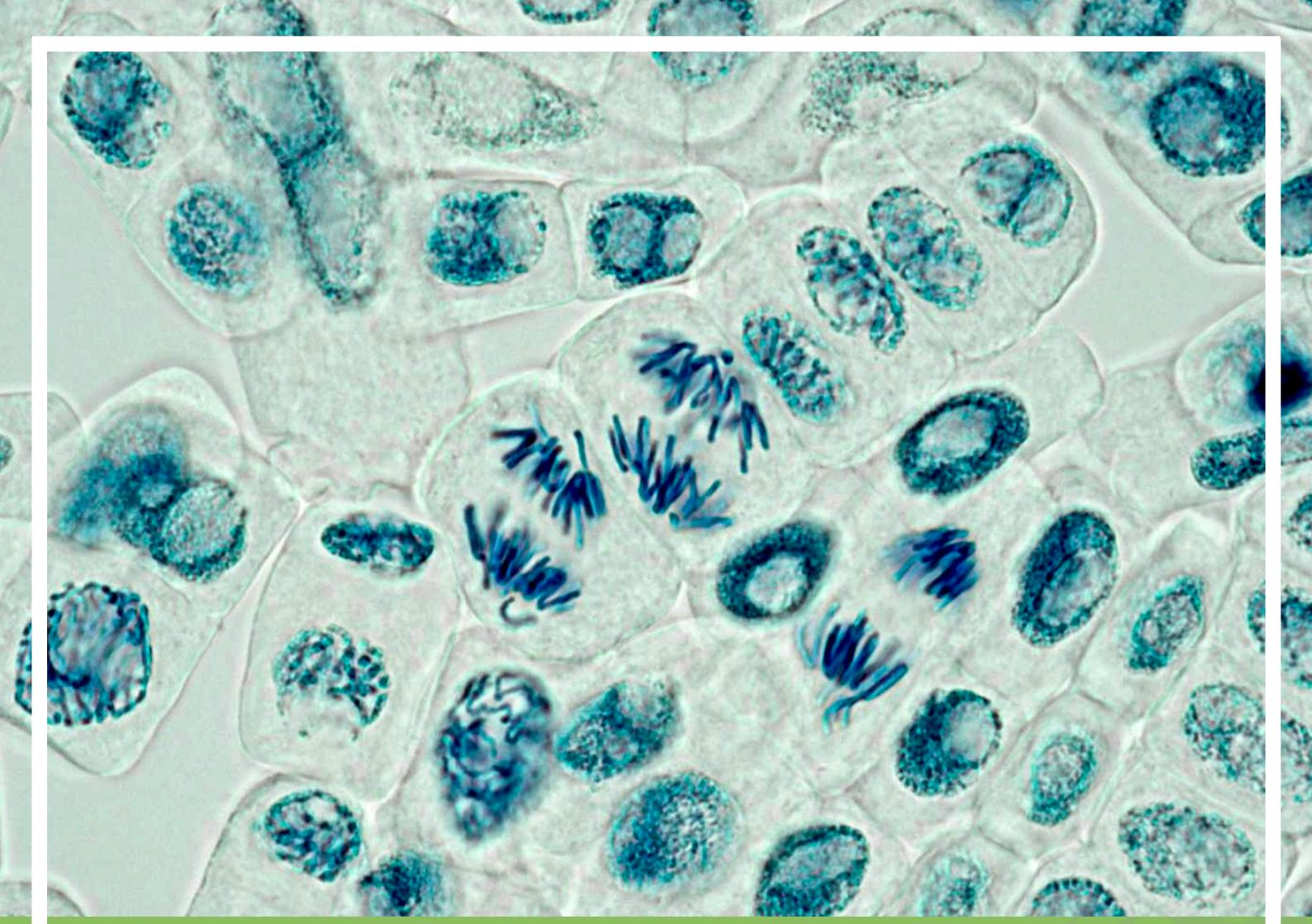


ISSUE 6

Processes

Under The Microscope

December 2022

ISSUE 6 DECEMBER 2022

Under The Microscope

Processes

Younger years
STEM club runs every week for year 7 and 8 Monday lunch 2

Aspiring medics
MedSoc runs every week on a Friday lunch 2 for those interested in pursuing a career in medicine.

PIE
PIE talks happen every Thursday lunch 2 - often covering topics in the field of STEM.

Laila:	Miranda:	Holly:	Liv:	Hannah:	Ghazal:
Features Editor	Copy Editor	Editor in Chief	Commissioning and Development	Creative Editor	Features Editor

Editors' Note

For our last edition of Under the Microscope before handing over to the new team, we chose the theme of Processes as we felt that it covered all areas of STEM and had scope for imagination. This edition includes articles from many different year groups and saw topics from drug trials to the process of uncooking an egg being discussed! We have worked so hard on this edition and hope that you all enjoy reading it as much as we enjoyed creating it!

CONTENTS

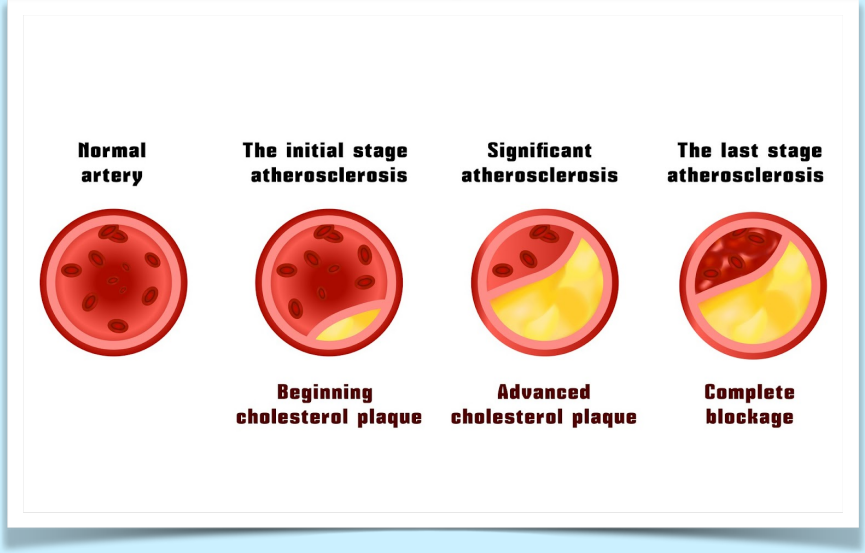
Gene Editing Lowers Cholesterol

Rawnaq Islam

In New-Zealand a volunteer for an experiment has become the first person to undergo DNA editing to lower their blood cholesterol - an exciting medical breakthrough which could be the future of disease prevention.

Cholesterol is a type of lipid (fat) produced by the liver and is present in the blood. It is vital for the human body, playing an important role in the brain, nerves and skin. It makes up part of cell membranes; is used to make vitamin D, which maintains healthy teeth and bones; and is used to make bile, which emulsifies fats.

So, if having cholesterol is important to maintain healthy body function, why is being able to lower cholesterol a good thing? Well, there are actually two main types of cholesterol: LDL (Low-density lipoprotein) cholesterol and HDL (High-density lipoprotein) cholesterol. HDL cholesterol is commonly referred to as the "good" cholesterol because it absorbs cholesterol and carries it back to the liver, where it is flushed from the body. High HDL cholesterol levels can reduce the risk of heart diseases and stroke. However, when there is excess LDL cholesterol ("bad cholesterol") it can be problematic, as too much can cause arteries to clog up and harden with time (also called atherosclerosis) - this increases the risk of heart diseases, heart attacks and strokes.

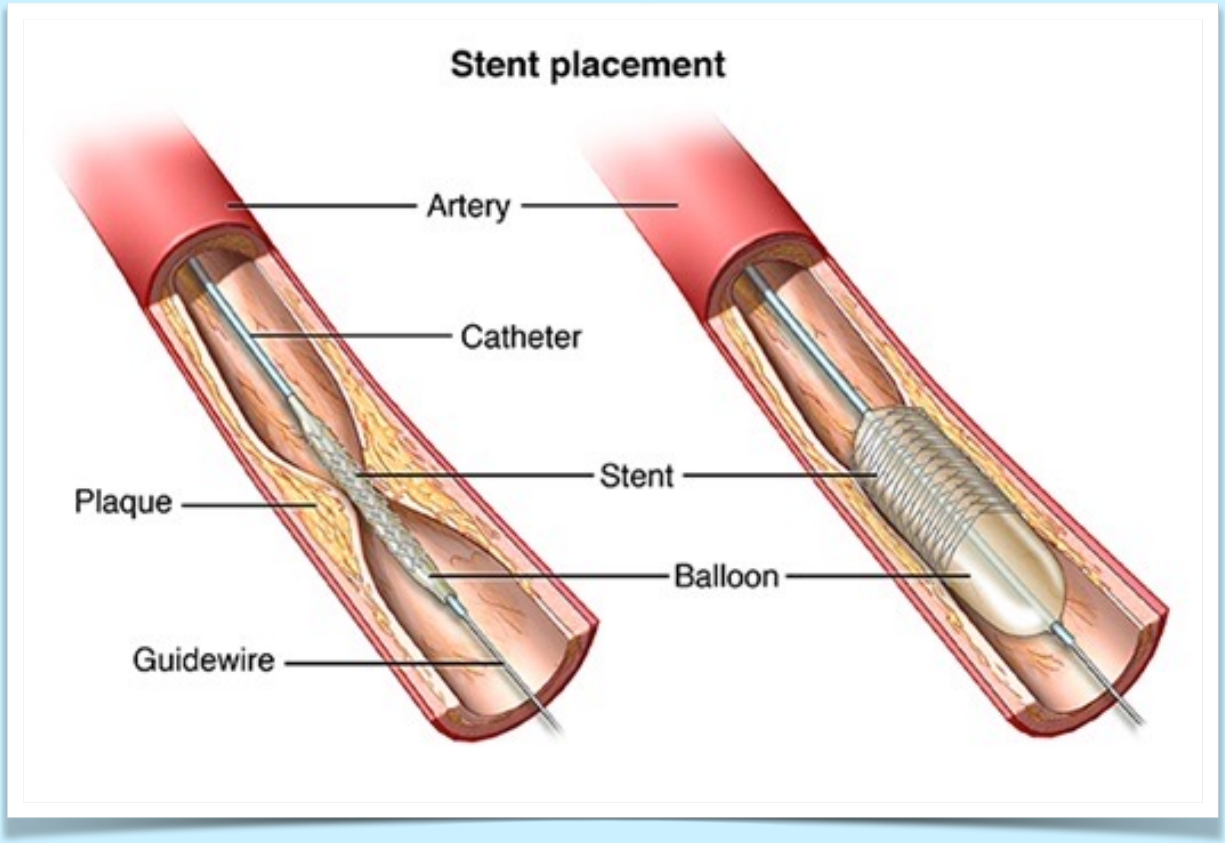


The experiment was part of a clinical trial by the US company Verve Therapeutics. It involved injecting a version of the gene-editing tool, CRISPR, so that a single letter of DNA in the patient's liver cells could be modified.

Interestingly, CRISPR is actually a natural process that has long-functioned as a bacterial immune system. CRISPR consists of two components: the Cas9 enzyme, which can cut DNA, and a guide RNA, which can recognise the sequence of DNA to be edited. After the DNA has been cut, scientists are able to edit the existing genome by choosing to either modify, delete or insert new sequences. Essentially, CRISPR/Cas9 is a "cut and paste" tool for DNA editing.

According to Verve Therapeutics, the small edit in the patient's liver cells was enough to permanently lower their "bad" LDL cholesterol. The patient had already been suffering with heart disease and had a greater risk of extra-high cholesterol. However, the company is hopeful that this technique may eventually be used on millions of other people to prevent, and even cure, cardiovascular diseases.

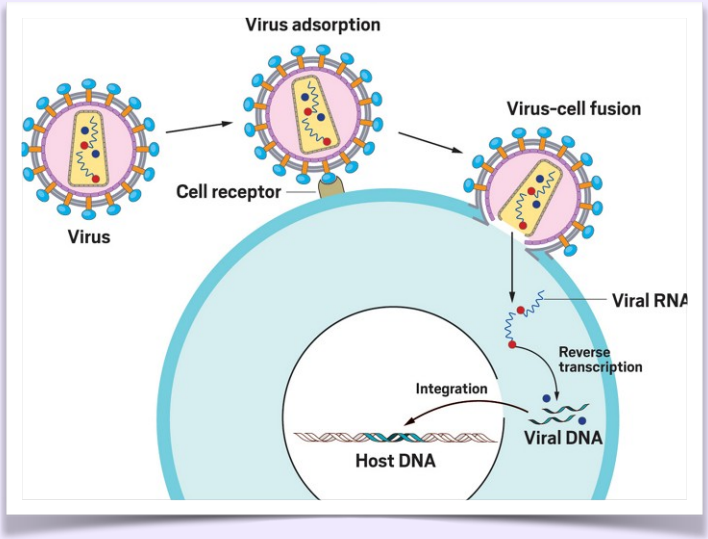
This gene-editing tool, however, isn't the only possible form of treatment of high cholesterol. There are different stages of atherosclerosis; lifestyle changes such as regularly exercising and maintaining a healthy diet may be all that is needed to treat it in its earlier stages. There are also many different medications available which can be used to treat atherosclerosis. Some include: aspirin, which helps to thin the blood and prevent blood clots; and statins, which effectively lowers LDL cholesterol. It can slow down, stop or even reverse the buildup of fatty deposits in the arteries, although sometimes more immediate and aggressive forms of treatment are needed, such as surgeries and other procedures. An example of this is an angioplasty and stent placement; this procedure involves inserting a catheter into a blood vessel (typically from the wrist or groin) where it is then guided to the blockage. A balloon, on the tip of the catheter, is then inflated to open the artery, while a mesh tube is usually placed to keep the artery open - this procedure helps to open a blocked or clogged artery.



