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MIDDLE PHASE

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XENOTRANSPLANTATION— THE FUTURE OF HUMAN ORGANS?

Renee Au 11E



Let's begin with a case that took place in 1984.

On October 14th, Stephanie Fae Beauclair was born — and expected to die. The left ventricle of her heart was extremely undeveloped, a congenital heart defect known as hypoplastic left heart syndrome. At that time, there was nothing doctors could do. However, Dr Leonard Bailey, from Loma Linda University Medical Center, had a different idea. He approached the infant with a baboon's heart and attempted to perform an organ transplant on the infant on October 26th.

She survived for 21 days, which was 2 weeks longer than earlier cases of transplantation using baboon hearts in humans.

Baby Fae's unique surgery is just one example of xenotransplantation since the breakthrough of human transplants in the 1950s. The success of human transplantation has saved the lives of millions ever since. However, its increasing demand has also become a burden. According to the American Transplant Foundation, approximately 114,000 people are on the waiting list for an organ transplant. However, 20 people die with their needs unfulfilled, and a new name is registered to the waiting list every 10 minutes. Hence, scientists and doctors are exploring how xenotransplantation may overcome the crisis of organ shortages.

What is Xenotransplantation?

Xenotransplantation is the utilisation of animal cells, tissues or organs in the human body; xenografts are the organs, tissues or cells transplanted into the human body. Xenotransplantation brings the advantage of having an unlimited supply of organs that can be bred economically by alternative animals, such as pigs. On the contrary, most human organs can only be obtained after death or under certain preliminary conditions which limits the availability of organs. In the future, scientists anticipate xenotransplantation to be a cure for various diseases requiring organ transplants involving the liver, lungs, heart, kidneys and pancreas.

Xenotransplantation might offer treatment to many other medical conditions as well. For example, Type 1 diabetes can be cured by transplanting pig islet cells into humans. These clusters of cells are located in the pancreas and produce the hormone insulin to control blood glucose levels. Pigs are an ideal donor since 98% of pig insulin is identical to that of humans' and as human islet transplantation is not widely available to most patients, xenotransplantation may offer treatment to more people.

Parkinson's disease, caused by a lack of dopamine from the loss of nerve cells in the brain's substantia nigra, may also be cured. Pig cells creating dopamine may be introduced into the human body for this purpose.

Trauma patients or those who suffer chronic diseases such as sickle cell anaemia may possibly benefit from transfusions using pig's blood as well. Patients with sickle cell anaemia are known to produce antibodies which reject human blood cells due to multiple blood transfusions previously, which makes xenotransplantation a possible remedy.

Furthermore, infants with congenital heart defects can temporarily rely on pig hearts until a suitable human donor is available. Unlike adults, artificial hearts have not been developed for the use of infants and being on the waiting list for over 3 months also risks a mortality rate of over 50% for newborns. Hence, xenotransplantation increases the infant's chance of survival.

Primate... or pig?

Deciding on an appropriate animal has been debated amongst many experts.

Non-human primates are often seen as the best match. Humans and primates share many anatomical and physiological similarities, as well as immunity to some human diseases. However, these similarities also make them the most controversial species amongst the public and are difficult to breed in large numbers to satisfy organ demand. More importantly, they are likely to transmit diseases and infections to humans, being so closely related to humans. For example, HIV was discovered to be derived from chimpanzees and is one example of a disease that could infect humans upon transplantation. These viruses that originate from animals are known as zoonosis.

In contrast, pigs have a short gestation time of 4 months and large litters which enable pig farming to be delivered at a mass scale economically. They also provoke less ethical controversy due to their prevalence in the food industry and have organs very similar to humans. Pigs have also been used medically for purposes such as pig valves for heart transplants.

However, pigs are far from perfect either.

More harm than good?

Scientists today experiment with xenotransplantation using pig organs in primate donors. But despite rigorous research, scientists still struggle with it for various reasons. Most attempts at xenotransplantation in laboratories do not last for long enough in primates to be reliable for humans' long term dependence. One reason for this is organ rejection.

In xenotransplantation, organ rejection occurs when antibodies in the human blood bind to the antigens of pig endothelial cells from the xenograft. These antigens contain a carbohydrate known as *galactose-alpha-1,3-galactose (also known as α -gal)*, which is present in all mammals— but not humans or primates. This allows antibodies to recognise the cell to be non-human. Therefore, the cell becomes destroyed and the organ undergoes hyperacute rejection— a form of organ rejection that only takes 5 minutes after transplantation.

Hyperacute rejection also occurs with human organs when using donors with different blood types to the recipient. Doctors can prevent this today by matching the recipient to the most suitable donor through blood tests and tissue typing, along with the use of immunosuppressant drugs. However, effective immunosuppressants are not strong enough for the human body during xenotransplantation.

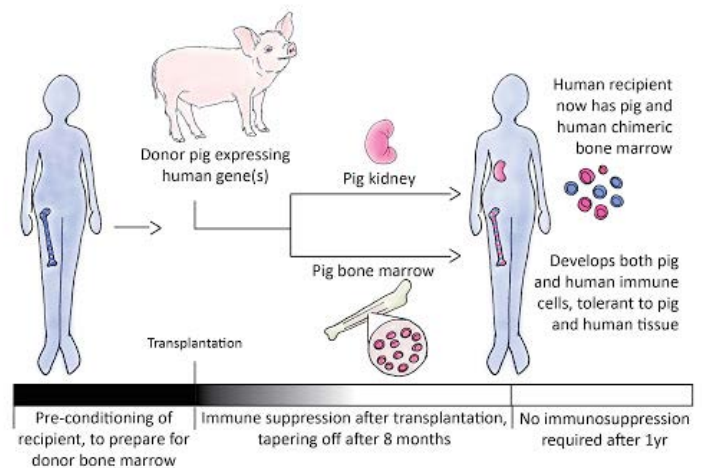


Scientists also fear that new, unfamiliar diseases may be created through xenotransplantation. For example, pig organs may carry or create new bacterial pathogens after transplantation, while viruses in their DNA may have serious consequences on humans despite being harmless in their natural hosts. The porcine endogenous retrovirus (PERV) is an example of a virus that is found in the DNA of all pigs. Although there have not been cases of infection due to PERV, it nevertheless poses a risk to humans as scientists fear that this could cause the rise of a new epidemic if infection occurs. Furthermore, infections from transplantation are especially life-threatening due to the use of immunosuppressants.

