdf



Links

Click on icon to go to website



Click on icon to go to website



References

SOURCES BY CHAPTER

1. Chapter 1 - Why we use primates in medical research
2. Chapter 2 - Which primate species do we use?
3. Chapter 3 - History of medical advances with primates
4. Chapter 4 - Medical advances
5. Chapter 5 - Primate welfare
6. Chapter 6 - Law and regulation

Chapter 1 - Why we use primates in medical research

<http://www.understandinganimalresearch.org.uk/why/>

Chapter 2 - Which primate species do we use?

Section 1 - Macaques

http://en.wikipedia.org/wiki/Crab-eating_macaque

http://en.wikipedia.org/wiki/Rhesus_macaque

<http://www.nc3rs.org.uk/page.asp?id=1858>

<http://www.nc3rs.org.uk/page.asp?id=238>

http://pin.primate.wisc.edu/factsheets/entry/rhesus_macaque

Section 2 - Marmosets

http://en.wikipedia.org/wiki/Common_marmoset

<http://www.marmosetcare.com>

http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_publishing_group/documents/resources/wtx041908.pdf

Section 3 - Other monkeys and apes

<http://en.wikipedia.org/wiki/Baboons>

http://en.wikipedia.org/wiki/Squirrel_monkey

http://en.wikipedia.org/wiki/Common_squirrel_monkey

Luc Viatour / www.Lucnix.be

<http://www.understandinganimalresearch.org.uk/news/2011/03/artificial-blood-vessel-success-in-animals/>

http://en.wikipedia.org/wiki/Great_apes

<http://www.animalresearch.info/en/listing/114/ebola-vaccine-western-gorillas/#ebolavirus>

<http://news.sciencemag.org/scienceinsider/2011/02/entering-a-wild-frontier-testing.html>

http://wwf.panda.org/what_we_do/

Chapter 3 - Medical advances

Images from wikimedia, Oregon Primate Centre, Wisconsin and photobank.

Chapter 4 - Medical advances

Section 1 - Alzheimer's disease

<http://www.alzheimers.org.uk>

<http://animalresearch.info/en/designing-research/261/primates/>

Section 2 - Anxiety

<http://www.news.wisc.edu/15363>

<http://www.med.wisc.edu/news-events/decreased-gene-activity-is-likely-involved-in-childhood-risk-for-anxiety-and-depression/39097>

Section 3 - Colour blindness

<http://www.nature.com/nature/journal/v461/n7265/full/nature08401.html>

<http://www.colour-blindness.com/general/prevalence/>

Section 4 - Hepatitis

<http://animalresearch.info/en/listing/457/hepatitis-e/>

Section 5 - HIV/AIDS

<http://animalresearch.info/en/listing/1/aids-hiv/>

Section 6 - Malaria

<http://www.who.int/mediacentre/factsheets/fs094/en/index.html>

Section 7 - Parkinson's Disease

<http://www.parkinsons.org.uk/>

<http://animalresearch.info/en/listing/25/parkinsons-disease/>

Section 8 - Polio

<http://animalresearch.info/en/search/results/?q=polio>

<http://www.who.int/topics/poliomyelitis/en/>

Section 9 - Reproductive system

<http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002558>

Section 10 - Schistosomiasis

<http://www.unhco.org/schistosomiasis/>

<http://www.who.int/tdr/diseases-topics/schistosomiasis/en/>

<http://animalresearch.info/en/listing/8/schistosomiasis/schistosomiasis/>

Section 11 - Stroke

<http://who.int/mediacentre/factsheets/fs310/en/>

<http://jama.jamanetwork.com/article.aspx?articleid=217622>

<http://www.ncbi.nlm.nih.gov/pubmed/9876870>

Section 12 - TB

[http://www.tuberculosisjournal.com/article/S1472-9792\(02\)00059-8/abstract](http://www.tuberculosisjournal.com/article/S1472-9792(02)00059-8/abstract)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3248283/pdf/JCI46252.pdf>

