Why they don't catch Covid

How do bats stay safe from the viruses they harbour?

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Bats have been implicated in several outbreaks of viral diseases that come to humans from animal sources. And the current pandemic of Covid-19, caused by severe acute respiratory syndrome coronavirus-2 (Sars-CoV-2), has affected 96 million people and claimed two million lives.

Aaron T Irving, Matae Ahn, Geraldine Goh, Danielle E Anderson and Lin-Fa Wang, from Duke-NUS Medical School and Duke-NUS Global Health Institute, Singapore, and the Zhejiang University, China, in a paper in the journal, Nature, examine the immune system and defences of the bat, which enable the animal to play host to viruses, but steer clear of being affected by them. "Lessons from the effective host defence of bats would help us to better understand viral evolution and better predict, prevent and control future viral spillovers," the authors say.

A reason for the "spillover" of pathogens from animal hosts, which have adapted to the pathogen, to humans, who are susceptible, is that human disturbance of an ecosystem raises the fraction of animals that are host to pathogens, over those that are not. Why this happens is that smaller and shorter-lived animals are more likely to survive and stay on when humans encroach an environment. These smaller animals, with lesser body weight, cannot afford the large investment of energy that immunity requires. Hence, they do not throw out several pathogens, as do the larger animals. The capacity to tolerate foreign bodies in the bloodstream without severe immune reaction being provoked enables them to adapt to changes and remain in the new areas that humans inhabit.

Smaller animals are also short-lived. This has been related to the higher resting-metabolic-rate in small animals. The higher rate of metabolism leaves the animals with less energy to support immunity, and hence makes them, in their short life-spans, host to more pathogens than larger animals.

The bat, the paper points out, in respect of the life-span, is an exception. For its diminutive size – bats are rarely larger that common rats – it has a life-span associated with a much larger animal. The result is that the bat is both host to many viruses and stays around for a long time. The paper points out that as the only mammal that is capable of flight, the advantages of this capacity come at a high metabolic cost, a feature associated with smaller animals.

The life-span, however, is substantially greater than non-flying mammals of the same size. "When adjusted for body size, only 19 species of mammals are longer-lived than humans: 18 of these species are bats (the other is the naked mole-rat)," the paper says, "As a mammalian model of anti-ageing, bats may offer vital clues in human attempts to delay mortality and enhance longevity."

The paper says that apart from possible mechanisms to regulate the body responses to infection, the species richness of bat communities may be a reason for the ability to harbour a variety of viruses. This idea flows out of research that shows that the number of pathogens an animal order can host increases with the richness of species within that order. In the case of bats, this richness is unprecedented – out of the 6,400 species of mammals, 1,423 are of bats. And they are widely distributed, being found in all parts of the world, except the poles, extreme desert climes and a few remote islands.

While bats have long been associated with infectious diseases, the discovery of Sars-related coronaviruses in bats, the paper says, has led to identifying them as the richest source of genetically diverse coronaviruses. The paper adds that apart from several coronavirus diseases in humans, bats can affect other animals, like pigs and horses. There is even the case of a reversal of infection – from humans to domestic pets or zoo animals. And where civets or pangolins were suspected as sources of Sars or Sars-CoV-2, this is seen not to be the case, as these animals take ill when infected, and could not be the reservoirs. Whereas bats show no signs of disease even when infected by most viruses.

How do they do it?

The authors refer to proposed answers based on factors that reduce the viral load in bats. But they discount these suggestions, as bats do carry and tolerate high viral loads. And evidence indicates that what makes bats special might not be their ability to overcome the virus, but rather their ability to avoid the disease that follows. What is likely, they suggest, is that there is an effective balance between the immune reaction of the body, which would protect against viruses, and moderation of the reaction, so that it does not harm the body itself. This could also be the reason that bats have long life-spans and low incidence of cancer.

The immune reaction gets activated when a foreign body, like microbes, viruses or certain toxins are detected. When a cell is infected by a virus, the cell releases a protein, called interferon, as a signal to other cells and to trigger immune cells to set up defence action. The fever or body pain that accompanies viral fever in humans is caused by the immune system, which acts on healthy tissue too. And there are many bat-borne viruses, the paper says, which set the innate immune system of humans on a course of prolonged or strong response, leading to serious disease.