How to Beat a Virus

Sofia Cobham

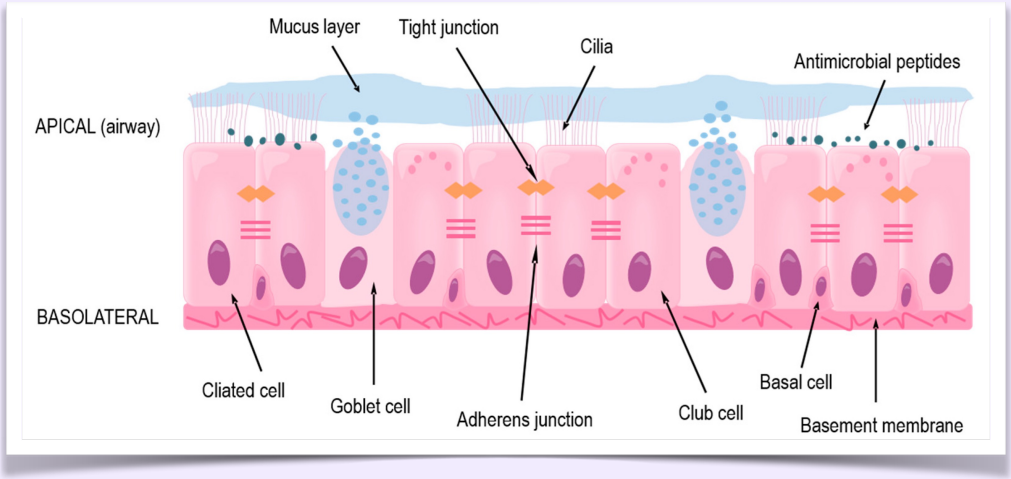
Viral eukaryogenesis is the theory that the first, more complex cells were derived from viruses – it has been hypothesised that a virus took over a bacterial cell, where the virus became trapped. It still continued to produce more viruses, eventually infecting other cells. This cycle repeated itself until the first stable eukaryotic cell was formed. From this cell, millions of new specialised cells were born, leading to four new kingdoms: Protoctista, Fungi, Plants and Animals. Yet, despite having potentially been derived from viruses, no organism is able to completely defend themselves from them, but instead, can only try to: bacteria use CRISPR-Cas9 to retain a piece of a virus' genetic material if they survive the infection; protoctista are able to form cysts to allow them to go for periods of time without any nutrients or oxygen to protect themselves from harsh conditions; fungi use chemical defence and release toxins; plants create thick cell walls to block off any connections to the infected site; and animals have an immune system. The human immune system is one of the most complex defence systems, each cell intricately linked and designed, with its own specific function.



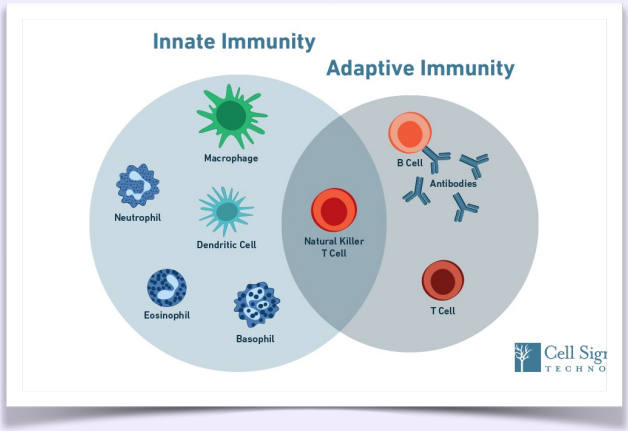
When a virus infects a cell, for example in the bronchi, it inserts its genetic material (e.g. RNA or DNA) into the host cell. The genetic material then replicates by either using RNA-dependent RNA synthesis or RNA-dependent DNA synthesis. As the only function of a virus is to replicate itself, its genetic material then begins to undergo transcription and translation within the host cell's organelles. This process continues until the host cell is no longer able to hold any more virus particles, leading it to then burst, releasing a new wave of viruses into the lungs. It is at this point that the immune system would begin to take notice of the virus. Alveolar macrophages, which are more 'relaxed,' are a special version of the macrophage. Their primary function is to 'patrol' the airways, ensuring that any pathogens are destroyed before

a large scale infection can begin. Using pathogen receptors, such as TLRs (toll-like receptors), macrophages are able to detect foreign antigens present on the surface of any cell that is not a part of the body. Normally, macrophages would detect a foreign entity, such as dust, and then activate parts of the innate immune system (the part of the immune system that is immediately used when an infection is detected), such as neutrophils, which ingest pathogens, and release toxic enzymes that break them down, or complement proteins, which mark pathogens, and activate and guide other immune cells. Whilst these methods are effective elsewhere in the body, each of these cells causes inflammation, and inflammation in the lungs could easily become deadly. As the lungs intake about 11 000 litres of air each day, that results in millions of pathogens and particulate matter entering the lungs, meaning that if our alveolar macrophages responded to everything, we would most likely be dead. To help deal with this, the airway epithelium was formed.

The airway epithelium acts as a barrier between foreign bodies and the blood. It consists of three main layers: the basement membrane, the layer of cells and the mucosal membrane. The basement membrane is effectively a sheet of proteins, which epithelial cells can attach to, and acts as a transport medium for the absorption of nutrients (e.g. oxygen or glucose). Goblet and basal cells are some of these epithelial cells which attach themselves to the basement membrane. Goblet cells are key in the function of the airway epithelium as they secrete mucin, which creates the mucosal membrane – a layer of mucus which traps particulate matter and pathogens. In order to remove these trapped pathogens, goblet cells are surrounded by ciliated epithelial cells, allowing them to 'sweep' mucus up the throat,where it can then be swallowed and dissolved in hydrochloric acid found in the stomach. The airway epithelium means that the immune system does not need to be summoned, and therefore protects the lungs from damage.



Should, however, a virus slip past these defences and begin to infect epithelial cells, a new protein of the immune system is called to action: the interferon. Interferons are used to slow down the rate at which viruses can infect your cells, since the adaptive immune system's more potent cells which fight off the virus are considerably slower to react. Epithelial cells contain receptors which are similar to what those of macrophages have, except, the difference being that epithelial cells can scan their own insides for specific chemicals and bodies which would mean that they were infected. If found, this triggers the release of cytokines – chemicals which are responsible for navigating your immune system around an infection. Interferons can be found amongst these cytokines. They attach to receptors on the outsides of other, nearby epithelial cells, causing protein production to slow down, which inherently results in virus production slowing down, as they are, effectively, protein shells with key genetic information stored inside. The next key cell is the plasmacytoid dendritic cell. They move through the blood and lymphatic network, picking up signs of viruses: either an actual virus itself, or interferons. If they came across either, they would release significantly more interferons than the epithelial cells, causing all protein production in the lungs to slow down, reaching cells that are further away. Whilst the release of interferons won't stop an infection, it will slow it down considerably, allowing for the adaptive immune system to be awakened.



The adaptive immune system is a particularly deadly part of the immune system, with cells specialised to attack certain antigens, as opposed to everything. For the duration of the infection, dendritic cells have been sampling virus remnants, and then trying to find the correct B lymphocyte to produce the complementary antibody to the virus. B lymphocytes produce antibodies – each slightly different to target a different pathogen. In your body, you have a plethora of B lymphocytes, meaning that there is a lymphocyte that will produce the complementary antibody, however, due to the sheer size of the lymphatic system, and the number of lymphocytes, it takes time to find it – this time is being supplied by the interferons. Dendritic cells contain a molecule called HLA class II at the end of their cytoplasmic extensions which has a sample of the viral antigen. These extensions can then brush against the receptors on B lymphocytes and if the

receptor on the B lymphocyte binds to the sampled antigen, it can be activated and begin to produce antibodies. Antibodies are incredibly useful proteins which can bind to viral particles to prevent them from binding to their host cells and stopping infection, and also label other pathogens such as bacteria for destruction by phagocytosis or neutralise the toxins that bacteria release making you feel ill.

Antibodies alone aren't enough to stop a viral infection: the host cells producing them need to be killed to. The Killer T Cell is responsible for this. Every cell in the body has a molecule known as HLA class I on it which allows for the Killer T Cell to detect if a virus is present in the cell. Dendritic Cells are able to perform a function called cross-presentation which means that they can bind a small sample of virus on to molecules of HLA class I. They then carry this sample with them, and wait for a Killer T Cell to bind to the sample. This process activates the Killer T Cell which then orders any cell carrying a sample of the antigen to kill itself.

Of course, it is possible for viruses to inactivate expression of these HLA molecules, and they often do so that the immune system cannot destroy the cell, and so, the Natural Killer Cell was born. Natural Killer Cells constantly scan cells (whether there is a known infection or not) for HLA class I molecules. If there is no HLA class I present on the surface of the cell, it orders the cell to kill itself. These cells are not only integral to the removal of viruses from the body, but also for the detection of cancer cells, which also hide HLA class I molecules.

In combination, every single one of these cells creates a deadly force that is very much capable of battling viruses. However, it is not flawless, and the immune system severely depletes the resources of your body, as well as damaging it through the release of proteins like cytokines (inflammatory chemicals) and pyrogens (fever inducing chemicals). Sometimes, a virus replicates too fast, sometimes our immune cells just aren't enough, and sometimes, the collateral damage is too much to handle. Despite our complex cellular structure, viruses, a capsid and core genetic machinery, are sometimes able to beat us solely due to the fact that they are able to replicate so quickly, meaning that they can evolve faster than us. This therefore means that viruses that survive can take over another cell, and create thousands of replicas of themselves, making the infection (and virus) ever stronger. Whilst viruses are deadly, so is our immune system, and, whilst viruses adapt to become more infectious, the body has adapted to become more swift and deadly should an infection occur.

Does Over Consumption of Processed Foods in 2022 Have a Bigger Social or Environmental Effect?

Annabel Jagusch

From Néstle to Pepsi, the food processing industry is constantly advancing, becoming one of the biggest industries globally. In 2022, processed and fast foods are cheap, easily available and increasingly popular, despite the scientifically proven health issues associated with overconsumption of these foods. However, an arguably more significant concern with ultra-processed foods are the effects they have on the environment. When considering factors from CO2 emissions to obesity and diabetes, what is the most significantly harmful effect of the food processing industry?

SOCIETY:

With 2.8 million people dying from it each year, obesity has reached epidemic levels. The side effects of obesity include: coronary heart disease, type 2 diabetes, potential strokes, breathing difficulties, mortality, and depression/anxiety or other serious mental conditions. Although it has been scientifically proven that fast and processed foods are associated with a 70% rise in obesity, for many people these foods are the only option. Processed foods are mass produced, which makes them

cheaper and therefore the easiest choice, especially given the ever-increasing cost of living today (although, arguably it is better to eat unhealthily than not to eat at all). The trans fats in foods sourced by fast-food industries lower 'good' cholesterol levels and increase 'bad' cholesterol levels – which causes excess fat and potential heart disease. On the NHS website, the leading cause of obesity is considered to be the over-consumption of processed or fast foods, demonstrating just how serious obesity and its detrimental effect on society are.

ENVIRONMENT:

As indicated by its name, processed foods are 'processed' which is defined as 'to perform a series of mechanical or chemical operations on something in order to change or preserve'. This system uses machinery, factories, and transportation etc. Clearly, the transport of millions of tonnes of food per day across the globe is harmful – but just how bad is it?

Here is an example: One of my favourite

foods – instant ramen. Cheap, but heavily processed. On a packet of ramen noodles, they were labelled 'sourced in Singapore', so using the food miles calculator online, I researched how many CO2 emissions were needed to transport the ramen noodles from Singapore to London. The distance was 6744 miles (10851 kilometres) – and a commercial plane journey of the same length results in roughly 3.72 tonnes of CO2 production. To put this into context, 3.72 tonnes of CO2 is equal to: growth of 200 trees for 1 year; 500,000 litres of coca cola; or electricity consumption of 2.5 households in 1 year. On top of this, the food industry generates roughly a third of the world's greenhouse gases. Think about how much better it would be for the environment if there was less of a demand for these processed foods and food could be produced more sustainably – and that's only considering CO2 emissions.

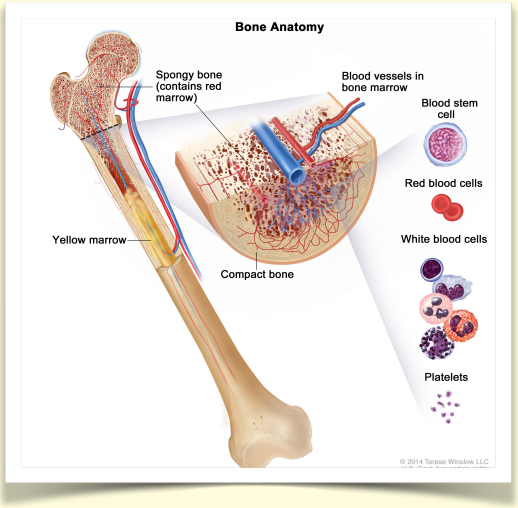
Surprisingly, however, processed foods could be considered more environmentally friendly. Although it is evident that fresh, locally sourced foods have a lower carbon footprint, many scientists argue that some processed foods have an equally sustainable impact. This is because the energy (in the form of freezing, storing, preserving, cooking, etc) required to 'process' a meal at home can expend more waste than bulk-processed foods in factories. "It's therefore the type of ingredient, rather than whether it's processed or not, that drives the environmental impact of a food," states Shelie Miller, an associate professor at the University of Michigan's School for Environment and Sustainability. For example, fresh red meat is one of the most problematic foods regarding emissions, as it's harder to store and requires cattle farming to produce.

Furthermore, processed foods could potentially even help with the environmental crisis. Because ultra-processed foods (for example pasta, crisps, canned soups) are designed to have a long shelf life, they get wasted less. One study found that waste from processed foods is around 14% lower than that of fresh fruit and vegetables, demonstrating how processed foods can be considered as more sustainable.

Overall, I think the primary conclusion to be drawn is that processed foods can be beneficial, when consumed in small quantities. They are typically cost-effective and last for a long period of time so result in less waste. However, the extreme health risks associated with over-consumption of processed and ultra-processed foods combined with the major carbon footprint of transportation of these foods make them a bad choice, when consumed in higher proportions. It is essential to consider the optimum choices for society whilst trying to take environmental action by reducing food waste and minimising the world's carbon footprint as best we can.

A Stem Cell Transplant

Ginevra Bocchi



Stem cells are cells produced by bone marrow (a spongy tissue found in the centre of some bones) that can turn into different types of blood cells. A stem cell or bone marrow transplant replaces damaged blood cells with healthy ones. It can be used to treat conditions affecting the blood cells, such as leukaemia and lymphoma.

The first successful stem cell transplant was in 1958 when a French oncologist, Georges Mathé, performed the first stem cell transplant of bone marrow to save six nuclear researchers who were accidentally exposed to radiation. From then on, millions of lives have been saved thanks to stem cell transplants.

A stem cell or bone marrow transplant is a long and complicated process that involves 4 main stages: harvesting, conditioning, transplanting, then recovery.

Before a stem cell transplant can be carried out, you'll need a series of tests and examinations to ensure you're healthy enough for the procedure to be carried out.

The first stage is harvesting, which is the process of collecting the stem cells to be used in the transplant either from the person having the transplant or a donor. Then there is conditioning where doctors prepare the body for the transplant. After this stage, doctors transport the stem cells to the necessary place which is a high-risk procedure. The final stage is the recovery where the patient will stay in the hospital for at least a few weeks until the transplant starts to take effect.