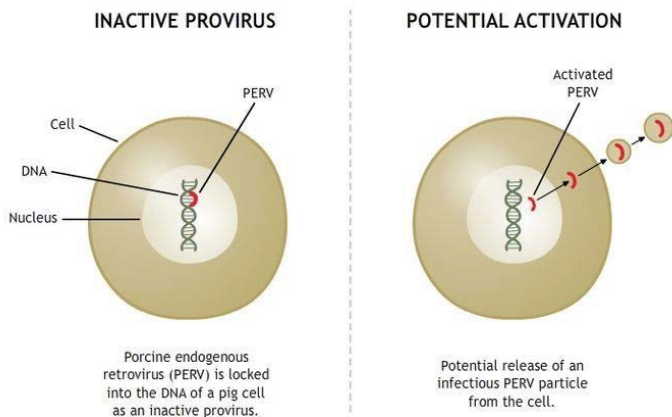
Ethical considerations are also raised by animal activists. Some people question whether we have the right to use pigs as organ donors or expose them to multiple surgical operations, as this could have a detrimental effect on their welfare. Certain cultures or religions, such as Islam and Judaism, also view pigs as unclean and may reject pig organs. Most people are also likely to feel uncomfortable with the prospect of a pig's organ inside of them after receiving a transplant.

As a result, the pig's genes would express human proteins—therefore making it harder for the human immune system to recognise the organ being porcine when human antibodies bind to the organ's antigens. For example, scientists may modify pig genomes by adding human thrombomodulin into its genes. It forms a coating over the pig's antigens and allows it to appear more 'human'.

Furthermore, the removal of the α -gal sugar molecules found on pig antigens has also led to improvements in pig to primate xenotransplantation trials. Some scientists also suggest that pig bone marrow cells can be transplanted into the human body before an organ transplantation. This could mean that immune cells released from the bone marrow would not recognise the pig organ to be foreign. Thus, patients become tolerant and become less dependant on immunosuppressants after a period of time.



Nevertheless, the success of xenotransplantation remains a long journey to becoming a reality. In the future, it may bring solutions to various forms of disease such as diabetes, Parkinson's or other desperate conditions requiring organ transplants. However, this will require scientists and doctors to overcome the difficulties of organ rejection, closely study possibilities of porcine infection and discuss the ethical implications of xenotransplantation. Perhaps one day, the relationship between humans and pigs will become much closer than we think.



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The Future

Although the risks of xenotransplantation are well-known and its ethics remain controversial, scientists are keen to find solutions to organ rejection. One method that scientists have pursued is by breeding transgenic pigs. These pigs are genetically modified using CRISPR technology. In theory, scientists can alter fertilised pig eggs by inserting DNA that closely resemble the sequence of human genes.

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BLOOD TYPES

Bonnie Tsui 11E

Blood may appear to be the same, but when looked closely under a microscope, it can be very different. Blood types are used for blood transfusions - a common medical process which helps replace the blood lost through surgeries and injuries in patients. The discovery of blood types has aided the advancement of medical discoveries and have become vital in life-saving procedures worldwide. But little is known about blood types to the general public. How are blood types defined and why are they so important?

Who discovered blood types?

In the early 1900s, doctors gave blood transfusions to patients who lost a lot of blood. They realized that the medical condition of the person who received the blood sometimes became worse instead of improving, but they didn't understand why. This was because the doctors at the time didn't know about the different blood types and assumed that everyone had the same blood. As a result, they conducted experiments to find out what was going on.

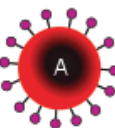
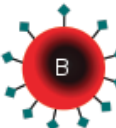
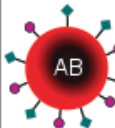
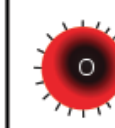






In one experiment, Austrian American immunologist and pathologist Karl Landsteiner mixed blood from numerous people in a petri dish. He discovered that when certain combinations of blood were mixed together, red blood cells clumped together (also known as agglutination), while other combinations remained as a liquid after mixture. From this experiment, he concluded that agglutination occurred as the host produced antibodies against donated blood from another blood type.

In 1901, Karl Landsteiner published his discovery of the classification of the different known blood types as we currently know: A, B, AB and O. Karl Landsteiner was also awarded the 1930 Nobel Prize for Physiology or Medicine due to his fascinating findings regarding the human blood types.

How do you differentiate between blood types?

Blood types can be differentiated by identifying the type of complex protein on the surface of the cell membrane - antigens. These antigens allow the immune system to recognise your body's own cells. The presence of the antigens means that the white blood cells do not attack your own red blood cells. Red blood cells in blood type A have A antigens, whereas B antigens are present in blood type B. People with blood type AB have both A and B antigens while neither A nor B antigens are present in blood type O.

The antigens you have are determined by alleles inherited from your parents. Since we inherit one copy of each gene from each parent, everyone has two alleles which determine their blood type. When the blood types of each parent are different, one allele overrides the other depending on their relative dominance. A and B alleles are dominant while the O allele is recessive.

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	 A antigen	 B antigen	 A and B antigens	None

Another significant antigen in the blood is called the Rh D antigen, also known as the Rhesus factor. People with the Rh D antigen have positive blood while people without the Rh D antigen have negative blood. The Rhesus factor can cause severe problems in pregnancy. If a mother with Rh-negative blood carries a child with Rh-positive blood, the mother's body may produce antibodies that attack the fetus, possibly leading to a fatal condition to the fetus known as the hemolytic disease of the newborn.

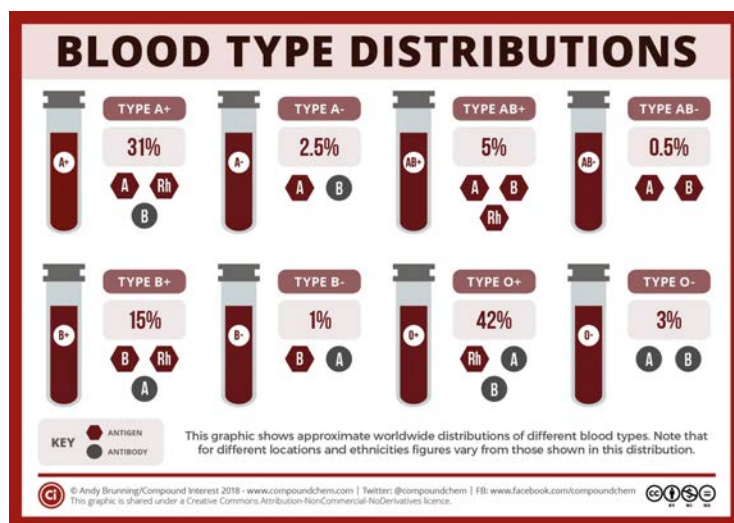
People with O- blood can donate their blood to almost anyone and are known as universal donors. This is because O- blood does not have neither A nor B antigens and there is no Rh D antigen on their red blood cells. This is advantageous as type O- blood is safe for almost everyone to receive. However, having negative blood types is very rare, and so it is only used in emergency situations when there is insufficient time to test the patient's blood type. People with blood type AB+ can receive blood from almost anyone and are known as universal recipients.