Bats, on the other hand, show no signs of disease even with high levels of virus infection. The paper explains that the recognition of invasion by a virus is by way of stimulation of genes that code for the interferon protein. This mechanism is called "stimulation of interferon genes", or STING, and the paper says that STING-dependent interferon response has been found to be dampened in several bat species.

The paper also cites a recent study, where three of the current authors took part, which found that a protein which senses an indicator of stress, to set off inflammation, is dampened in the case of bats. The result is that whatever the load of viruses, in bats, there is reduced inflammatory response. That allows the bat to act as a viral reservoir without showing symptoms of infection.

"Deeper understanding (of the mechanism of robust defence and immune tolerance) will provide insights and strategies not only to aid in the prediction, prevention or control of zoonotic virus spillover from bats to humans, but also to potentially combat ageing and cancer in humans," the paper says.

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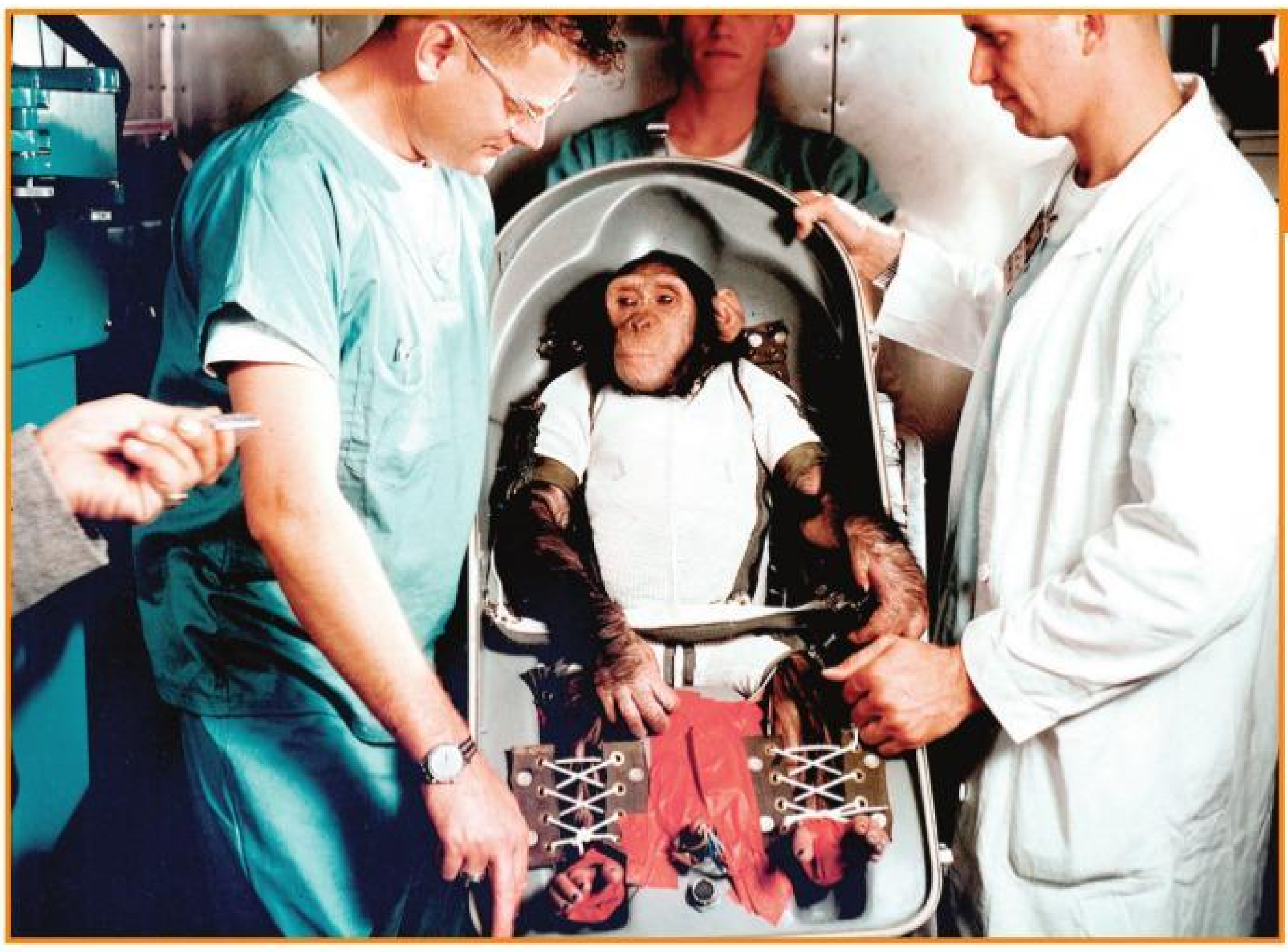