FUN FACTS

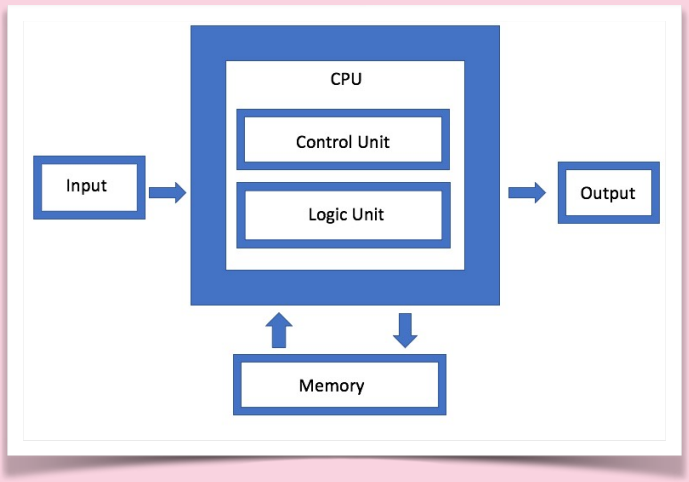
More than 50,000 stem cell transplants are done per year with an increase of 10 - 15% per year.

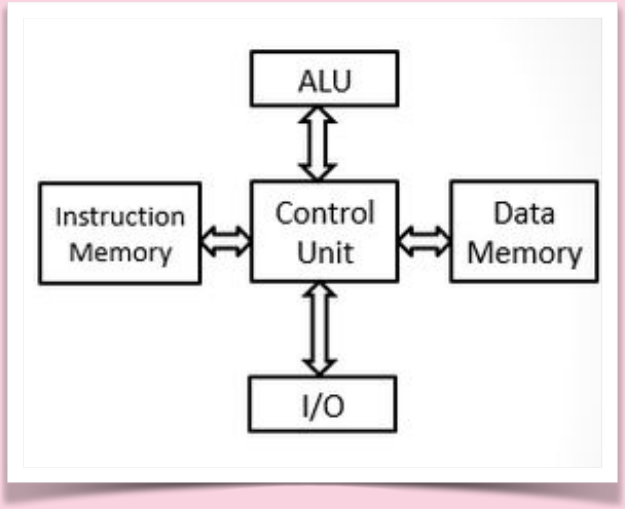
Up to 80% of stem cell transplants done are successful

How Computers Process Data and Factors Affecting Processing Speeds - Zoë Hopkins

Zoë Hopkins

To successfully run, a computer must perform multiple processes simultaneously. It does this in the central processing unit (CPU) which processes data and commands and tells the rest of the computer what it needs to do. It's basically the brain of the computer! To perform actions and run programs, the computer needs to access the data, process it and then execute any actions. The CPU does this by using the Fetch-Decode-Execute cycle. In the fetch stage of the process, the CPU receives data from the random-access memory (RAM) using an address bus. This contains the location of the necessary data in the RAM. The data stored in this location is then taken to the CPU on the data bus. Next the data needs to be decoded by the CPU so that it can be understood. Finally, the instruction is executed, the data is processed and the cycle repeats so that the CPU can carry out more processes. There are many different types of processors which are used in various computers or devices. The most common CPU architecture is Von-Neumann. We think of computers as being modern but it was actually developed in 1945. This architecture is cheap to manufacture and uses memory very effectively. There is also the Harvard architecture which is more complex, making it more expensive to manufacture, however it can process data faster due to being able to use parallel processing. Harvard architecture is often used in the cache memory which I'll discuss later.





An alternative option to a CPU is a graphics processing unit (GPU). As the name implies, historically GPUs were intended for graphics and were stored in a graphics card which connects to one or more monitors. Over time GPUs became increasingly powerful as gamers required more graphics. Over the last 10-15 years, those looking to perform repetitive complex tasks such as machine learning and bitcoin mining have found that GPUs can provide them with the computing power they need. They can process large

amounts of data very quickly and can use parallel processing due to containing many cores. GPUs for high intensity processing are specialised and expensive, this causes them to not be used frequently in most computers for processing despite their high processing speeds. Despite this, most computers still have a GPU for display processing.

It is possible to change the performance of the CPU and therefore alter processing speeds. One of the main factors affecting the CPU processing speed is clock speed. Clock speed is measured in Hz, and it determines the number of cycles the computer runs per second. If the computer runs more cycles per second, it is able to process more data more quickly. It is possible to speed up the clock speed of a computer by using a method called overclocking. Overclocking can be a very effective way of making your computer run faster than the manufacturer-specified speed; however it can also be detrimental to the computer, causing it to heat up or crash, shortening its life expectancy!

Another factor impacting processing speed is cache size. I mentioned cache previously when talking about architecture and it is memory with a very fast read/write speed which is stored on the CPU. It is faster than RAM and therefore increasing the size of the cache will cause the computer to run faster due to it being able to access data more quickly. Unfortunately, cache is expensive and therefore most computers only contain a small amount (a few megabytes) used mainly for storing data used frequently by the CPU. It is possible to buy computers with larger or smaller cache memory, however computers with more cache will be more expensive.

The number of cores can also massively impact the processing speed of a computer. This is the number of CPU chips in one computer, so increasing the number of cores means that the computer can run multiple programs simultaneously. This means that more instructions can be carried out at once and allows the computer to use parallel processing. It is very common for computers to have multiple cores. Unfortunately, these cores need to interact which uses up some of the extra speed you gain from increasing the number of cores. Pipelining is a way for the CPU to organise tasks. It is only possible in some CPU architectures, but it can massively increase processing speeds. It allows the CPU to fetch the next piece of data whilst still processing the current piece of data, greatly speeding up the process of moving data from the RAM to the CPU. This allows the computer to complete tasks faster, however it only works when the CPU knows which instruction needs to be fetched next.

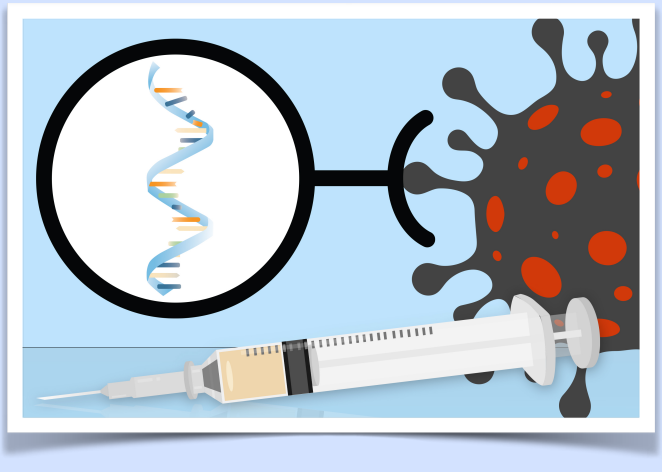
Computers have evolved amazingly quickly over the last 70 years, practically doubling in speed every couple of years and there are sure to be many amazing new advances in the future!

The Processes Involved in Developing a Vaccine

Ghazal Ershadi-Oskoui

There are many different types of vaccines: whole virus vaccines, RNA vaccines, subunit, toxoid vaccines, and viral vector vaccines. A vaccination introduces a small quantity of a dead or weakened form of pathogen (disease-causing microorganism) which is known as an antigen. This causes our bodies' immune systems to produce antibodies which are specific to that pathogen. The antibodies target and attach to the pathogen and therefore destroy it.

However, there are also mRNA vaccines (very well-known examples are the Pfizer and Moderna COVID vaccines). They work by introducing the body to an mRNA sequence (the molecule which instructs cells what to make). This mRNA sequence is coded for an antigen which is specific to a disease. This mRNA will instruct our cells to make a protein which will trigger an immune response (once again, producing antibodies to protect us from getting ill by preparing the body to fight the real thing).



Discovery Research & Preclinical Stage

Discovery research usually takes 2-5 years. It involves lab-based research as researchers search for ways to induce an immune response at a molecular level.

In order to determine which antigen the vaccine must contain, all vaccines under development must first undergo screening and evaluations. This is known as the preclinical stage. It takes up to two years. Unfortunately, experimental vaccines are first tested on animals to evaluate their safety and potential to prevent disease (according to the RSPCA, national and global laws require that new medicines are tested on animals before being licensed for use). If an immune response is triggered, it is then tested in human clinical trials which consists of three phases.

The 3 Phases of Human Clinical Trials

Phase 1 (2 years): The vaccine is given to a small number of volunteers (generally involves young, healthy adult volunteers). This is so that researchers can assess its safety, confirm it generates an immune response, and determine the right dosage.

Phase 2 (2-3 years): The vaccine is then given to several hundred volunteers. In

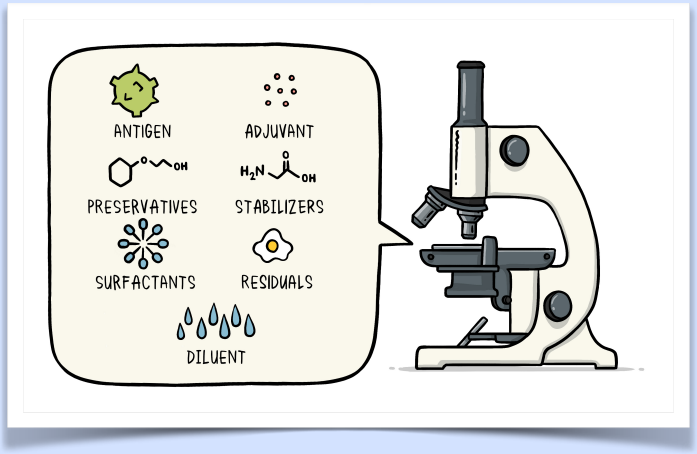
order to ensure the validity of the trial, the participants must have the same characteristics (such as age and sex) as the people whom the vaccine is intended for. Usually, multiple trials are carried out in this phase for reliability. This helps evaluate various age groups and different formulations of the vaccine. A control group is also necessary so that researchers can see whether the changes in the vaccination group are attributed to the vaccine or have happened by chance. They are usually given a placebo vaccine (containing water, for example).

Phase 3 (5-10 years): Next, the vaccine is given to thousands of volunteers and is compared to a similar control group. This is done to determine if the vaccine is effective in its function (to combat the specific disease it is designed for) and to study its safety. Usually, phase 3 trials are conducted across multiple countries and multiple sites within a country so that the findings apply to various populations.

Manufacturing the Vaccine

Each "ingredient" in a vaccine has a specific purpose and has been tested in a manufacturing process to ensure their safety. The key component of a vaccine is the antigen (a protein or sugar) so the body can learn the specific way to combat it whilst preventing itself from getting sick.

As vaccines contain complex biological molecules that are inherently unstable (and, therefore, prone to degradation if left on their own), vaccines usually contain preservatives to prevent the vaccine form from becoming contaminated once the vial has been opened (if the vial is being used to vaccinate more than one person). On the other hand, vaccines which are stored in one-dose vials do not contain preservatives as the vial will be discarded following the administration of the vaccine. Preservatives are normally considered to be harmful due to their negative associations in the food industry but the most commonly used preservative (2-phenoxyethanol) is used in a range of baby care products and is completely safe to use in vaccines as it has little toxicity in humans.



Vaccines also contain stabilisers. These protect the vaccines from the effects of heat or freeze-drying and also help to maintain the shelf life of the vaccine. Examples of stabilisers are sugars (disaccharides such as lactose and sucrose), amino acids (glycine), gelatine (the routine UK vaccines containing this are the MMR and nasal flu vaccines and

many faith group leaders have stated it is acceptable and does not break any religious rules), and proteins (recombinant human albumin which is derived from yeast).

Some vaccines contain adjuvants. This is an ingredient that improves their function as the vaccine is kept at the injection site for a little longer, or by stimulating local immune cells. For example, aluminium adjuvants are used in vaccines such as hepatitis A and hepatitis B. However, they are not used in live, viral vaccines such as the MMR vaccine. This is because they already contain naturally occurring adjuvants so an additional adjuvant can induce robust immune responses in the body.

Regulatory Approval (can take 2 years)

This process involves submitting data and information to regulatory authorities for review. This is about the vaccine's safety and efficacy. Once it gains the authorities' approval, the vaccine is now licensed. However, pharmaceutical companies continue to monitor safety and efficacy after this process as well.

RNA Vaccines

A very important advantage of RNA vaccines is that they are much quicker and less expensive to produce, meaning there is a faster response to emerging outbreaks (like COVID). This is because the RNA can be produced in the lab from a template of DNA using materials that are readily available.

There are many pharmaceutical companies and initiatives that are interested in RNA vaccines. Examples include the Merit Consortium, which is a European initiative to develop cancer vaccines as well as UniVax: a research collaboration to develop a universal influenza vaccine. Companies such as Moderna, CureVac and BioNTech are involved in phase I trials of RNA vaccines in cancer and infectious disease. In cancer vaccines, the immune system is triggered into targeting the cancer. In both dendritic cell vaccines and personalised cancer vaccines an RNA sequence is designed to code for antigens that are cancer-specific.

These companies are also researching the broader use of RNA therapeutics for diseases where important proteins are missing or defective. Therefore, mRNA treatments could be used to express a functional copy of the protein.

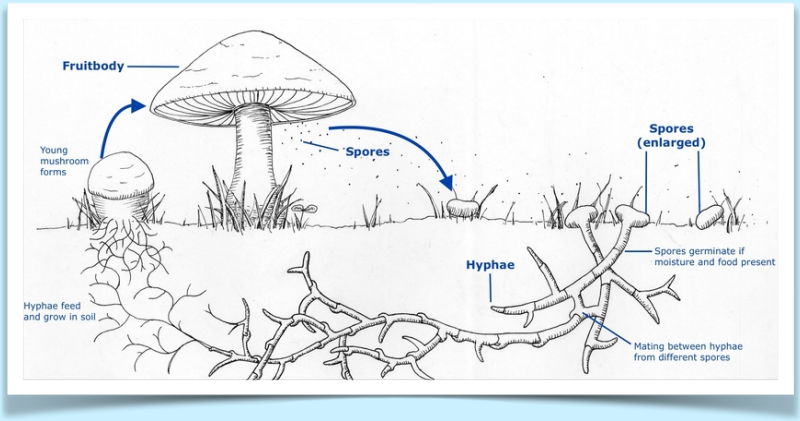
You can see that a vaccine usually takes over 10 years to develop. The COVID vaccine development only took around a year. This incredible speed is not because any of the vital stages which I have mentioned were skipped. Instead of the $500 million usually spent, investment increased dramatically (at least 4 times the usual amount) and a much larger number of volunteers were available. This allowed for each stage to only take a few months rather than a few years.

Anastomosis: The Secrets Within Fungi

Ysaline Pauwels

Fungi are very special things, but why? Firstly, the definition of a fungus is any group of spore-producing organisms feeding on organic matter, including moulds, yeast, mushrooms and toadstools. Not only are fungi one of the five kingdoms, but they also play a key role in the cycle of nutrients in the environment. They are responsible for the break down of organic matter and releasing carbon, oxygen, nitrogen, and phosphorus into the soil and the atmosphere. Without them, the leaves, dead trees, and other organic matter that build up in forests wouldn't have their nutrients available for other plants to use. They are also essential for the making of bread, wine, beer and certain cheeses.