<http://sciencenordic.com/new-vaccine-could-eradicate-tuberculosis>

Chapter 5 - Primate welfare

Section 1 - Accommodation

<http://www.nc3rs.org.uk/page.asp?id=25>

<http://www.nc3rs.org.uk/category.asp?catID=26>

<http://www.marmosetcare.com/care-in-captivity/housing.html>

http://www.marmosetcare.com/downloads/EAZA_HusbandryGuidelines.pdf

<http://www.nc3rs.org.uk/downloaddoc.asp?id=418&page=277&skin=0>

<http://www.psgb.org/captivecare.php>

<http://www.marmosetcare.com/care-in-captivity/housing.html>

http://www.marmosetcare.com/downloads/EAZA_HusbandryGuidelines.pdf pp72-80

Section 2 - Enrichment

<http://www.marmosetcare.com/care-in-captivity/what-is-enrichment.html>

Section 3 - Handling

Chapter 6 - Law and regulation

Section 1 - UK law

<http://www.homeoffice.gov.uk/science-research/animal-research/>

<http://www.understandinganimalresearch.org.uk/how/regulation>

Section 2 - EU law

http://ec.europa.eu/food/animal/welfare/index_en.htm

<http://www.understandinganimalresearch.org.uk/policy/european-directive/>

<http://animaltestingperspectives.org/transposition/>

Section 3 - US law

<http://speakingofresearch.com/facts/research-regulation/>

<http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf>

http://www.aphis.usda.gov/animal_welfare/awr.shtml

<http://www.nap.edu/readingroom/books/labrats/>

http://www.avma.org/issues/animal_welfare/euthanasia.pdf

<http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples>



About Us



Dr. Bushmitz Mark Moshe

Understanding Animal Research



UNDERSTANDING ANIMAL RESEARCH (UAR)

Understanding Animal Research aims to achieve broad understanding and acceptance of the humane use of animals in biomedical research in the UK, to advance science and medicine.

The information provided by Understanding Animal Research is based on thorough research and understanding of the facts, historical and scientific.

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What we do

Understanding Animal Research provides information and educational materials and seeks to engage with and inform many sectors to bring about its vision of the acceptance of the humane use of animals.

Key stakeholders include members of the public, the media, policy makers, schools and the scientific research community.



Bushmitz Mark Moshe



Dr. Moshe Bushmitz is a vet specialized in lab animals and primates. He has been involved in Israel with “Helping Hands”, a primate training project assisting Israeli war handicapped soldiers by Capuchin monkeys.

In 1990 Dr Bushmitz founded BFC Israel a SPF *Macaque fascicularis* breeding facility dedicated to high animal health & welfare standards. In the last 10 years he is the research & scientific director of Bioculture Mauritius and consults on primate breeding, husbandry & welfare at different institutes and primate centers.

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AIDS

a disease in which there is a severe loss of the body's cellular immunity, greatly lowering the resistance to infection and malignancy.

Related Glossary Terms

Drag related terms here

Index

Find Term

Alzheimer's disease

progressive mental deterioration that can occur in middle or old age, due to generalized degeneration of the brain. It is the commonest cause of premature senility.

Related Glossary Terms

Drag related terms here

Index

Find Term

Ape

large primate that lacks a tail, including the gorilla, chimpanzees, orang-utan, and gibbons.

Related Glossary Terms

Drag related terms here

Index

Find Term

ASPA

Animals (Scientific Procedures) Act (ASPA) - law that controls the use of laboratory animals in the UK

Related Glossary Terms

Drag related terms here

Index

Find Term

Baboon

a large Old World ground-dwelling monkey with a long doglike snout and large teeth.

Genera *Papio* and *Mandrillus*, family *Cercopithecidae*: several species, including the drill and mandrill.

Related Glossary Terms

Drag related terms here

Index

Find Term

Cynomolgus monkey

Macaca fascicularis - most commonly used macaque species in medical research

Related Glossary Terms

Drag related terms here

Index

Find Term

Gorilla

a powerfully built great ape with a large head and short neck, found in the forests of central Africa. It is the largest living primate.

Gorilla gorilla, family *Pongidae*: three races (two lowland gorillas and the mountain gorilla)

Related Glossary Terms

Drag related terms here

Index

Find Term

Hepatitis

Hepatitis is a medical condition defined by the inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the organ.

There are many causes including a range of virus.

Related Glossary Terms

Drag related terms here

Index

Find Term

HIV

human immunodeficiency virus, a retrovirus which causes AIDS

Related Glossary Terms

Drag related terms here

Index

Find Term

Macaque

a medium-sized, chiefly forest-dwelling Old World monkey which has a long face and cheek pouches for holding food.