MORE THAN ANIMAL, LESS THAN HUMAN

This year marks the 60th anniversary of Ham the chimpanzee's foray into space

ALICE GORMAN

On 31 January 1961, an intrepid chimpanzee called Ham was launched on a rocket from Cape Canaveral in the United States, and returned to Earth alive. In this process, he became the first hominin in space.

In the 1950s, it was unclear whether humans could survive outside Earth – both physically and mentally. The science fiction writer and warfare expert Cordwainer Smith wrote about the psychological pain of being in space.

Plants, insects and animals had been taken to high altitudes in balloons and rockets since the 18th century. The Soviet Union sent the dog Laika into orbit on Sputnik 2 in 1957. She died, but from overheating rather than the effects of space travel itself.

While the USSR focused on dogs, the US turned to chimpanzees as they were the most like humans. The stakes became higher when US President John F Kennedy promised to land humans on the Moon by the end of the 1960s.

Biography of a non-human astronaut

Ham was born in 1957 in a rainforest in the Central African nation of Cameroon, then a French territory. He was captured and taken to an astronaut school for chimps at Holloman Air Force Base in New Mexico.

The astrochimps were trained to pull levers, with a banana pellet as a reward and an electric shock to the feet for failure. The chosen chimp would test life support systems and demonstrate that equipment could be operated during spaceflight. Ham showed great aptitude, and was selected the day before the flight.

On 31 January 1961, Ham was launched into space, strapped into a capsule inside the nose cone of a Mercury-Redstone rocket. The rocket travelled at 9,000km/h, and reached an altitude of 251 km. The whole flight took 16 minutes from launch to return.

Throughout the journey Ham was obliged to pull a lever. He received two shocks for not doing this correctly, out of 50 pulls. He achieved this with a 16 cm rectal thermometer in place to monitor his temperature.

He experienced 6.6 minutes of free fall and 14.7g of acceleration on descent – much greater than predicted. The biomedical data showed Ham experienced stress during acceleration and deceleration.

Jane Goodall, an expert in primate behaviour, said she had never seen such terror in a chimp's expression. However, Ham was calm when weightless.

Ham survived the flight itself, but nearly drowned when the capsule started filling with water after its ocean splashdown. Fortunately, the helicopter recovery team reached him in time. Ham's treat on emerging from the spacecraft was an apple, which he devoured eagerly.

After his flight, Ham lived for 20 years by himself, in a zoo in Washington DC. People wrote him letters, and some were answered by zoo staff signed with Ham's fingerprint. In 1980 he was sent to another zoo to live with a group of chimps. He died in 1983 at the age of 26.

A proposal to stuff and display his body was abandoned after an outcry. But he did undergo a post-mortem. Ham's flesh was stripped from his skeleton, cremated, and buried at the Space Hall of Fame in Alamogordo, New Mexico. The National Museum of Health and Medicine in Washington DC retains his bones.

Cyborg and simian, man and machine

Ham sits at an interesting intersection of race, gender and species. "Ham" was an acronym for Holloman Aero Medical, but as American philosopher of science Donna Haraway has pointed out, "Ham's name inevitably recalls Noah's youngest and only black son".

While the chimps were in training at the Holloman Airforce Base, women were actively excluded from spaceflight. Pilot Jerrie Cobb said she would take the place of one of the chimps if it meant having a shot at space.

The astronauts of the 1960s Mercury programme felt their masculinity threatened by performing the same tasks as chimps. In a scene from the 1983 film *The Right Stuff*, based on Tom Wolfe's book for which he did extensive interviews with the astronauts, one says, "Well none of us wants to think that they're going to send a monkey up to do a man's work... what they're trying to do to us is send a man up to do a monkey's work."