Fungi carry out a process called anastomosis. Anastomosis is the process by which fungal cells fuse together. This process is very important for filamentous fungi because it allows them to form networks, share nutrients and is a key part to sexual reproduction.



When a spore germinates, it sends out a hypha (a cylindrical thread of fungal cells). This hypha branches and the new branch grows outwards to avoid the other branch. Eventually, the hyphae are growing outwards in a full circle around the original spore. To maintain this type of growth, the hypha, tips have to be repelled by one another. If the branch gets close to another hypha, the tip will change direction or stop growing. This ensures that new areas of substrate are efficiently colonised. This means that the substrate of which the mycelium has grown out into is ready for a mushroom to be grown from, usually turning white as an indication. However, in anastomosis, hyphae are attracted to one another instead of repulsed. It is not clear what causes this change in behaviour, but it seems to have a link with the maturity of the mycelium and the density of the hyphae. Anastomosis predominantly occurs in older parts of the mycelium, which tend to have hyphae that are closer together and have fewer available nutrients since the fungus has already consumed most of them. In these

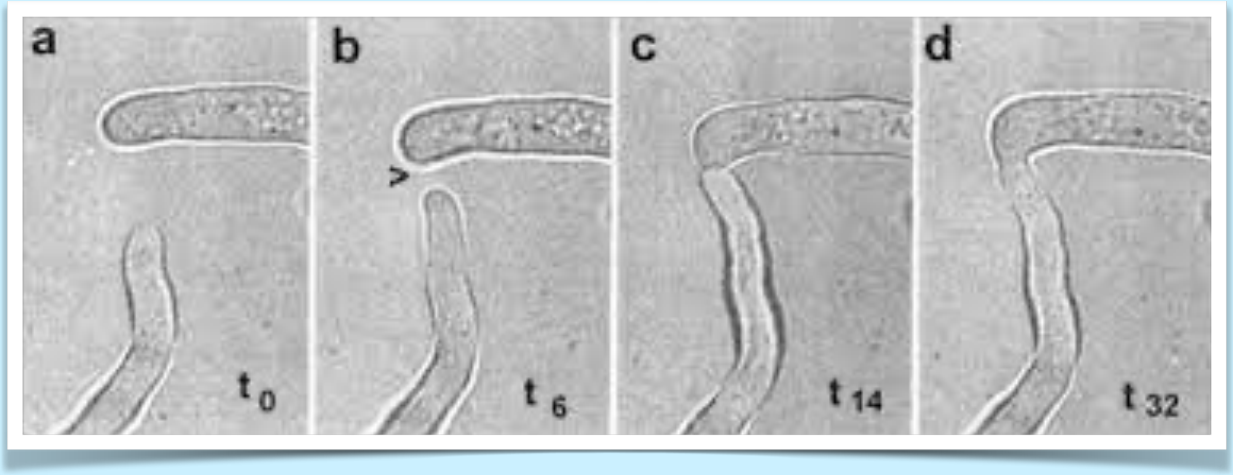
areas, hyphae anastomose when growing close together. This results in the formation of links between the different sections, like a net or web. This also allows the fungus to transfer resources and communication molecules from one part of the mycelium to any other part, which lets the mycelium act as a single organism! Alternatively, anastomosis can be dangerous due to incompatibility but also if one fungus uses the fusing of the cytoplasm to steal another's resources.

Anastomosis is what sets fungi apart from most other forms of life on earth. Their ability to fuse with each other is unparalleled in plants, animals, and nearly all other kingdoms. Consider this : you have a fungus growing on an agar dish, it's clearly an individual. You then cut the fungus in half and put each half in a new dish to have two individuals. You then put the two fungi in the same dish. They grow toward each other and, through anastomosis, fuse to become one organism again. So how many individuals did you really have? There is no good way to answer this question in nature.

Anastomosis has not yet been discovered completely, but mycologists have determined the behavioural sequence of it in five steps.

1. Recognition : all fungi secrete low levels of hormones in their environment. These are a way of communicating to hyphae nearby. Two hyphae will not react to each other unless they are close enough to detect the hormones of the other.

2. Attraction : When an approaching hypha encounters these hormones, it has three options : repulsion, attraction, defence. As mentioned, hyphae in young areas of the mycelium will most likely be repulsed, while in older areas will be attracted. If the hypha recognises the hormones as being different from itself, it may secrete proteins to defend its territory from the other fungus. The only reaction resulting in anastomosis is



3. Fusion : Once the hyphae are in contact with each other, they secrete enzymes to break down their cell walls at the point of contact. The cell wall must then be restricted to support the new bridge forming. Finally, the plasma membrane must be fused so that the cytoplasm of each cell can meet.

4. Compatibility reaction : Once the cytoplasm merges, the two hyphae can exchange nuclei, organelles and signalling molecules. To ensure that this only happens between hyphae of the same organism or of closely related organisms, there are a variety of genes that must be identical. If the two fused hyphae have a different version of any genes, one or no the cells directly involved in anastomosis kill themselves. The process of cell death is programmed into the cell's DNA and minimises the risk involved with anastomosis.

5. Next steps : What happens after anastomosis depends on the fungus's life cycle. If the two hyphae involved are part of the same individual, communication between separate parts of the fungus is initiated, but things get complicated if the two hyphae are from different individuals.

- If each individual has a haploid nucleus (one copy of each chromosome), the different nucleus may be copied and sent to the rest of the mycelium. As a result, the two genetically distinct individuals can become one genetically identical one.

- The fused cell which contains two different haploid nuclei may produce a new hypha, resulting in a new mycelium growing from that centre.

- The nuclei can also remain in the same cell without moving or growing

As humans, we are using fungi more and more everyday, for example for plant based meats. Even mycelium has a rubbery texture so it can be used for materials such as leather and is even biodegradable!

The Process of Treating Trauma Patients

Tilly Bowden

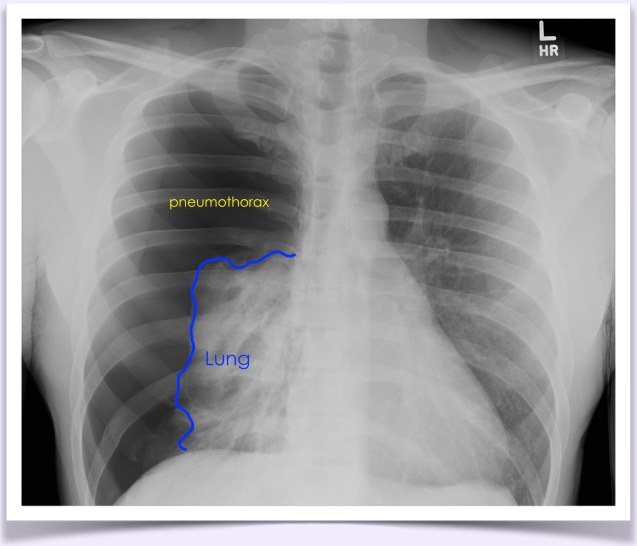
Major trauma events in the UK such as knife crime, car crashes and gun violence are on the rise. It has therefore become increasingly important for the NHS to provide effective trauma care. 2022 marks ten years since the first major trauma centre (MTC) in the UK was opened, but what does its process of treating patients look like?

On admission to an MTC the team will take a patient's vitals using devices including cardiac monitors, blood pressure monitors, and pulse oximeters. They also conduct a primary survey, using the mnemonic ABCDE: airway, breathing, circulation, disability and exposure.

'A' stands for Airway. One member of the team checks the airway for potential blockages, including blood clots and foreign bodies, which inhibit a patient's ability to oxygenate the lungs. A common method to check for obstructions is to ask a patient their name, so the doctor can assess how clearly they are able to speak. If a blockage is identified, the patient may need an endotracheal or nasotracheal intubation to assist normal breathing. Doctors will assess the possibility of intubation using the LEMON mnemonic as a checklist. This involves:

- Look – can you see anything that would make intubation difficult.
- Evaluate – use the 3-3-2 rule which helps measure the size of a patient's mouth and jaw.
- Mallampati – scored from I-IV, evaluates how much the tongue is blocking the oesophagus
- Obstruction – does the patient have any conditions or injuries that could make intubation difficult, for example maxillofacial fractures, burns, haematomas.
- Neck – how mobile is the neck and can it be extended, does the patient have a cervical collar to stabilise spinal cord.

The next stage of the primary survey is 'B' which stands for breathing, checking the lungs function properly. A blunt force injury to the chest can cause problems such as a pneumothorax (collapsed lung),



haemothorax (where blood pools in the pleural cavity), and flail chest (three or more ribs broken in multiple places cause part of the rib cage to become detached).

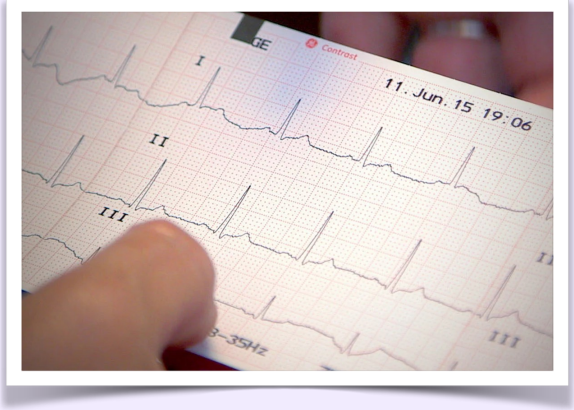
These injuries can severely increase mortality, so doctors use intubation or mechanical ventilation to increase the volume of the chest cavity, improving lung function and increasing oxygen levels in the blood. When the patient is more stable, imaging such as x-rays and CT scans are used to determine further treatment.

The third stage of the survey is 'C' for circulation, the movement of blood around the body, checked using cardiac and blood pressure monitors. The average blood pressure is 120/80, anything significantly lower or higher indicates a severe issue. Many trauma patients experience haemorrhages, decreasing the volume of blood in their body and therefore the oxygen supplied to organs. Cells become unable to aerobically respire efficiently, they begin to respire anaerobically producing lactic acid. Blood pH is decreased and enzymes, including those responsible for clotting, are thereby denatured and bleeding increases. Furthermore, this acidosis kills muscle tissue in the heart, which will decrease cardiac function. Circulatory problems must therefore be treated extremely quickly using a tourniquet, gauze and blood transfusions.

'D' is for disability, which doctors must consider in their treatment of trauma patients. This includes speech and neurological disability caused by head trauma. The Glasgow Coma Scale (GCS) is used to assess these traumas for brain injury. GCS assesses eye opening, verbal and motor response by scoring patients - each category combines to give an overall score. A score of 8 or less shows a severe head injury, 9-12 a moderate injury and 13-15 a mild head injury. The GCS helps to evaluate the current state of a patient and thus their ongoing treatment.

The survey is concluded by assessing 'E', exposure. Doctors perform further detailed checks, including a temperature assessment to monitor hypothermia or hyperthermia. Extreme temperatures are dangerous as they also cause enzyme denaturing, interrupting bodily functions. Hypothermia is included in the trauma triad of death – hypothermia, acidosis and coagulation, which combine to dramatically increase mortality rate.

Following the primary survey, a secondary survey is conducted once the patient has stabilised. Doctors will consider the patient's medical history, assess further signs and symptoms, allergies, medications and the events experienced during the trauma. Follow up testing such as CT scans, ECGs, lab tests and toxicology screening may be necessary.

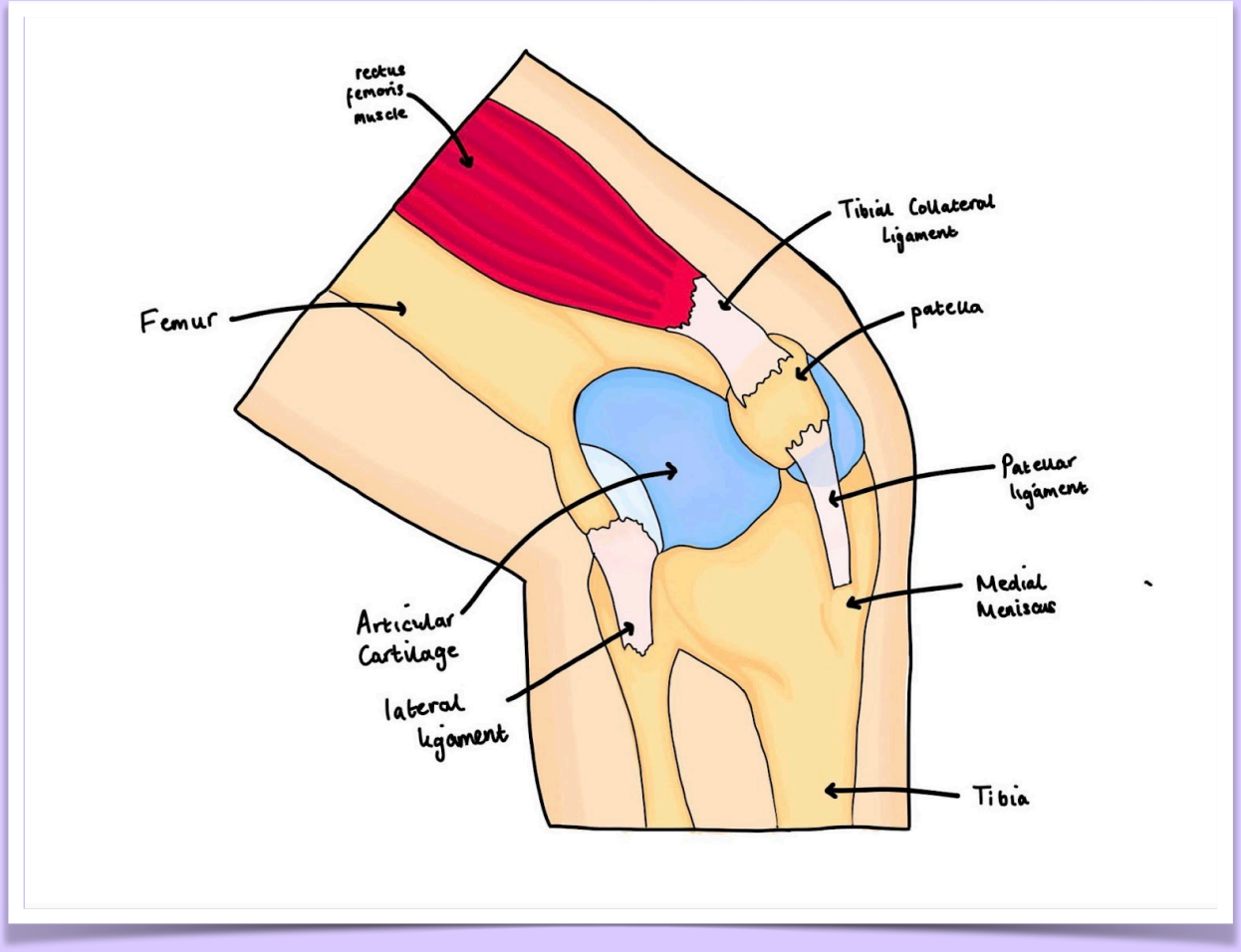


Furthermore, a patient's care doesn't just end when they leave the hospital. According to the Major Trauma Group, 75% of people need rehab following a traumatic event, for example physiotherapy and psychological support.