The eight different blood types that are most commonly known are classified in the ABO and Rh D systems. However, there are actually 35 different blood type groups recognised by the International Society of Blood Transfusion. The other blood type groups such as Kell, Vel, MN and Lewis are less well known because the vast majority of people have these antigens, and writing them out would be unnecessary, as incompatibility is rare or does not cause life-threatening medical problems.

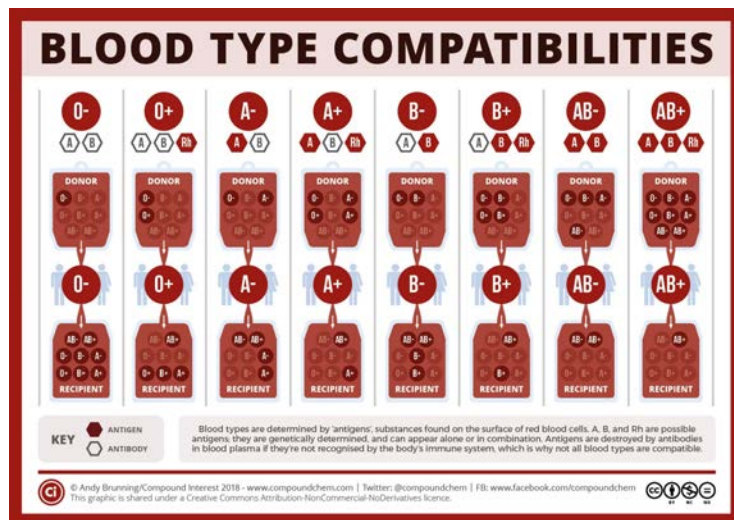
Blood Transfusions

Blood transfusions help to replace the blood lost through injuries or surgeries. In the process, blood is transferred through an IV into your vein. Blood transfusions are generally very safe, and any donated blood is checked in blood banks before it is sent to hospitals for use and is transferred to patients. Volunteer donors answer questions about their health before they donate blood, and testing is also conducted to check blood types or possible diseases within donated blood. Blood banks are constantly searching for donors because the blood can only be stored for a short period of time before they have to be thrown away.

For blood transfusions, blood types are vital to determine the patient's life or death. If a transfusion with an incorrect blood type is made, the foreign antigens are rejected by the antibodies within the patient's blood. This causes the transfused blood to clot, also known as agglutination. This could lead to hemolysis, which is when the destruction of red blood cells leads to the release of haemoglobin into the bloodstream. Serious consequences could lead to severe illnesses or even death.



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Rh Null Blood: The Golden Blood Type

Rh Null blood is the rarest blood globally, and is known as the “golden blood type” with only 43 reported cases and 9 active donors. People with Rh Null blood completely lack Rh antigens on the surface of their red blood cells. Rh Null blood was first discovered in 1961, in an Australian woman. Before then, doctors assumed that an embryo missing all Rh antigens would not survive.

Researchers found that Rh Null blood occurred due to two completely random mutations on pure chance. Although having Rh Null blood makes you extremely special, it can also be really dangerous to live with. If you have Rh Null blood type, receiving a transfusion of blood types with any Rh antigens will cause your body to reject the blood. Finding a blood donor for people with Rh Null blood can also be nearly impossible as only 43 individuals in the entire world have it. As a result, people with the golden blood type are encouraged to donate their own blood in case they ever need blood in the future. Additionally, Rh Null blood can be life-saving - within the field of medicine, it is seen as a universal blood donor as it contains no Rh antigens to be rejected, and can be used for those with rare blood types. However, it is only given to patients in extreme circumstances as it is extremely rare.

Conclusion

The development of knowledge about blood types with regards to the classification of blood types using their antigens has proved to be vital for medical processes such as blood transfusions. Despite the ever-growing amount of research we are discovering about blood

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SLEEP PARALYSIS: A PHANTOM MENACE?

Clarissa Ki 11F

A LIVING NIGHTMARE...

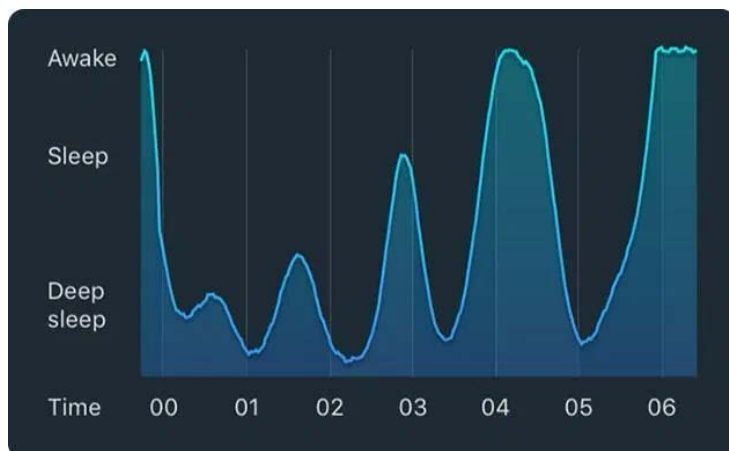
Imagine being jolted awake in the dead of the night-- your eyes are wide open, and you can't move a single muscle. In the corner of a room, a grotesque figure hovers, and you watch in silent terror as it advances on you, a phantom menace siphoning the breath from your lungs-- then the moment is gone, and you are safely tucked in your bed with only beads of cold sweat as evidence of your supernatural encounter.

Except there is nothing supernatural about this experience, as many people in history, and even now, believe. Nor is it a myth, or a scene from a horror film. This phenomenon is called sleep paralysis, a frightening but fairly harmless neurological condition.

WHAT IS SLEEP PARALYSIS?

To learn why sleep paralysis happens, it is important to understand what happens during a normal sleep cycle, especially during the REM stage.

A sleep cycle is a 90- to 120-minute period consisting of three NREM (non-REM) stages and a REM (rapid eye movement) stage.



For reference, NREM sleep refers to 'non-rapid eye movement'. A sleeper's eyes don't move rapidly as brain waves are relatively slow, which is also why one doesn't experience dreams under the three stages categorized as NREM. Stage 1 is light sleep, which refers to a transition from a wakeful to sleeping stage. In stage 2, brain waves slow with rapid bursts called 'sleep spindles' to prevent the brain from awakening. Stage 3 is deep sleep, and is restorative in allowing the brain and body to heal and grow. During this period, heart rate slows down, while body temperature and blood pressure decrease.