In the *I Dream of Jeannie episode* "Fly me to the Moon" (1967), astronauts Tony Nelson and Roger Healey train Sam the chimp for spaceflight. They are envious that Sam gets to go to the Moon before them. "He can't make any decisions, we might as well have a robot up there," says Major Nelson.

This refers to the then ongoing battle among both Soviet and US astronauts about how much autonomy they would have as pilots. On both sides of the Iron Curtain, being controlled by machines was felt to diminish masculinity.

Chimps in space also threatened the accepted evolutionary order. In some versions of the famous "March of Progress" illustration of human evolution, the first figure is a knuckle-walking ape and the last is an astronaut. Ham was leapfrogging to the front of the evolutionary queue in a *Planet of the Apes*-style interspecies competition. Ham's spaceflight made him more than animal, but still less than human

A mere 10 weeks after Ham's feat, Soviet cosmonaut Yuri Gagarin became the first human in space when he orbited Earth on 12 April. On 26 November, Enos the chimp completed an orbit.

We don't send animals into orbit any more as proxies for human experience. But there is one chimp still in space. The calls of a wild chimp were recorded on the Voyager Golden Records, now heading out beyond the Solar System.

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PLUS POINTS

Obesity may affect brain health

New research has found being overweight is an additional burden on brain health and may exacerbate Alzheimer's disease. The pioneering multimodal neuroimaging study revealed obesity may contribute toward neural tissue vulnerability, whilst maintaining a healthy weight in mild Alzheimer's disease dementia could help preserve brain structure.

The findings, published in The Journal of Alzheimer's Disease Reports, also highlight the impact being overweight in mid-life could have on brain health in older age.

Lead author of the study, professor Annalena Venneri from the University of Sheffield's Neuroscience Institute and NIHR Sheffield Biomedical Research Centre, said, "More than 50 million people are thought to be living with Alzheimer's disease and despite decades of ground breaking studies and a huge global research effort we still don't have a cure for this cruel disease.

"Prevention plays such an important role in the fight against the disease. It is important to stress this study does not show that obesity causes Alzheimer's, but what it does show is that being overweight is an additional burden on brain health and it may exacerbate the disease."

She added, "The diseases that cause dementia such as Alzheimer's and vascular dementia lurk in the background for many years, so waiting until your 60s to lose weight is too late. We need to start thinking about brain health and preventing these diseases much earlier.

Educating children and adolescents about the burden being overweight has on multi-morbidities including neurodegenerative diseases is vital."

Researchers from the University of Sheffield and the University of Eastern Finland examined MRI brain scans from 47 patients clinically diagnosed with mild Alzheimer's disease dementia, 68 patients with mild cognitive impairment, and 57 cognitively healthy individuals.

The novel study used three complementary, computational techniques to look at the anatomy of the brain, blood flow and also the fibres of the brain. The international team compared multiple brain images and measured differences in local concentrations of brain tissues to assess grey matter volume – which degenerates during the onset of Alzheimers – white matter integrity, cerebral blood flow and obesity.

In mild dementia patients, a positive association was found between obesity and grey matter volume around the right temporoparietal junction. This suggests obesity might contribute toward neural vulnerability in cognitively healthy individuals and those with mild cognitive impairment. The study also found that maintaining a healthy weight in mild Alzheimer's disease dementia could help preserve brain structure in the presence of age and disease-related weight loss.

Joint author of the study, Matteo De Marco from the University of Sheffield's Neuroscience Institute, said, "Weight-loss is commonly one of the first symptoms in the early stages of Alzheimer's disease as people forget to eat or begin to snack on easy-to-grab foods like biscuits or crisps, in place of more nutritional meals.

"We found that maintaining a healthy weight could help preserve brain structure in people who are already experiencing mild Alzheimer's disease dementia. Unlike other diseases such as cardiovascular disease or diabetes, people don't often think about the importance of nutrition in relation to neurological conditions, but these findings show it can help to preserve brain structure."

The study was conducted in collaboration with the University of Eastern Finland. Professor Hilkka Soininen, joint author of the paper, said, "The results emphasise different perspectives on lifestyle and nutrition in the prevention and treatment of Alzheimer's disease. It's important to avoid obesity for brain health, but for patients with Alzheimer's disease, it is essential to take care of proper nutrition and maintain a healthy weight."