Following the 'Trauma, who cares?' report, made in 2007, which heavily criticised trauma care in the NHS, the setting up of the MTCs revolutionised treatment. Between 2012 and 2018 the NHS has saved the lives of an extra 1600 people and has increased the survival odds of those admitted by almost 20%. Considering that trauma is the primary cause of death of the under 40s in the UK, this improvement in care has been crucial to saving many lives. Therefore, the successful creation of MTCs highlights that the NHS and its staff must continue to adapt to the demands of the population in order to create positive change.

SCIENTIFIC ARTWORK OF THE ISSUE:

THE KNEE BY ELSA FRASER

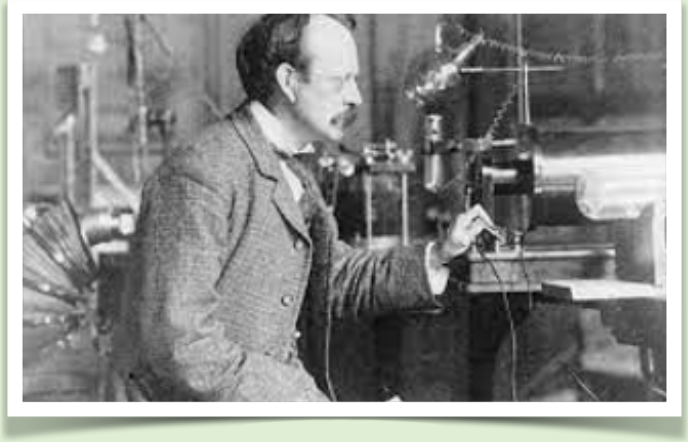


The Electron

Laila Samarasinghe

I recently listened to a podcast called 'The Electron' on BBC Radio 4 for my chemistry homework and found that it really went into depth about this subatomic particle. I really recommend listening to it as it explains the process of its discovery and role in our lives today.

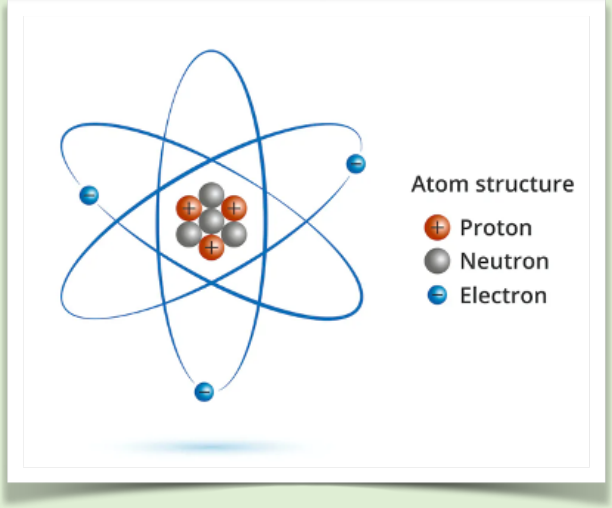
So, how was the electron discovered? In 1897 JJ Thomson discovered a new subatomic particle with a tiny mass and negative charge (the electron). He did this by directing cathode rays between charged aluminium plates, so that the cathode rays repelled negative plates and were attracted to positive ones. This shows they have a negative charge.



Following this in 1932, was the discovery of the positron (a particle like the electron, but with a positive charge). Carl Anderson used a cloud chamber to see electrons travelling through, leaving a trail of water droplets. However, when he applied a magnetic field he saw the particles curving in the wrong direction, showing a positive charge. This particle became known as the positron.

This had been predicted by Dirac some years before, when he had come up with an equation which described the behaviour of an electron but found that sometimes he found it had a positive charge. The positron can be described as the antimatter of the electron.

So what does an electron look like? Electrons can be described as point-like particles which are extremely round, similar to what they look like in our diagrams of the atom. They are so spherical that if they were enlarged to the size of our solar system, they would be completely round to the strand of a hair. It is this spherical shape which suggests to us that electrons are fundamental particles, so are not made of anything smaller. We cannot be sure about the exact size of an electron, as they are so small. However we can say that they are smaller than $1x10^{-15}m$ in diameter.



Electrons' role in our lives

Electrons help make up atoms, which make up all the objects that we see in our day to day lives. Electrons are also what stop us from sinking through the ground, as the negative charge between electrons in our feet and the floor create a repulsive coulomb force. We also use electrons in everyday appliances such as those that use electricity. They are used in certain types of microscopes which work by projecting a beam of electrons at the sample you want to look at. This can magnify the sample x500,000 and give a resolution of 0.002 micrometres, which is incredibly detailed. These are just a few examples of how electrons play a key role in forming everything around us.

PHYSICS RECOMMENDATIONS

The Infinite Monkey Cage Podcast

Lara Tanner

This Brian Cox podcast explores scientific discoveries, both present and past, through a humorous and witty approach. With every episode a combination of experts and comedians join a panel where they discuss such explorations. An educational, entertaining, exhilarating programme which is recommended by all who listen to it.

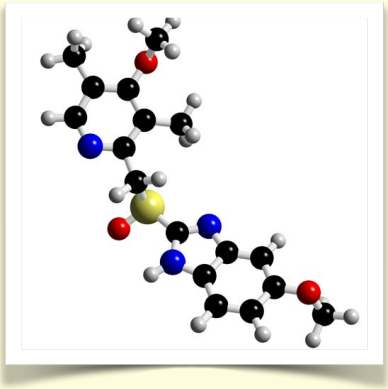
The NASA "Houston We Have a Podcast"

Lea Boucher

Simplified guide of what NASA is up to at the moment. Allows you to keep up to date with the current astronomy projects. Easy listen but still feels like you are learning something from it. You get a different astronomer each week and learn about things you wouldn't otherwise.

Omeprazole: the process of inhibiting proton pumps

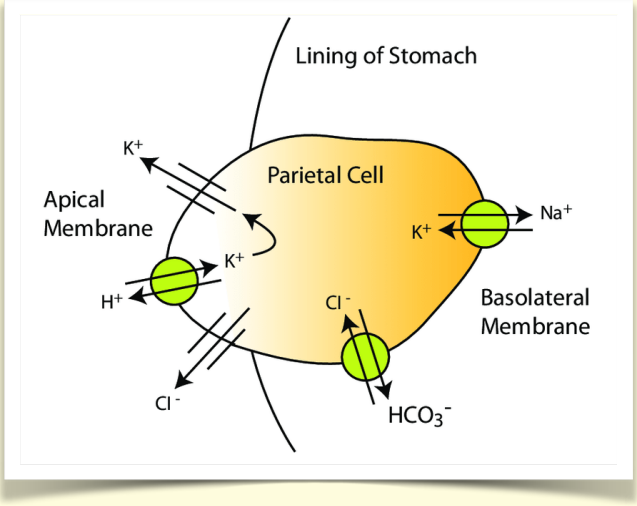
Liv Crawshaw



Omeprazole is a commonly prescribed medication used to treat gastro-oesophageal disease and peptic ulcers. It is a proton pump inhibitor, the first of its kind, made in 1979 and readily prescribed 10 years later.

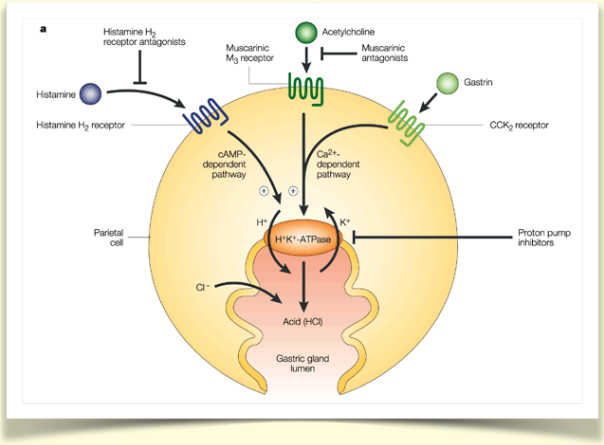
The drug contains a sulphur sulfinyl group where a sulphur atom is joined to an oxygen atom by a double bond. In this case, it has a coordination number of three and is in a pyramidal structure. This allows the compound to form 'S' or 'R' optical isomers. The molecule is therefore chiral or unsymmetrical and therefore distinguishable from its mirror image. Omeprazole can be described as a racemic mixture because it contains equal concentrations of both optical isomers. When in the body, it will undergo a chiral shift which converts the inactive 'R' isomer to the active 'S' form.

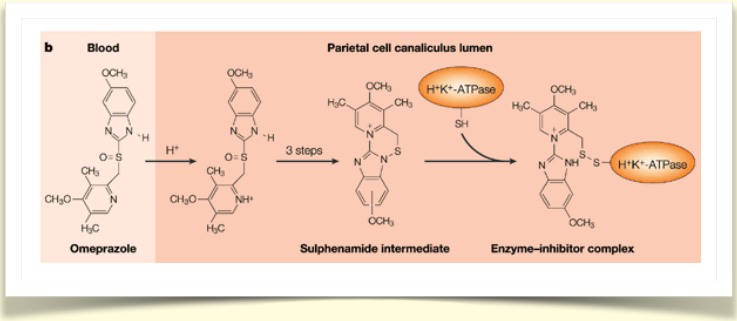
The medication aims to reduce the secretion of acid in the stomach produced by parietal cells. These are a type of epithelial cell that line the inside of the stomach and release hydrochloric acid. The first stage of this process is the formation of carbonic acid from water and carbon dioxide using carbonic anhydrase. Subsequently, the carbonic acid dissociates to form hydrogen ions (H+) and bicarbonate ions (HCO3-). The latter is exchanged through an anti-porter for chloride ions (Cl-) and the bicarbonate ions enter the blood, resulting in the alkaline tide phenomenon or a temporary increase in pH. The chloride ions exit the cell from the opposite side through a channel into the stomach lumen. Simultaneously, the proton pump, hydrogen potassium ATPase, pumps the hydrogen ions into the stomach lumen in exchange for potassium ions. The hydrogen and chloride ions can now combine to form hydrochloric acid.



Omeprazole is a competitive and irreversible inhibitor of the hydrogen

potassium ATPase pump, therefore stopping the secretion of hydrogen ions into the stomach lumen. With all proton pump inhibitors, omeprazole only works on active ones stimulated by food and so should be taken before a meal. Despite the half-life being only 30 minutes to an hour, the duration of inhibition is usually 72 hours as it is covalently bonded to the pump. Occurring mainly in the liver, the drug is fully metabolised by a family of enzymes called the cytochromes P450. Not everyone has these enzymes in equal proportion so effectiveness varies. It has been suggested that dosage should now be tailored to one's ability to metabolise the medication.





It is commonly prescribed to relieve indigestion, heartburn, acid reflux and prevent stomach ulcers. On occasion, it is used in the treatment of Zollinger-Ellison syndrome. This is a rare digestive disorder and results in larger volumes of gastric acid. The condition arises due to tumours on the pancreas or duodenum leading to increased secretion of the hormone gastrin. This is a peptide hormone that stimulates parietal cells to secrete acid.

An important consideration whilst prescribing omeprazole is its possible interactions with other medications. For example, it is not recommended for a patient to be taking both omeprazole and clopidogrel. Clopidogrel is an anti-platelet medication used to reduce the risk of heart attacks and strokes. It is described as a prodrug and so is inactive until metabolised in the body to its active form. This process partly requires the enzyme CYP2C19, which omeprazole inhibits. Additionally, any medications that depend on an acidic environment in the stomach will likely be poorly absorbed and unable to carry out the desired effect. These include ketoconazole, used to treat fungal infections and atazanavir, an antiretroviral medication used to treat AIDS.

The process of manufacturing a drug to inhibit proton pumps was a remarkable one and marked a breakthrough in the treatment of suffering patients.

The Use of Cannabidiol (CBD) in Veterinary Medicine

Holly Dulieu

As cannabis-derived products have become more readily available, veterinarians have seen an increase in interest among clients in using these products for their pets. Cannabinoids, most notably cannabidiol (CBD), appear to hold therapeutic promise in areas such as the treatment of osteoarthritis, epilepsy, anxiety, and inflammation. They have been used medicinally for the last six centuries in both humans and animals as they are non-psychotropic, so are mood-altering substances. When using CBD in treatments, there are questions regarding its safety and whether it is legal for medicinal use. In the US, in 2018, use of cannabis hemp extracts in veterinary medicine became legal, although in some states it had been legal for human medicinal use since 1996 due to its success in treating seizure disorders. In the UK, there are no current CBD products that have been authorised for use in animals.

There is limited evidence for the medicinal benefits of CBD, however, anecdotally it has been shown to improve many areas of the body. These areas include pain management, seizure control, the gastrointestinal tract and cancer. The greatest outcomes when using CBD have been for the treatment of arthritis and anxiety in geriatric dogs. Although in some cases it causes a marginal increase in liver enzymes, once a certain level is reached the concentration of liver enzymes subsides. CBD works by inhibiting the endocannabinoid system, but what is this system?

The endocannabinoid system (ECS) is a neuromodulatory system that plays an important role in the central nervous system; regulating homeostasis and synaptic plasticity. The “runner's high” effect is also caused by the ECS. It works at the synapse, e.g. when a pain receptor is disturbed. Impulses fired, are slowed down by endocannabinoids present at the synapse therefore reducing inflammation. The ECS is made up of three parts: cannabinoid receptors, endocannabinoid molecules, and metabolic enzymes. The primary targets of the ECS are the CB1 and CB2 receptors which are involved in analgesic pathways and immune-related tissues respectively.

CBD is able to affect the ECS by targeting the CB1 receptor (CB1R) which resides on the pre synaptic neuron. It acts as a non-competitive inhibitor as it binds to CB1R’s allosteric site, so changes its shape and alters the potency of other primary ligands, including endocannabinoids. As a result of this, endocannabinoid signalling is inhibited and, due to its lack of intrinsic efficacy, CB1R activity is decreased without any CB1 related side-effects occurring as often happens with other drugs. Due to its generally high safety profile, as only mild side effects have been reported in animal preclinical studies, coupled with the fact that there is limited abuse liability of the substance, CBD is a good therapeutic option for vets to prescribe where it is legal!