In contrast, REM sleep, also called the dreaming stage, is characterized by the sleeper's rapid eye movement (and hence, its name). The two significant parts of REM sleep include vivid dreaming, where the sleeper experiences sensory stimuli like visions and sounds due to active brain waves, and muscle paralysis--called REM atonia, which is believed to protect the sleeper from hurting themselves trying to move according to the things happening in the dream. The paralysis is induced by two neurotransmitters, gamma-aminobutyric acid (GABA) and glycine. GABA and glycine are inhibitory neurotransmitters which reduce excitability of neurons. During REM sleep, increase in both GABA and glycine work together to switch off motoneuron activity. Motoneurons transmit messages that control muscle movement. With their activity switched off, muscle paralysis is triggered. Muscle movement returns only after the effects of both GABA and glycine on motoneurons are diminished.

In normal REM sleep, its two significant aspects happen while the brain is unconscious. However, during sleep paralysis, the REM and wakeful stages overlap, causing the person to be paralysed, and sometimes hallucinate (in place of dreaming), while the brain is fully conscious. REM usually happens at the end of each sleep cycle, after the brain has gone through all three NREM stages (not necessarily in chronological order) which is the case when sleep paralysis occurs while waking up. When a person experiences sleep paralysis while falling asleep, they skip all of the NREM stages and jump to REM straight away.

CAUSES AND ASSOCIATIONS

The truth is, many things about sleep paralysis remain a mystery to scientists, and this includes its causes. However, it is one of the symptoms of a neurological sleep disorder called narcolepsy that disrupts the brain's control on sleep-wake cycles, causing people to have sudden sleep attacks throughout the day and night-time sleep being disrupted by hallucinations and sleep paralysis. For those suffering from narcolepsy, their hypothalamus loses cells that produce a chemical called hypocretin, which is in charge of activating the brainstem to send out signals to wake them up. This means they are often in a state where REM sleep and the wakeful stage are overlapped. Sleep paralysis is, in certain ways, similar to narcolepsy, sharing similar causes with respect to the overlapping stages in the sleep cycle.

Another significant cause is stress. Most kinds of stress, including life stress, traumatic events like war, bereavement and assault, were associated with increased prevalence of sleep paralysis, while the victims of child sexual abuse tended to have greater frequency and intensity of hallucinating about intruders and incubuses.

There is also a significant relationship between poor general mental health and sleep paralysis. One study from the University of Wisconsin found that those with more severe symptoms of depression tended to have sleep paralysis, while anxiety was strongly associated with hallucinations. For example, the study by Munezama and colleagues (2011) found that 11.9% of people with poor mental health suffer from sleep paralysis, compared with only 5.3% among those with good mental health. This means that those with poor mental health are 1.54 times more likely to have sleep paralysis.

Lastly, there is a possible hereditary component in sleep paralysis. In a study conducted in Hong Kong, one-fifth of the subjects who had experienced sleep paralysis had family members with history of this condition. A twin study showed that sleep paralysis may be moderately influenced by genetics, with 53% of the cases being related to genes.

THE INFLUENCE OF BELIEFS AND CULTURE

It is not uncommon that when humans encounter a phenomenon they don't understand, they attribute it to the paranormal. This has been the case for sleep paralysis over the course of history, and as such, many cultural interpretations have been developed. For example, African-Americans believe that the episode is a witch attack, whereas the Chinese think they are being visited by ghosts that bring bad fortune, called "Ghost Oppressions". These collective beliefs sometimes spiral into folklore and mythology, like the Scandinavian 'mare'-- a horse summoned by a sorceress to trample on bodies and suffocate them-- or the Brazilian 'Pisadeira'-- an ugly old woman with long fingernails who prepares to victimize sleepers while lurking on their roofs.



Recent researchers even argue that the pre-existing cultural or religious beliefs contribute to the different interpretations of sleep paralysis in the first place. One study compared the explanations of the causes of sleep paralysis among the Danish and the Egyptians who had such experiences. Denmark and Egypt differ in religiosity, with Denmark being mostly secular and Egypt having a strong influence of Islamic faith. When asked about the causes of their sleep paralysis, most Danish people believed the phenomenon to be caused by biological factors, whilst the Egyptians attributed it to supernatural causes. The specific belief systems may prime people to interpret certain experiences in different ways, causing them to have different reactions.

In turn, cultural interpretations of sleep paralysis may influence the recurrence, intensity and the reaction towards the experience. The salience hypothesis -- or how important something is perceived to be--states that the stronger the belief that sleep paralysis was a supernatural experience, the more afraid the person is of the experience, further activating the amygdala--the fear system--of the brain, conditioning the brain to be even more sensitive to future symptoms of sleep paralysis.

CONCLUSION

Sleep paralysis, though a fascinating and sometimes horrifying phenomenon, is still quite under-researched to this day. Albeit being mostly harmless on its own, understanding more about this strange condition may help to identify other medical problems and uncover the relationships between culture, belief and human psychology. Besides, most people would presumably prefer to know they did not, in fact, encounter a demon in their sleep.

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STEM CELLS

Grace Zheng 11F



Packed: Your Friday Night Steak, Nutrients Aside

With the gradual popularization of events like 'Meatless Monday' in schools and communities alike, rises once again the age-old question of: 'Should I eat meat or not?' Whilst many believe meat is a key staple of any diet, others avoid it entirely. Whether it is for health or ethical reasons, is vegetarianism in the 21st century truly the right way to go?



'Naturally' Carnivorous?

Firstly, are humans designed to eat meat? At a glance, it might not be obvious that humans are meat eaters. Anatomically, our small 'canine' teeth and soft fingernails are incomparable to the strong, large claws of natural carnivores. While carnivores' jaws have relatively more centralized up and down movement that aid in tearing flesh, our jaws are more similar to that of herbivores, moving in all four directions. Most of the nutrients from the food we eat is absorbed in the small intestine and predators have short intestinal tracts which allows meat to

quickly pass through, whilst human intestines are longer, designed to take in nutrients from fibrous food (plant matter) as well. Our stomach acid is also much weaker in comparison and leaves us vulnerable to the many types of pathogens found in raw meat. Pathogens are organisms that can cause diseases, such as viruses and bacteria. Simply put, the human digestive system is most similar to our closest relatives - chimpanzees, whose diets are largely based in fruits, nuts and leaves and are only occasionally supplemented through pieces of animal matter.

Judging by our biological factors, it would appear we'd thrive off a plant-based diet - and our extinct ancestors, the other members of our family hominidae did. There are a lot of theories as to why meat was gradually integrated into their diet. One proposal was the Expensive Tissue Hypothesis, which argued that the human brain was very 'expensive' because it requires over 22 times the amount of metabolic energy needed by the same amount of muscle tissue. Leslie Aiello and Peter Wheeler proposed in 1995 that in order to sustain our brain, our guts (which also used a lot of metabolic energy) became shorter. However, this meant our food had to be more nutrient-rich and easier to digest, hence why we began eating and even more importantly, cooking our meat. Scientists hypothesise that the change in the length of our guts combined with our newly adapted diets is why we are able to have much larger brains compared to our primate counterparts. However, research done within a sample of 100 mammals at the University of Zurich shows that there is no negative correlation between brain size and any other 'expensive organ', thus refuting the hypothesis.