- Genus *Macaca*, family *Cercopithecidae*: several species, including the Cynomolgus and rhesus monkey

Related Glossary Terms

Drag related terms here

Index

Find Term

Malaria

an intermittent and remittent fever caused by a protozoan parasite which invades the red blood cells and is transmitted by mosquitoes in many tropical and subtropical regions.

- The parasite belongs to the genus *Plasmodium* (phylum *Sporozoa*) and is transmitted by female mosquitoes of the genus *Anopheles*

Related Glossary Terms

Drag related terms here

Index

Find Term

Marmoset

a small tropical American monkey with a silky coat and a long tail.

Family *Callitrichidae* (or *Callithricidae*): genus *Callithrix* (three species), *Callithrix jacchus* most commonly used in research; and the pygmy marmoset (*Cebuella pygmaea*)

Related Glossary Terms

Drag related terms here

Index

Find Term

Monkey

a small to medium-sized primate that typically has a long tail, most kinds of which live in trees in tropical countries.

Families *Cebidae* and *Callitrichidae* (or *Callithricidae*) (New World monkeys, often with prehensile tails), and *Cercopithecidae* (Old World monkeys, without prehensile tails)

Related Glossary Terms

Drag related terms here

Index

Find Term

Parkinson's disease

a progressive disease of the nervous system marked by tremor, muscular rigidity, and slow, imprecise movement, chiefly affecting middle-aged and elderly people. It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine.

Related Glossary Terms

Drag related terms here

Index

Find Term

Poliomyelitis

Polio - an infectious viral disease that affects the central nervous system and can cause temporary or permanent paralysis.

Related Glossary Terms

Drag related terms here

Index

Find Term

Primate

a mammal of an order that includes the lemurs, bush-babies, tarsiers, marmosets, monkeys, apes, and humans. They are distinguished by having hands, hand-like feet, and forward-facing eyes, and are typically agile tree-dwellers.

Related Glossary Terms

Drag related terms here

Index

Find Term

Rhesus monkey

Macaca mulatta - a small brown macaque with red skin on the face and rump, native to southern Asia. It is often kept in captivity and is widely used in medical research.

Related Glossary Terms

Drag related terms here

Index

Find Term

Schistosomiasis

Schistosomiasis (also known as bilharzia, bilharziosis or snail fever) is a collective name of parasitic diseases caused by several species of trematodes belonging to the genus *Schistosoma*. Snails serve as the intermediary agent between mammalian hosts. Individuals within developing countries who cannot afford proper water and sanitation facilities are often exposed to contaminated water containing the infected snails.

Although it has a low mortality rate, schistosomiasis often is a chronic illness that can damage internal organs and, in children, impair growth and cognitive development. The urinary form of schistosomiasis is associated with increased risks for bladder cancer in adults. Schistosomiasis is the second most socioeconomically devastating parasitic disease after malaria.

This disease is most commonly found in Asia, Africa, and South America, especially in areas where the water contains numerous freshwater snails, which may carry the parasite.

The disease affects many people in developing countries, particularly children who may acquire the disease by swimming or playing in infected water. When children come into contact with a contaminated water source, the parasitic larvae easily enter through their skin and further mature within organ tissues. As of 2009, 74 developing countries statistically identified epidemics of Schistosomiasis within their respective populations.

Related Glossary Terms

Drag related terms here

Index

Find Term

Squirrel monkey

a small South American monkey with a non-prehensile tail, typically moving through trees by leaping.

Genus *Saimiri*, family *Cebidae*: five species, in particular *S. sciureus*

Related Glossary Terms

Drag related terms here

Index

Find Term

Stroke

A stroke, sometimes referred to by the older term cerebrovascular accident (CVA), is the rapid loss of brain function due to disturbance in the blood supply to the brain.

Related Glossary Terms

Drag related terms here

Index

Find Term

Tuberculosis

Tuberculosis, MTB, or TB (short for tubercle bacillus) is a common, and in many cases lethal, infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis*.

Related Glossary Terms

Drag related terms here

Index

Find Term

Vervet

a common African guenon with greenish-brown upper parts and a black face. Compare with green monkey, grivet.

Cercopithecus aethiops, family *Cercopithecidae*, in particular the race *C. a. pygerythrus* of southern and eastern Africa

Related Glossary Terms

Drag related terms here

Index

Find Term