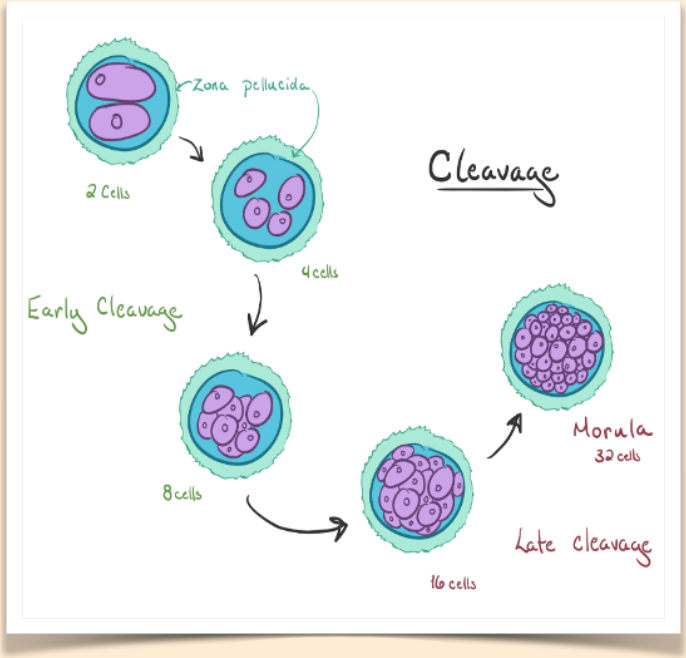
Embryogenesis: The Journey From One Cell to a Conscious Mind

Beatrice Crachilova

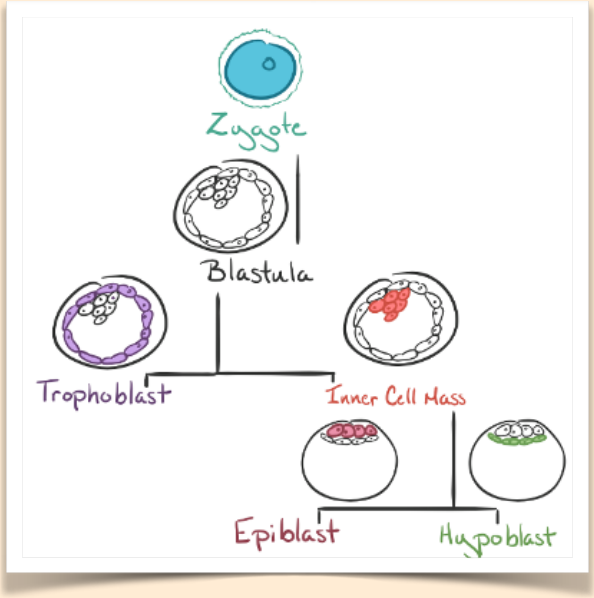
Embryogenesis is one of the most incredible things that exists on earth. It is the fascinating process of a single cell, transforming over a period of time into a fully formed organism. Embryogenesis is the science of you, your friends, your family and everyone you see around you; embryogenesis is the reason for their existence. So, I invite you to embark on an incredible journey through the enchanting process of embryogenesis.

At first, the egg cell is fertilised by a sperm cell (this creates a zygote), this will initially create the very first stem cell that can make nearly any other cell present in the human body, these are called omnipotent stem cells. This takes place inside the Fallopian tubes of a woman, and is how we start our journey.

After this the cells begin to divide at a very fast rate, in fact the rate of division is so fast that the zygote doesn't even have time to grow! The process of splitting without growth is also called cleavage. This cleavage process will repeat numerous times, starting with 2 cells, then 4 cells, then 8 cells, and so on. This will repeat until the soon to be embryo has now 32 cells, the zygote then adopts a new name called a morula. This is actually the Latin word for mulberry due to their similarity in appearance.

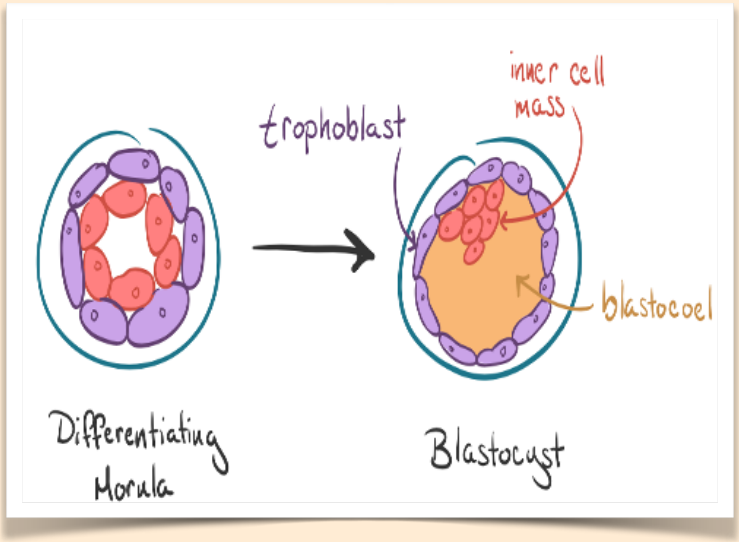


The next stage is called compaction, this is where those many cells are slowly starting to squeeze into the middle of the zona pellucida, but one of the most significant differences from this stage is the way that the cells start to differentiate with each other. This process is called differentiation, and is one of the reasons why our bodies can carry out so many amazing functions that keep us alive and allow us to do everyday actions. The regular cells are located on the inside, these are called embryoblast and the slightly altered ones that surround them, these are called trophoblasts. The trophoblasts are vital to help develop different structures so the embryo can comfortably implant inside the mothers uterus, while the embryoblast will continue to differentiate and eventually become the embryo.



As well as this happening, the cells begin to compact so much to the point where they are pushed off to the side, to create something called the inner cell mass. The rest of the space remaining is filled with fluid, and this is called a blastocoel. To help you visualise it, you can think of it as a snow globe.

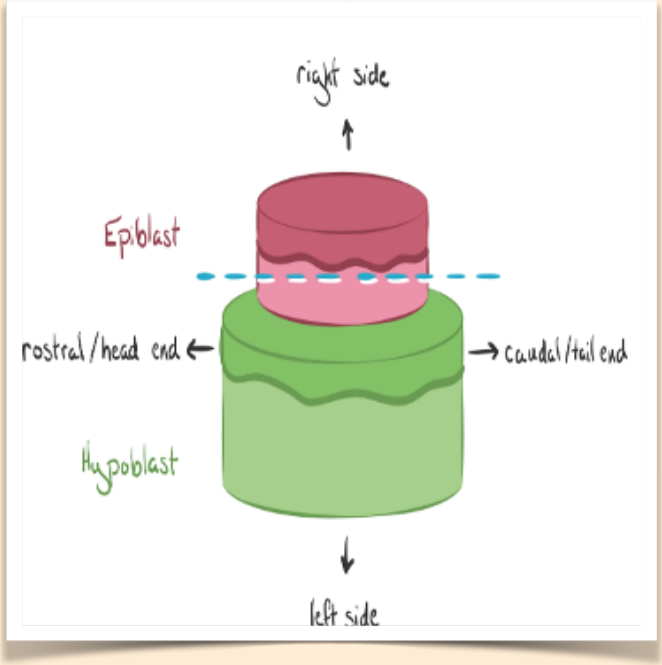
Next, the zona pellucida disintegrates as the structure is stable enough - this is where you are left with the trophoblasts on the outside, without anything to protect them. It is really important that the zona pellucida doesn't stay, as the trophoblasts need to change shape so that they can implant properly inside the mothers uterus. It's important to note that now the cells of the inner cell mass are pluripotent, which means that they can derive into different cells, but not all of the options available for omnipotent cells. But as this happens, another cavity develops inside of the internal cell mass. This cavity is called the amniotic cavity. Throughout this whole process, cells will start to differentiate more and more, at this stage we get a new type of cell called a hypoblast, these are located along the edge of the internal cell mass and we also get another type of cell called an epiblast. These two cells are part of something called the bilamitor disc. You can imagine this disc like a CD without the hole in the middle. This disc separates the blastocyst into 2 spaces, the epiblasts and the hypoblasts. This also creates two new cavities, the amniotic cavity and the primitive yolk sack.



Then the most important stage takes place which is implantation. As the name suggests the blastocyst implants itself into the lining of the mothers uterus - this is now a fixed position so the blastocyst can't move around. It is extremely important that this process happens as the blastocyst needs nutrition to be able to grow, it needs to get rid of any metabolic waste, and it also needs to be able to exchange gases from the mothers body. Where the blastocyst

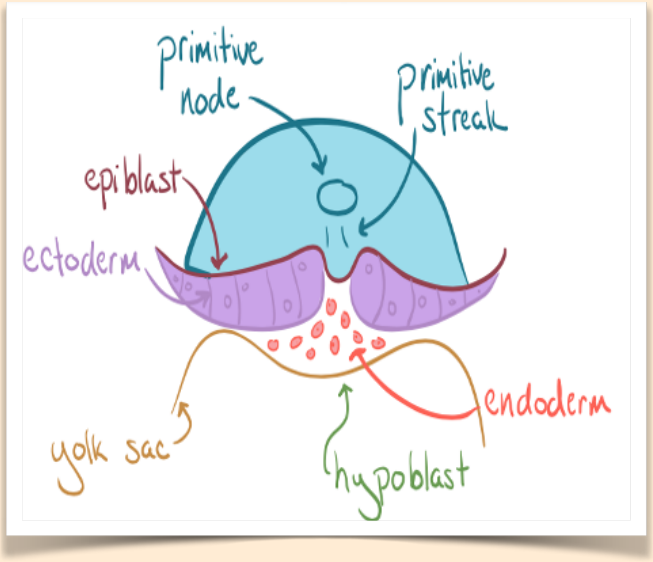
Where the blastocyst attaches, a placenta will form, the placenta is a very important organ that allows for the exchange of waste, nutrients and gases to take place. It is actually extremely common for mothers of all organisms to eat their placenta, many animals do this as food is unpredictable and scarce in their environments, and weirdly enough, the placenta is a very good source of protein that keeps them fuller for longer - even humans sometimes eat them too!

Next, a process called gastrulation happens. Three germ layers form any of our human organisational tubes. Organisational tubes are any tubes that we have present in our body, like our trachea, and oesophagus. The three layers that form are called the ectoderm, the mesoderm, and the endoderm. All of these layers have a different thing that it goes on to form. The ectoderm goes on to form our hair, nails, brain, spinal cord, peripheral nervous system, and epidermis (our skin is structured in different layers and the epidermis is on the top). The mesoderm layer is responsible for forming your muscle, bone, tissue, notochord (helps cue the development of the embryo) , kidney, gonads (part of the reproductive system which produces eggs and sperm), and circulatory system. Lastly the endoderm is responsible for the digestive tract, the stomach, colon, liver, pancreas, bladder, and lungs.



Initially, gastrulation is started by something called the primitive streak. Khan academy actually explains this process extremely well with the analogy of a cake. You can image the bilaminar disc as a two tiered cake - you can take your imaginary knife and cut the top layer horizontally.

The cut in this case acts as the primitive streak. The reason why the primitive streak is so important is because it determines the body's major axis. This allows humans to have bilateral symmetry which means that you can only split a human one way to create a mirror image. The primitive streak is located in between the bilateral disc, and it forms the three germ layers. The mesoderm then forms a thin rod of cells called the notochord - this also further helps define the major body axis of the body. It is vital for our next step,



neurulation. Gastrulation is the stage with the highest failure rate, that actually means that a lot of women have probably been pregnant at least once in their lifetime, but not know it as the baby died in the gastrulation stage.

Finally we can start to make the tubes of the body! After the notochord is made, it uses the ectoderm above it to create a circle of cells that looks a bit like a weight plate inside of a gym. This is called the neural plate. The neural tube then folds in on itself, and seals into a tube that we call the neural tube. The two sides that bent over meet at the neural plate borders, which we now refer to as the neural crest. The neural tube will later go on to form the brain and spinal cord. The neural crest will go on to form the sympathetic and parasympathetic nervous system (the fight or flight instinct and the rest and digest instinct), and some bones of the face. The process continues with many other fascinating steps!

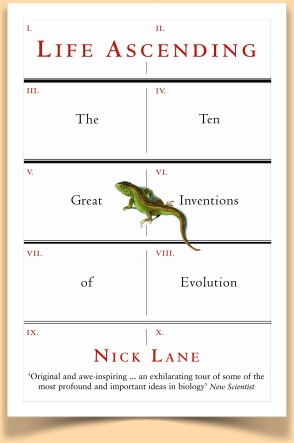
I wanted to present the amazing process of embryogenesis because it is so important. Each of us takes the journey from simple physics and chemistry towards high level cognition.

IF YOU ENJOYED EMBRYOGENESIS...

Life Ascending by Nick Lane

Vanessa Shaw

I really enjoyed reading Nick Lane's "Life Ascending" where he discusses the 10 greatest 'inventions' that evolution has produced. The most interesting of which was the evolution of death. I found the chapter on consciousness to be less convincing, however it was interesting nonetheless. If you are interested in the origins of life, DNA, photosynthesis and how eukaryotic cells may have arisen, this is a very informative read.



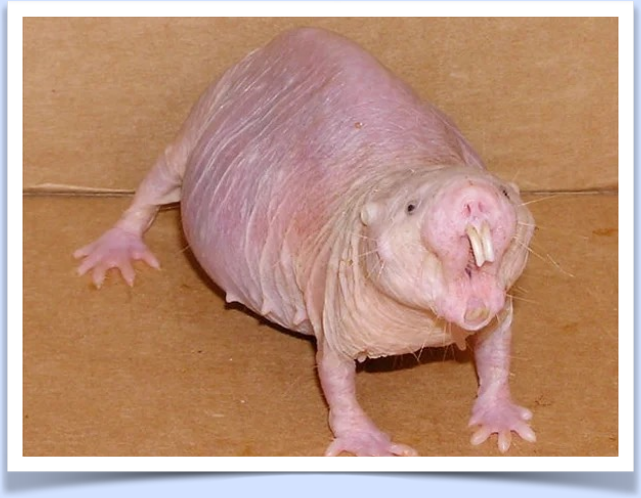
Negligible Senescence and Super-agers

Hannah Kelly

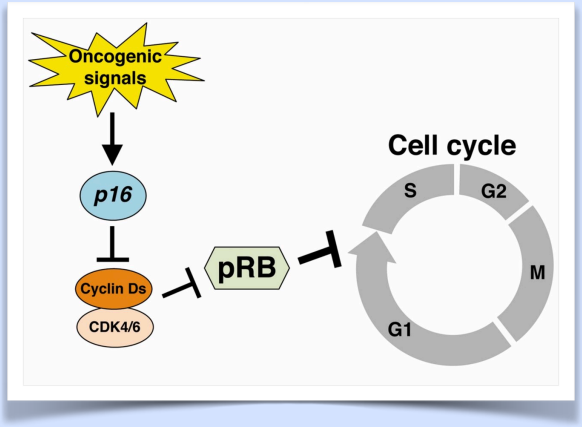
Negligible Senescence

Despite growing older, ageing is not a concern for a number of species. In order for an animal to be classified as negligibly senescent, the mortality risk must remain constant, independent of age. As a result these animals typically have extremely long lifespans, however, they are not immortal as one might expect, instead, their cause of death is simply unrelated to their age.