Another theory believes that a climate shift over 2.5 million years ago caused the earth to become much drier and hotter. Previously, hominins consistently fed on fruit and vegetation, but the change in temperature caused forests to diminish into grasslands and plains. Evolutionary pressure led some hominins to seek other alternatives for energy. Grasslands supported many grazing herbivores, and it is speculated that they began by scavenging meat left from carcasses by other carnivores. Our ancestors probably also fed regularly on nuts and seeds, which are poor in fibre but rich in fats. This might have prompted our caecum (where fibres are digested) to shorten and instead, our small intestines to become longer in order to better digest the lipids in our diet. The original tools used for grinding and pounding nuts would have also been easily adapted to fit the needs of the earliest hunter-gatherers. Though many theories have been provided, it is still uncertain why we began eating meat; however, it is certain that our basic need for survival has kept it through the evolutionary chain today.

Meat in the Modern World

Initially, our ancestors began eating meat for survival - now, it's the foundation of many diets across the world. Meat can be separated into red meat (does not turn white when cooked), white meat (light-colored, normally poultry) and processed meat (meat that has been preserved/contains additives). Made up of 'meat' ourselves, our muscle tissue is largely composed of water and protein. Within the body, protein is crucial to the repair of body tissue. As a macronutrient, it is made of smaller compounds called amino acids. Unfortunately, our body is incapable of producing the 9 essential amino acids we need which means they must be obtained through our food. Inside the body, their functions range from muscle regeneration and maintaining metabolism to producing neurotransmitters that aid in regulating immune response. Another component commonly associated with eating meat is iron, a mineral which aids in blood regulation and oxygen transportation. However, it has been found that some green foods such as broccoli and spinach can act as good substitutions as they contain high amounts of iron as well.

Another important component of meat are the natural fats and vitamins found within it. Many cold-water fishes are rich in Omega-3 fatty acids which can promote brain growth and development in infants, as well as combat autoimmune diseases. It also helps maintain healthy skin, hair and eyes. Just like vegetables, meat contains vitamins. Vitamin B12 for example is not only a crucial component in the maintenance of healthy blood and nerve cells, but aids in the production of DNA as well. Although other components such as protein and iron can be found in vegetables as well, natural sources of Vitamin B12 can only be found in animal products.

But as Aesop once said, it is possible to have too much of a good thing. The excess protein absorbed by your body is stored as fat and a high-protein diet will likely lead to weight gain over time. Although there is still limited evidence associating meat-eating with cancer, the World Health Organization have found links between eating red meat and pancreatic, prostate and colorectal cancer. In an analysis of 10 studies scientists estimated that your chances of colorectal cancer can increase up to 18% with every 50g of processed meat that you consume on a day to day basis. Even though the amount of meat that is considered 'safe' to eat will vary with every individual, high-intake of red or processed meat does increase your chances of developing coronary diseases.



Aerial view of a hog farm in North Carolina - the pink area represents a lagoon of hog excrement.²

However, the potential harms of meat aren't just limited to the human body - it affects our surrounding environment as well. According to policy institute Chatham House, a major driver of climate change is the consumption of meat. The emission associated with the meat industry is more than the emissions produced from powering all the world's road vehicles, trains, ships and aeroplanes combined" and "is considerably more than the emissions produced by the world's largest national economy."

Not only does the livestock sector directly contribute to 14.5% of the global total emission of greenhouse gas, there are even more indirect emissions from activities such as the transport of meat products. In just the U.S. alone, more than 500 million tons of manure are produced per year on factory farms. In areas that lack sewage processing plants, excrement is stored in lagoons but occasional 'run-offs' can enter our waters, bringing dangerous bacteria into our rivers and lakes. Airborne chemicals may be emitted from these lagoons, and when inhaled they can cause inflammatory reactions or even neurochemical issues in our body. Some farms practice spraying liquid manure into the air, creating a 'mist' which is then inhaled by civilians in surrounding areas. The process of producing red meat or more specifically, beef, consumes a much larger quantity of resources than others. Ruminant creatures, cows also release 70 to 120kg of methane per year. As a whole, the livestock sector makes-up roughly 37% of human caused methane emissions. Land for cattle-ranching is often created through deforestation and the practice as a whole requires 28 times more land than producing pork or chicken. It's been estimated that up to 90% of land cleared in the Amazon since the 1970's was used for grazing livestock.

Moving to our seas, commercial fishing methods are destroying our corals at a similar speed. Bottom trawling in particular is notorious for taking up a lot of by-catch. The method involves dragging a large net with heavy weights across the ocean floor. While it captures large amounts of fish, it also traps other wildlife, such as turtles and large corals. Meanwhile, coastal fish farms pose just as serious of a threat. Antibiotics and parasites from fish farms may leak into the larger ocean, while schools of non-native fish

(alien/invasive-species) can enter the ecosystem, threatening the number of local populations. Research published in the journal Nature indicated that there must be a shift in global meat and dairy consumption if the rise in global temperature is to be kept below two degrees celsius come 2050.



A technician from Impossible Foods weighs burgers inside the test kitchen.³

Meat Eating for the Future

Fortunately, these aren't new issues and scientists have been working long and hard to find healthier, greener alternatives for those of us considering a meat-free diet and there is an increasing number of plant-based meat options available. Although the first vegetarian burger traces all the way back to 1980s Oregon, foods such as Beyond Beef and the Impossible Burger are also entering the public eye. These foods are designed to replicate the taste, image and smell of real meat - through scientific data and testing. Meat is made up from a variety of proteins, but Myoglobin in specific contains Heme - a molecule that carries iron. When a piece of meat is cooked, heme catalyses reactions that create volatile compounds, helping give the appearance and smell of meat. However, it was discovered that the roots of soy plants carried a form of protein known as leghemoglobin which also contained heme. The problem was that in order to extract 1kg of leghemoglobin, you would need as much as one acre of soybeans. Harvesting soy plants would also increase soil erosion and become very unsustainable in the long run.

Instead, a process of fermentation occurs where genetically modified yeast that contains the coding for leghemoglobin is fed and grown until scientists can extract heme containing leghemoglobin from it. However, heme is not the only factor that influences the final taste of meat - scientists use the gas chromatography spectrometry system to help identify all the individual flavors. Firstly, the meat is volatilized and each component is separated (gas chromatography) with each substance containing a different retention factor. The retention factor indicates how soluble a substance is - a smaller retention factor indicates a less soluble substance and vice versa. The neutral atoms are then ionised by the mass spectrometer. The sample is first vaporized and hit by an electron beam which converts the vapors into ions, meaning it has either lost or gained electron(s), affecting its charge. Then, the mass spectrometer helps quantify these components and identify the individual compounds that create this flavor. This deconstruction of meat helps scientists better grasp an understanding of the specific compounds responsible for the creation of different flavors. Although the US Food and Drug Administration acknowledges that the leghemoglobin produced from the yeast is 'generally recognized as safe', it is still a genetically modified food and some have argued that it cannot be considered 'vegan' as animal testing is a part of the substance's production process.