There is not one specific reason that accounts for longevity in certain species, but instead a multitude of factors and adaptations. Naked mole-rats are an example of negligibly senescent animals which stop ageing once they reach maturity and have the longest lifespan of any rodent. The extremely efficient adaptive abilities of this species make them able to tolerate environmental changes very effectively. Naked mole-rats are able to reduce their metabolism in order to prevent damage by oxidative stress. Additionally, their genome was sequenced in 2011 which revealed an expression in DNA repair genes that was far higher than that measured in other rodents. This suggested that DNA repair is significant in relation to lifespan - a finding that is supported by the DNA damage theory of ageing which suggests

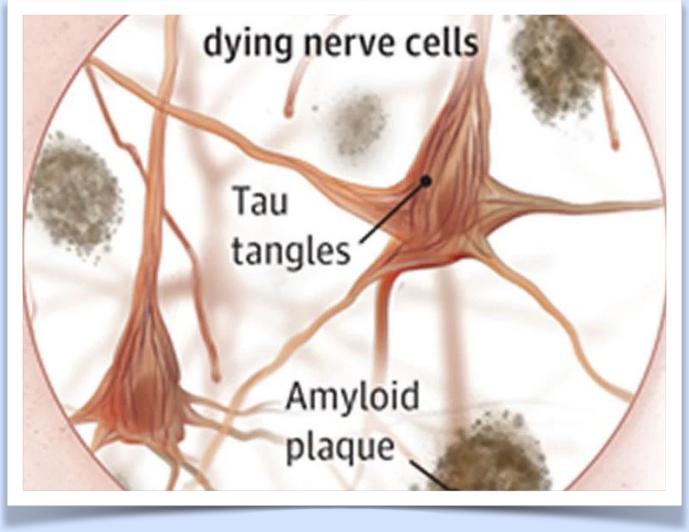


that ageing itself is a result of an accumulation of DNA damage. Damage can be to both nuclear and mitochondrial DNA. As a species, the naked mole-rat displays almost complete resistance to cancer and tumours - that largely underpins their negligible senescence. An impressive combination of action of both the P16 and P27 genes, act to stop uncontrolled cell division, and thus prevent tumour formation. In captivity, it has been found that malignancies are able to occur as a result of an unideal environment. This could be analogous to the growing prevalence of cancer in humans as the world continues to develop and diverge further and further from our natural conditions.



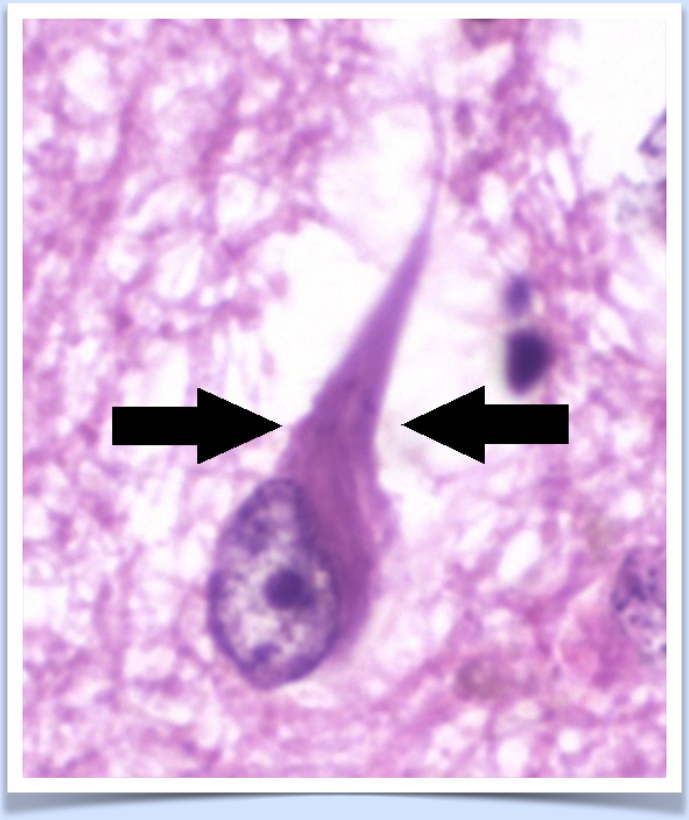
Super-Agers

Super-agers are people whose brains age far slower than average and as a result display the cognitive ability of someone far younger than themselves well into their 70s or 80s. Recently, scientists have been able to connect this previously confusing phenomenon to the size of neurones in the entorhinal cortex which is part of the hippocampal memory system. Both the large size of the neurones, in addition to the absence of tau tangles, are what make these people's



brains so efficient. Tau tangles are an accumulation of threads that form inside of neurones and affect cognitive function. These threads are formed from tau proteins which are normally bound to microtubules to stabilise them, however, with age they detach and bind to each other.

Researchers at Northwestern University discovered the large neurones at post mortem, and through comparison to those of younger individuals, they still stood out as being significantly larger. As a result it could be concluded that the presence of these bigger neurones was not something that was lost with age, but something that was present from birth and therefore may be hereditary. Despite this being the early stages of discovery, it is a particularly exciting scientific find on account of the strong links to Alzheimer's disease. Common markers of Alzheimer's are shrunken neurones and these tangled threads of proteins, so if the cause for larger neurones can be found, there is a great deal of potential for future use in neurological medicines.



How Does EMDR Therapy Help Patients Process Trauma?

Clarissa Soto-Rosa

What is EMDR therapy?

Eye movement desensitisation and reprocessing (EMDR) is a relatively new, non-traditional type of psychotherapy, developed by Dr Francine Sharpiro in 1987. It is designed to help individuals process and recover from past experiences that negatively impact their mental health and wellbeing, and facilitates the accessing and processing of traumatic memories and other adverse life experiences.

What can EMDR help with?

EMDR therapy was originally designed to alleviate the distress associated with traumatic memories and is best known as a therapy for treating post-traumatic stress disorder (PTSD) and can also treat C-PTSD (complex PTSD). Many mental health illnesses are rooted in trauma, so EMDR can be used to treat other disorders apart from PTSD including anxiety, depression, addictions, psychosis, borderline personality disorder, bipolar disorder, and other personality disorders.

How does trauma impact cognitive processes and quality of life?

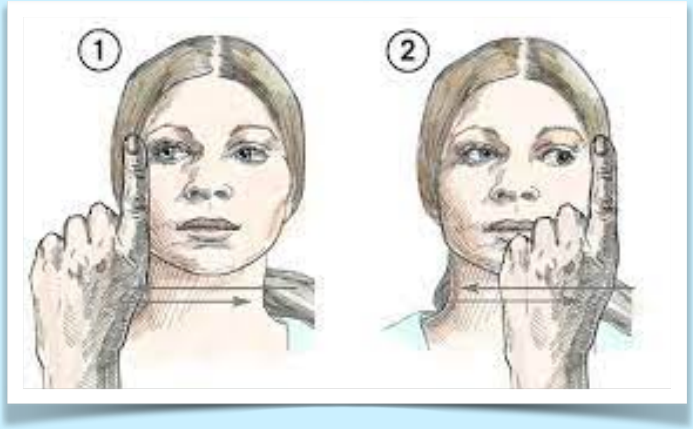
The American Psychological Association define trauma as 'any disturbing experience that results in significant fear, helplessness, dissociation, confusion, or other disruptive feelings intense enough to have a long-lasting negative effect on a person's attitudes, behaviour, and other aspects of functioning.' It is also important to consider that the dimension of the event is not necessarily directly proportional to the severity of the trauma. This depends on personal variables such as environment, history and the point at which an individual is in their life. Trauma can severely impact quality of life as if the experience is not overcome it can lead to the development of other mental health disorders. There can be both psychological and physical symptoms of trauma, with every individual experiencing different reactions. Psychological symptoms include difficulty concentrating, depression and irritability. Physical symptoms include panic attacks, fatigue and exhaustion, and psycho-somatization. The physical symptoms are believed to be an expression of what cannot be coped with or processed emotionally.

EMDR Therapy: the theory

EMDR therapy is based on the theory that traumatic events are not properly processed in the brain when they happen. Therefore, they continue to affect individuals after the trauma has occurred, such as with nightmares, flashbacks, and the feelings of trauma re-surfacing long after traumatic event. In many cases when something reminds the individual of the trauma, the brain and body react as if it is occurring again, unable to distinguish between the past and the present. EMDR uses the adaptive information processing model in order to "reprocess" this traumatic memory and change the way it is stored in the brain to help an individual move past it. The aim of the therapy is that once the brain properly processes the memory, the individual should be able to remember the traumatic event but not experience the accompanying intense emotional reactions.

EMDR Therapy: in practice

During an EMDR therapy session, a therapist will instruct an individual to briefly focus on a trauma memory. They will then be instructed to perform side-to-side eye movements whilst thinking of the memory. This is known as bilateral stimulation and is carried out in order to engage both sides of the brain. If an individual has visual processing issues, the therapist may use rhythmic tapping on both patient's hands or play audio tunes directed towards both ears. EMDR therapy is broken down into eight phases, so patients will need to attend multiple sessions: usually a minimum of six to twelve sessions.



Phases 1-3

During phases 1-3 (history and treatment planning, preparation, assessment), the therapist will review the patient's symptoms and health history, as well as briefly hearing about the patient's trauma and pinpointing potential trauma memories to address. The patient is then taught a few techniques to help manage and cope with the discomfort that is likely to arise during the treatment. The therapist then helps the patient select a memory to target and think about the uncomfortable sensations that may come from it before beginning.

Phases 4-7: Treatment

The 4 stages of the treatment are:

1) Desensitisation – patient will focus on traumatic thought, memory or image whilst simultaneously be lead through bilateral stimulation. They will then let the mind go blank and identify any thoughts and feelings that arise impulsively.

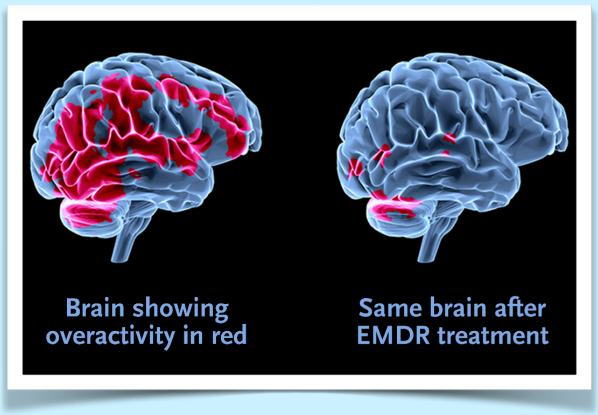
2) Installation – patient will "install" a positive image or self-belief to replace the unwanted one recognised in phase 3. This will be focussed on as the bilateral stimulation is continued.

3) Body scan – if the traumatic memory elicits any uncomfortable physical pain or sensations, bilateral stimulation will be repeated.

4) Closure – at the end of each session, the therapist will discuss the progress that the individual has made as well as other coping strategies that the patient can use in between sessions to sustain the recovery process.

Phase 8: Re-evaluation

At the beginning of the next session, the feelings and memories targeted in the previous session will be discussed to conclude how much progress has been made. If they continue to cause distress, thew will be targeted again in the same way as the previous session; if not, the treatment will be carried out but with a different traumatic memory.



How effective is EMDR therapy?

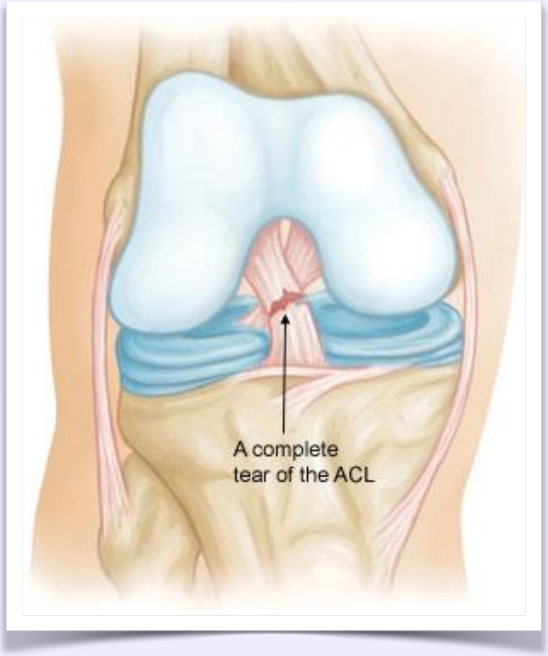
Research has shown that EMDR therapy can be very effective, quickly treating both PTDS and C-PTSD along with the symptoms they bring. There have been several studies that have investigated its effectiveness. One study shows that up to 90% of single-trauma victims no longer have PTSD after only 3 90-minute sessions. In another study, 77% of combat veterans no longer had PTSD in 12 sessions.

ACL Tears: From the Field to Recovery

Falak Awan

The ACL (anterior cruciate ligament) is a ligament found in the knee that joins your femur to your tibia. It is a thick band of tissue holding the cartilage and bone together whilst maintaining the knee's rotational ability. The ACL is one of four major stabilising ligaments in the knee alongside the MCL, LCL and PCL. Knee ligament injuries can be classified into different grades based on the severity. A grade 1 is usually a slight overstretch of the ACL. Grade 2 is a partial tear of the ACL and a grade 3 is a complete tear. People of all ages and physical conditions can tear their ACL but is most common in athletes in high demand sports with women 2 to 10 times more likely than men to obtain these injuries because of hormonal, neuromuscular and structural differences.

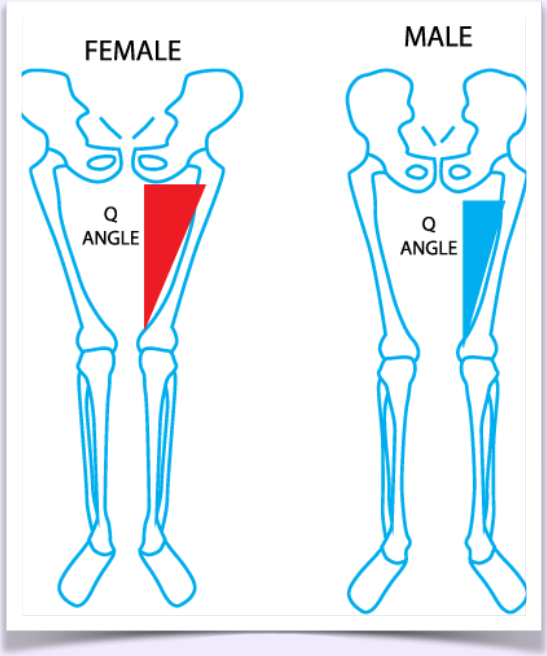
So what causes ACL tears? Nearly ¾ of ACL injuries are non contact. Some reasons for injury include rapid change of direction, change of pace when running, incorrect landing from jumping and direct collision. One of the most common mechanisms of ACL tears is when the foot is planted and direction is quickly changed. This is commonly known as "plant and cut" in sports where the deceleration required for this movement, combined with turning the knee, puts the ACL in a vulnerable position. Another



main function of the ACL is to resist extension as well as extreme varus and valgus. Valgus is a knee position where the kneecaps are pointing inwards and varus is a "bow legged" position. Any combination of these movements including rotation at a high speed can cause an ACL tear.