To conclude, there will always be a flood of ethical and scientific questions that surround our everyday proteins. With new discoveries occurring simultaneously around the world and both meat lovers and haters taking their stand, there is no doubt the 'meat debate' will continue - for many, many years to come.

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FARM FRESH TO LAB FRESH - CULTURED MEAT

Kimberley Ng 11N



BURGER PATTIES - HOW IT

Protein is essential to the human diet and we mostly obtain this from eating meat, but livestock production and meat cultivation make huge negative impacts to the environment. The industry is quickly using up resources and contributing to climate change, according to the United Nations, 14.5% of the world's greenhouse gas emissions are from livestock. The global demand for meat production will likely be more than can be provided, which is why scientists have started to experiment more with in-vitro meat in recent years.

The theory of in vitro meat was made known to us in the early 2000s by Jason Matheny, who also started the world's first non-profit in vitro meat research organisation called New Harvest. The practice of growing meat in the lab can be related to in-vitro fertilisation - where a sample of muscle tissue is injected into a cell culture, allowing the cells of the animal to grow without the animal being present.

The process starts by taking small samples of *myosatellite cells from a small section of a muscle cell from an animal. The cells are placed in a petri dish which contains nutrients such as amino acids and carbohydrates that create a similar environment to the insides of an animal which allow the cells to multiply as quickly as possible. All the cell differentiation takes place in a bioreactor which allows the cells to differentiate in their optimum environment while preventing any contact with bacteria.

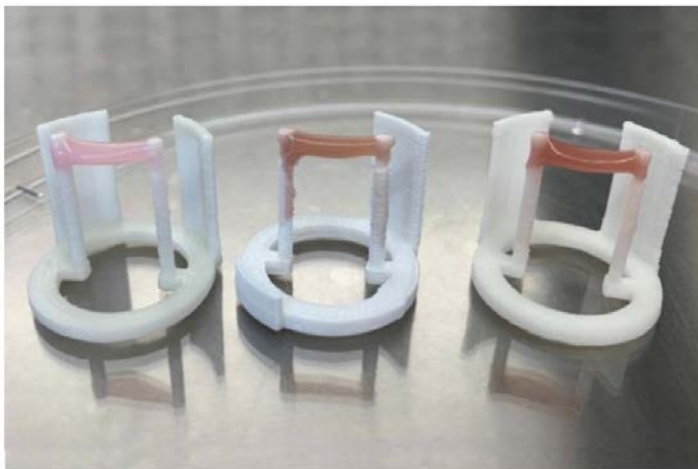
Once cells have multiplied they turn into *myoblasts, they are deprived of nutrients and other growth factors, which causes the cells to further differentiate into *myotubes - the myotubes are formed after myoblasts undergo the process of *myogenesis -. Myotubes are then placed in a medium which contains 99% water; this promotes the formation of muscle tissue, as the cells have a tendency to contract and fuse to become a small strand of tissue called *myofibres. By layering these fibres on top of each other, meat is formed. This meat can then be treated like regular meat, for example, it can be molded into any desired shape and seasoned with salt and pepper to make your own hamburger perhaps. According to Mosa Meat, "one tissue sample from a cow can produce enough muscle tissue to make 80,000 quarter pounders".



Bioreactor used in the lab to make cultured meat.

REFINING THE MEAT

Although the concept and process have been identified, there is still room for improvement. In order for customers to experience something almost identical to real meat; the taste and texture have to be as similar as possible, for customers to get over their hesitancy over the idea of lab grown meat. David Kaplan, professor of engineering at Tuft University said “we need to find the right conditions for cells to grow that replicate the formation of natural muscle”. A team of researchers at Tufts University have found that adding *myoglobin and *haemoglobin would make the cultured meat a better colour and better texture. Both myoglobin and haemoglobin are a type of haem-protein which means they both carry iron atoms which bring out the natural, meaty taste of beef. It is also responsible for the deep red color that people identify meat with, the more myoglobin in meat, the richer the red.



Skeletal muscles grown in myoglobin and haemoglobin to show color

Myoglobin plays an especially big role; it occurs naturally in the muscle and contains a single polypeptide chain. Polypeptides are components of protein, which help give the cultured meat a more authentic taste. Myoglobin is said to increase the rate of muscle fibres forming into strands and increase total yield, thus promoting *cell differentiation. This is because the myoglobin introduces more oxygen to the *mitochondria of the cell, providing more energy to help the cells differentiate.



Israel based Aleph Farms created the world's first strips of lab grown steak.

STEAK

Lab grown steak isn't as easy as making a burger, because of its tough texture and unique cutting. Creating a different scaffold for the muscle cells to grow on could change the texture of the product. As an attempt, Harvard scientists experimented with the type of scaffolding the meat would be grown on. They experimented with gelatin at different concentrations; gelatin is comprised of proteins and comes from collagen. According to Dr Parker (bioengineer at Harvard), “When meat rich in collagen - such as steak- is cooked, the heat melts the collagen fibers into softer gelatin, giving meat its succulent texture” .

To make the gelatin scaffold, gelatin was mixed into water and spun at high speed in a machine until layers of muscle fibres were interlinked to form a supported structure for cells to latch onto and differentiate. Other alternatives to gelatin scaffolding are also being trialed, for example the use of cellulose and starch are being experimented with as they would cost less to produce as well.



Sheets of gelatin fibres for muscle cells to grow on

OTHER TYPES OF MEAT

Research on cell based meat has come a long way, and has expanded far from just beef and hamburger patties. Although meats are similar in the fact that they all contain a large percentage of water, carbohydrates, fat, minerals and vitamins; their textures and tastes are different, therefore the raw materials needed will vary to create different products.

FISH

For example fish has a flaky and soft texture, compared to beef which is more chewy and firm. Growing these fish cells requires muscle and fat, rather than just muscle cells. The fat makes a huge impact on the fishiness in the meat as it is responsible for the omega-3 fatty acids present in fish and the resulting creamy, oily taste and the fall apart texture. Other than the addition of fat, the process of growing fish is the same as growing beef. The muscle and fat cells are drawn from fish and placed in a nutrient filled medium until layers of fibres are produced and 'fish' is created. Blue Nalu is the leading company in creating cellular-based aquaculture. They have already successfully produced whole cuttings of yellowtail, amberjack with just a small sample of muscle and fat from a fish. They have proven that their product can be cooked and treated just like you would a normal fish.



Blue Nalu's cell based amberjack, deep fried for a fish and chips dish

Cultured seafood should in theory be easier than culturing mammalian cells as fish live underwater and therefore can tolerate lower levels of oxygen and temperatures. The diffusing of oxygen to tissue can sometimes get complicated when developing 3D shapes, because seafood cells are already adapted to lesser amounts of oxygen, the process becomes easier.

CHICKEN

Chicken has also been widely tested with and is one of the few other types of meats where a successful product has been made for consumers to have a look at. Just Inc., a San Francisco based company has created a prototype of lab grown chicken nuggets which took \$50 US to make. They source these cells from feathers of chickens and take tissue samples from those chickens, which undergo the exact same process that cultured beef and fish go through. Making these chicken nuggets took approximately 2 weeks.



Just Incs. Fried chicken nuggets with vegan mayonnaise

CONCLUSION

Consumers' needs are rapidly changing as they are becoming more aware of how small things, such as farming, are affecting the planet. Manufacturers have to keep up with this and introduce new concepts to the market to accommodate buyers' needs and to keep up with the fast pace the world is moving at. With the basic concept already nailed down, more research needs to be done into the specific percentages of nutrients inside the mediums so that the cells can grow faster and to produce a higher yield which will hopefully be available to consumers by 2022.

In the future, it will be possible to make any type of meat, from beef to seafood, out of animal cells. As Winston Churchill said "We shall escape the absurdity of growing a whole chicken in order to eat the breast or wing, by growing these parts separately under a suitable medium". All meat and no slaughter will be our future. With more experimenting and researching, the market will continue to expand, who knows what will be on our shelves next?

GLOSSARY

- Myosatellite cells: Stem cells within an animal that create new muscle cells when the animal is injured
- Myotubes: A type of cell which will develop into a muscle fibre.
- Myofibres: Basic unit of a muscle cell
- Myoglobin: Iron and Oxygen binding protein found in muscle tissues.

- Myoblasts: An undifferentiated cell capable of becoming a muscle cell.
- Haemoglobin: A protein found in red blood cells that carries oxygen.
- Cell Differentiation: The process where a cell becomes a more specialised cell.
- Mitochondria: Powerhouse of a cell, where energy is stored.
- Myogenesis: Formation of muscular tissue.

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TURNING LEAD INTO GOLD

Yu Hang Hui 11R

Alchemy is perceived by many as a foolish and meaningless study related to magic, immortality, and spirituality. One recurring idea amongst alchemists was 'transmuting' lead into gold. They believed gold was spiritually perfect, and that lead - a lesser form of gold - could potentially become gold.

As we all know, these attempts made by alchemists in the past were unsuccessful. But what about efforts by modern scientists to turn lead into gold?

What does 'transmutation' mean?

The word 'transmutation' was traditionally used in alchemy; the Latin word 'transmutare' means 'to change from one condition to another'.

In physics, transmutation is the change of a chemical element or isotope to another, either occurring naturally through radioactive decay or by artificial means.

Radioactive Decay

To understand how lead can change into gold, radioactive decay must first be discussed. Radioactive elements can change into other elements naturally: the process of radioactive decay takes place when an atomic nuclei has an unstable number of protons and neutrons in the nucleus; it lacks the sufficient binding energy needed for the nucleus to remain together, so the nucleus emits ionizing particles and energy to stabilize the isotope. These are therefore radioactive.

In pop culture, radioactive substances are often portrayed as green poisonous substances that reduce society to abandoned ruins. However, we are also exposed to radiation on a daily basis through the sun, telephones and much more. So what does being radioactive actually mean?

There are three types of radioactive decay - alpha decay, beta decay, and gamma radiation. The type and strength of radiation, as well as the length of exposure, determines how dangerous the radiation is.



In alpha decay, the nucleus of the atom loses two protons and two electrons, otherwise called an alpha particle. Thin surfaces like paper can stop alpha particles and they are only dangerous if ingested.

In beta decay, an electron is emitted from the nucleus (the beta particle) when a neutron turns into a proton and electron. Beta particles are much smaller than alpha particles; they can be blocked by most solid objects but they can penetrate the skin and cause some harm to tissue. It is also much more dangerous if ingested.

Gamma radiation accompanies alpha and beta decay, emitting high-energy photons (light particles of electromagnetic energy with no mass) to reduce the energy in the nucleus. Gamma rays have no mass and are much more penetrating; a few centimeters of lead or even a few meters of concrete is required to block them. Upon exposure, gamma rays will pass through the entire body and damage skin, bones, and tissue indiscriminately.

Nuclear Transmutation

The number of protons in an atom is responsible for which element it is. Although the number of neutrons or electrons can change to form different isotopes or ions, each element has a certain number of protons. No chemical reactions can change the element of the atom,

Sometimes, radioactive decay changes the nucleus of the atom and causes unstable elements to change their number of protons, thus becoming a new element. This was first observed by Frederick Soddy and Ernest Rutherford in 1903 when they witnessed thorium changing into radium. It is now known that thorium is an unstable, radioactive element with 90 protons. By undergoing alpha decay and losing two protons, it turns into radium, which has 88 protons.

Upon witnessing this, Soddy had cried “Rutherford, this is transmutation!” Rutherford had notably replied. “For Christ’s sake, Soddy, don’t call it transmutation. They’ll have our heads off as alchemists!”

Arguably, however, it was transmutation.

Artificial transmutation

Since then, scientists have experimented with artificially changing stable isotopes of elements to other elements.

Because the strong nuclear force holding the nuclei together is incredibly strong (as the name implies), a lot of physical force is needed to change the nucleus of an atom. For this reason, particle accelerators are often used for artificial transmutation. Particle accelerators speed up subatomic particles to nearly the speed of light using either electric or electromagnetic fields. When these sped-up particles collide with atoms, it can force alpha decay and beta decay.

Artificial transmutation was first done by Patrick Blackett in 1921-1924 when he bombarded a stable nitrogen isotope with alpha particles and successfully created a stable oxygen isotope. Nowadays, the transmutation of elements is an important part of chemistry and physics.

Transmutation into Gold

Gold has 79 protons and lead has 82 protons. Theoretically, gold would form if lead atoms lost 3 protons.

In 1980, Glenn Seaborg and other scientists at the Lawrence Berkeley National Laboratory made a small amount of gold from bismuth. Using a particle accelerator, they bombarded carbon and neon nuclei onto bismuth foil and produced a few thousand atoms of 9 isotopes of gold.

While this may sound like a great accomplishment, this method of producing gold is not sustainable or recommended. This is because gold-197 is the only isotope of gold that occurs naturally and the only stable isotope. All other isotopes of gold are unstable and radioactive, with half-lives ranging from 2.7 days to 186 days. The gold atoms produced by the scientists were not enough to be seen with a naked eye, and the majority of gold atoms produced decayed within months, turning into other elements. In other words, the gold produced couldn’t be used.

Equally important is the extraordinary cost. Glenn Seaborg also said, “It would cost more than one quadrillion dollars per ounce to produce gold by this experiment.” At that time, an ounce of gold cost \$560. David J. Morrissey, one of the scientists who worked on the experiment, summarised: “The problem is the rate of production is very, very small and the energy, money, etcetera expended will always far exceed the output of gold atoms.”

Many other transmutation experiments have been conducted. Another example is creating bombarding stable platinum-198 with a neutron, creating unstable platinum-199 which turns into unstable gold-199 through beta decay. Similarly, the cost of platinum used would be more expensive than the unstable gold produced.



A dream come true?

Alchemists from medieval times would be delighted to know that their much sought-after transmutation is possible through science and technology.

However, it is clear that transmuting lead to gold in usable quantities using modern technology is not wise.

Regardless of this, it is fascinating how something that was once deemed impossible and crazy in the past could become common and accepted. As Ernest Rutherford once said, "It is impossible until you understand it, and then it becomes trivial."

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IS THE PALEO DIET THE OPTIMAL DIET FOR HUMANS?

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Introduction

The paleolithic diet, also known as the 'cavemen' diet prevalently comprises of meat, fish, shellfish, nuts, eggs, vegetables, roots, and berries. Grains, dairy, legumes, sugar, and salt are not allowed to be consumed. This diet surfaced around 10000 years ago and the theory that humans are genetically inclined to eat along these lines emerged in 1998 from the book, "The Paleolithic Prescription," written by Dr. S. Boyd Eaton. Nonetheless, as good as this sounds, a few scientists are having difficulties in accepting this. Yes, our DNAs were established in pre-agrarian societies, but anthropologists contend that our paleolithic ancestors most likely ate whatever they could find.

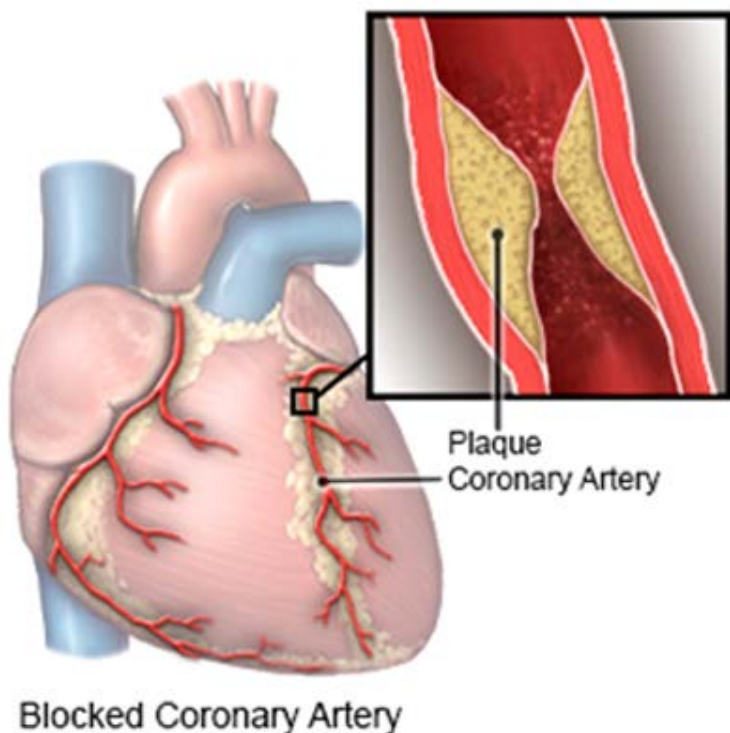
Did Prehistoric People Really Live on the Paleo Diet?

In reality, cavemen most likely had a substantially more broad, varied diet that changed with their environment than our understanding of the 'paleo diet.' For instance, groups settled in the desert wouldn't have had access to foods such as fish or meat, whilst groups in cold areas may have had scarce measures of vegetables and fruits.

Ultimately, we may never know if our ancestors ate like this because humans, as well as food, have changed through evolution. Our bodies have gotten relatively smaller, our jaws smaller as well as an increased diversification of physical characteristics, which may have changed our diet patterns. Besides, we live in a society where it is impossible to eat exactly what our ancestors ate. For example, livestock consisted of higher omega 3 fats in the past, but due to differences in how we raise cattle today, meat is higher in saturated fat, which is unhealthy.

Sugars and additives are a detriment to our health. Since the paleo diet impedes the consumption of sugar, salted, or processed foods, low sugar levels are regulated in the blood. Therefore, a condition of slow metabolism of sugar can be prevented by consuming a paleo diet. In addition, the lack of additives in the diet can fight diseases, prevent the increase in calories, and prevent adverse side effects such as impaired growth and development.

Eating a paleolithic diet reduces your weight, the number of triglycerides, and systolic blood pressure - the force which occurs in your heart when blood is pushed through arteries. A case study from the European Journal of Clinical Nutrition in 2009: "Metabolic and physiologic improvements from consuming a paleolithic diet" showed a significant decrease in triglycerides (by 35%) and LDL cholesterol (by 22%) in the body after consuming a paleo diet for ten days (Frassetto et al., 2020). Although this showed some commending effects, further studies must be warranted as correlation does not indicate causation. 120mmHg or below is considered as normal systolic pressure. Having a pressure too high (hypertension) or pressure too low (hypotension) is neither desirable. Similarly, LDL (low-density lipoproteins) is a 'bad' type of cholesterol that can build up in arteries over time, forming plaques that restrict blood flow. Two factors determine blood pressure; how much blood is pumped by the heart and the amount of resistance to the flow of blood. The buildup of plaques not only causes cardiovascular diseases, but the effect is more widespread than you think. For instance, the accumulation of plaques in vessels results in less blood reaching the brain causing mental impairment, such as dementia.



However, as desirable as this diet may seem, consuming just the paleo diet itself eliminates whole food groups, which can diminish our body. By consuming a paleo diet, we miss out on some essential fibers, vitamins, minerals, and calcium that comes from grains and dairy foods. Seafood, which is rich in calcium, could be considered as a substitute, but you would need to consume large amounts to meet your body's daily needs. Some symptoms of calcium deficiency include hypocalcemia (problems relating to the nervous system), muscle cramps, and soft, deformed bones. Furthermore, if you are not exposed to the sun or adhere firmly to this diet, you may be at risk for vitamin D deficiency. This is often associated with osteoporosis, the deformation of bones.



Conclusion

Everyone has a perspective on the 'optimal' human diet, and years of research hasn't added any clarity. But, one thing that we can clarify is that there is no such thing as one 'ideal' diet. There are contrasts in our DNA, behavior, environment and even our gut contents. Even the concentration of the gut microbiome can influence our abilities to absorb nutrients! In conclusion, there are essential differences in each and everyone one of us that determines our 'optimal' diet.

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