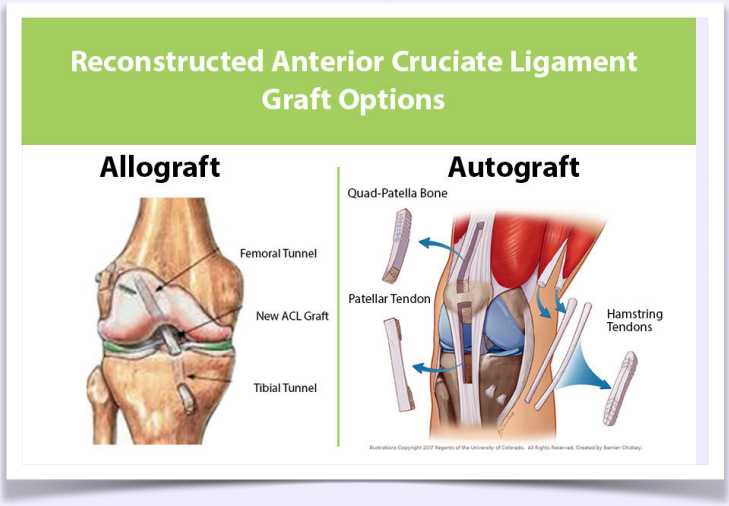
Another interesting concept is how women, especially female footballers, are more likely to undergo an ACL injury than men, with a 8:1 ratio respectively. Football in general is a fast paced sport with many unpredictable movements, tackling, and changes of pace which all contribute to ACL tears. However, what factors make women more susceptible to injury? The first factor is the hormonal difference between sexes. Testosterone, the hormone predominant in men, stimulates something called fibroblast proliferation, whereas the hormone oestrogen in women inhibits this. Fibroblasts are cells

that contribute to the formation of connective tissue by producing collagen and other fibres. Evidence has shown that women are more prone to ACL injury during the ovulation phase of the menstrual change. The second factor is anatomical. The “Q-angle” is a space between the line from the front of the hip to the middle of the kneecap and the line from the middle of the knee to the front of the shin. A female's Q-angle can be 5.8 degrees greater than in males which is



disadvantageous as the larger the Q-angle, the more it pulls on the kneecap, leading to rupture. Another factor is neuromuscular. Women usually have more muscle mass on the front of their thighs compared to the back. The muscle at the back of the thigh helps to pull the shin bone backwards, reducing stress on the ACL. The outer thigh muscles tend to have more muscle fibres than the inner thigh which results in the knee being positioned further away from the body and increasing the risk of injury.

Finally, how are ACL injuries treated and prevented? It is possible to reduce the risk of ACL injury by being aware of how the body moves. ACL injury prevention programmes are evident in reducing injury and modifying poor biomechanical movements. Prevention training that incorporates plyometrics and strengthening exercises can help reduce risk. Depending on the severity of the tear, ACL recovery after surgery can take up to a year. During surgery, the damaged ligament is replaced with a graft, which is



a segment of tendon. Physical therapy after surgery is the most important to help strengthen the muscles and restore stability and function of the knee.

A Cracking Guide to Unboiling an Egg

Mollie Patterson

Firstly, what happens when you boil an egg?

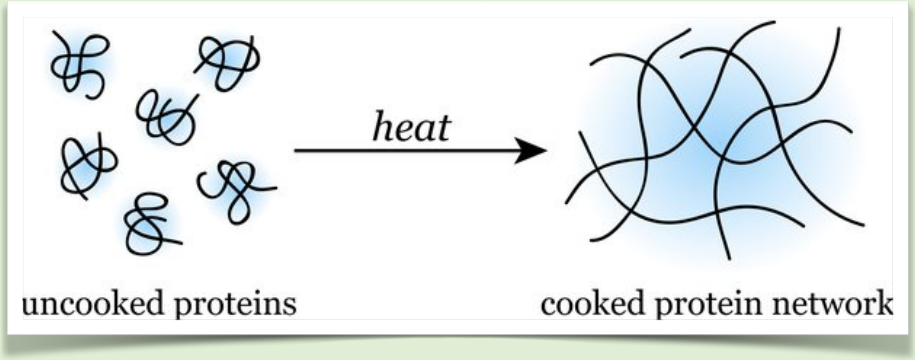
One of the main components found in eggs are proteins; when raw, these globular proteins are in the form of compact, knot-like structures held together by 4 types of bonds:

- peptide bonds that form the primary amino acid chain

- weak hydrogen bonds that fold the amino acid chain into secondary structures

- ionic (and disulphide bonds) that, together with peptide bonds and hydrogen bonds, determine the protein's final shape.

By boiling the egg, these proteins are subject to a lot of thermal energy which results in the weak hydrogen bonds and ionic bonds to break, changing the shape of the protein. As heating continues, the proteins form new bonds which restrict their movement, resulting in a solid, boiled egg.



How can this be reversed…

To reverse this change, the clumped together proteins must be broken apart, and the proteins must be converted back to their original shapes. The egg whites must first be chopped and dissolved in urea and water- this helps to liquify the solid egg whites and break down some of the bonds between proteins.

In order to re-fold the proteins back to their original state, a Vortex Fluidic Device is used to spin the egg-urea solution really, really fast (5000 rotations/minute). The proteins spread out into a thin layer when spun, with the velocity of the solution being greatest at points closest to the container wall. The proteins are flung at the

container and the difference in velocity causes them to undergo continuous stretching and compression; this action is what allows the proteins to regain their original shape. This demonstrated the principle that proteins could have their shape changed but keep their bonding patterns and connectivity the same.

…and more importantly, why?

This process has many more pressing applications than un-cooking your breakfast; the use of the Vortex Fluidic Device will make working with proteins easier and less wasteful. For example, this technique has been adapted to be able to re-fold lab-created proteins associated with cancer, making cancer research more time and cost effective.

FOR RANDOM SCIENCE INTERESTS...

New Scientist Weekly Podcast

Elsa Fraser

Each week the New Scientist releases a podcast and I have been listening to them for several months. What I find particularly enjoyable about this podcast is that I am able to easily explore my subjects beyond the specification by listening to experts from many different scientific areas. The most recent episode I listened to explored the geoengineering plan to slow the melt of Arctic ice, which I think is a really innovative and important solution to a problem affecting many habitats across the world. It builds on GCSE knowledge and therefore I would recommend it to all STEM students.

Entangled Life

Miranda Barron

Recently, I read 'Entangled Life' by Merlin Sheldrake, in which he explores different aspects of the Fungus kingdom and their significance in ecosystems, symbiosis, biotechnology, and more. In particular, I found the discussion of symbiosis between fungi and plants fascinating - without the presence of fungal counterparts, land plants may have never diverted from aquatic algae in early evolution, and terrestrial life as we know it may have never come into existence. It was a fascinating read - I would definitely recommend it to anyone thinking of studying Biology at A level or beyond.

How Does Dementia Affect Psychological Processes?

Clarissa Soto-Rosa

What is dementia?

Dementia is a syndrome associated with an ongoing decline of brain functioning. The word 'dementia' describes a set of symptoms that over time can affect memory, problem-solving, language and behaviour. Alzheimer's disease is the most common type of dementia. According to the NHS, over 850,000 people in the UK have dementia. It is most common amongst the elderly, with 1 in 14 people over the age of 65 and 1 in 6 people over 80 being affected by it. This number is increasing due to people living longer. It has been estimated that by 2025, over 1 million people in the UK will have dementia.

Symptoms and consequences of dementia

Dementia is a group of symptoms. It is caused by different diseases that damage the brain. Some of the symptoms include:

· Memory loss

· Decline in thinking speed

· Difficulty with language, such as using words incorrectly, or trouble speaking

· Confusion and needing help with daily tasks

· Problems with judgement and understanding

· Problems with regulating mood

· Hallucinations

Some of the consequences of these symptoms include:

· Loss of interest in usual activities, which sometimes leads to problems managing behaviour or emotions

· Difficulty with social situations and loss of interest in relationships and socialising

· Parts of their personality changing, this can include a loss of empathy

· As a result of losing the ability to remember events, or not completely understand situations or their environment, it may seem as though they are choosing to ignore problems or are not telling the truth

· Difficulty to maintain independence as dementia affects their mental abilities, so planning and organising can become a problem

Dementia is progressive, meaning that the symptoms get worse over time. So, although they may be relatively mild at

first, in the late stages of dementia, people often cannot take care of themselves and sometimes become unable to communicate.

What causes dementia?

Dementia is caused by a disease damaging nerve cells in the brain. As nerve cells are responsible for carrying messages between different parts of the brain and to other parts of the body, as more nerve cells become damaged, the brain becomes less able to work properly. Dementia can be caused by different types of diseases, which impact the brain in different ways and can result in different types of dementia. Some causes for the damage to brain cells include, advance in age, family history, damage to blood vessels of the brain, metabolic and genetic disorders, accumulations of clumps of protein in the brain, brain tumours and certain medications.

Types of dementia

Approximately 19 out of 20 people with dementia have one of the main four types. Some people also have mixed dementia, which is where they have symptoms of more than one type. Although the effects of dementia vary from individual to individual, each type has some common early symptoms (listed in the symptoms above).

Alzheimer's disease Early signs: problems with language, vision, thinking, or perception. Caused by an abnormal build-up of proteins in and around brain cells. As brain cells become affected there is also a decrease in neurotransmitters (chemical messengers) involved in sending signals (messages) between brain cells. Over time, different areas of the brain shrink. The first of these tend to be those that are responsible for memories.	Vascular dementia Early signs: problems with planning or organising, making decisions or solving problems. Caused by a reduced blood flow to the brain cells, damaging them, and eventually they are killed. This is usually due to a stroke, lots of "mini strokes" (also known as TIAs that cause tiny but widespread damage to the brain), or the narrowing of the small blood vessels inside the brain (known as small vessel disease).
Dementia with Lewy bodies (DLB) Early signs: confusion or sleepiness, experiencing hallucinations, problems with movement and sleep, tremors and slow movement . Caused by clumps of protein forming inside brain cells. These abnormal deposits are called Lewy bodies. The same deposits are found in people with Parkinson's disease, and they build up in areas of the brain responsible for functions such as thinking, visual perception and muscle movement.	Frontotemporal dementia: Early signs: changes to personality and behaviour, difficulties with language, difficulties with mental abilities, memory problems. Caused by clumps of abnormal protein forming inside brain cells, which damage the cells and prevent them from working properly. The proteins mainly build up in the frontal and temporal lobes of the brain at the front and sides. These are important for controlling language, behaviour and the ability to plan or organise. There is often a genetic link, though it is not fully understood why this happens.

Treatments for dementia

At the moment there is no cure for dementia, but there are medicines and treatments available which aim to reduce and slow the progression of the condition. Some medicines are taken to treat the chemical processes in the brain, such as acetylcholinesterase inhibitors which prevent enzymes from breaking down a substance in the brain called acetylcholine which helps nerve cells communicate with one another. Other medicines treat related conditions or some of the symptoms of dementia, such as stroke, diabetes or depression. Some also treat behaviour, particularly in the later stages, where many people develop what are known as "behavioural and psychological symptoms of dementia (BPSD)". Some of these symptoms include anxiety, hallucinations and aggression. Other treatments do not involve medicines and support those with the difficult symptoms of dementia, particularly involving interacting with one another. For example, cognitive stimulation therapy, which involves taking part in group activities and exercises designed to improve memory, problem-solving skills and language ability. Also, reminiscence and life story work which involves talking about events and possessions in your past can help.

FOR MORE ON AGEING

Being Mortal - Auto Gawande

Lottie Ward and Ella Ng

This book discusses the importance of quality of life and how people can better live with age-related frailties. Doctors should help patients have those conversations regarding their priorities for their end of life care to ensure that it is the most comfortable. He also discusses how important hospices are for alleviating suffering and helping people enjoy the time that they have left, as an alternative to surgeries or extensive treatments. He discusses how medicine has changed the way people enjoy ageing - people think of it as a failure rather than a natural process. Because of this, ageing can be an uncomfortable topic to discuss so most people aren't prepared to make important decisions later in life. This was a very interesting and moving read and would recommend it to any future medics!

Fibonacci Numbers, Complex Numbers and the Golden Ratio

Dr Rolfe

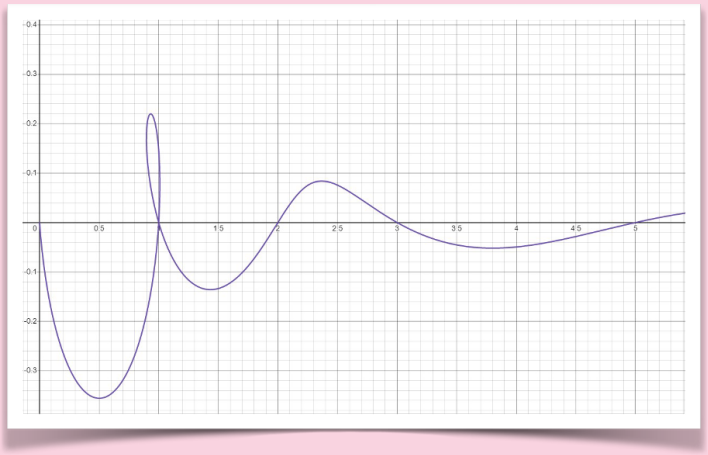


Figure 1

Figure 1 contains a graph that I was shown recently. At first glance, the graph has an unusual loop before oscillating above and below the x-axis. Identifying the x-intercepts reveals an interesting pattern: the graph crosses the x-axis at 0, 1, 1, 2, 3, and 5. In fact, this graph only crosses the x-axis at the Fibonacci numbers.

Most students will be familiar with the Fibonacci sequence of numbers:

0, 1, 1, 2, 3, 5, 8, 13, 21…

Where each term in the sequence is obtained by adding the previous two terms. Some students will also be familiar with the fact that the ratio of two consecutive numbers tends to the golden ratio, φ. For example, 21/13 = 1.6154 to 5 significant figures, while φ = 1.6180 to five significant figures.

The link between Fibonacci and the golden ratio may not be apparent at first. To explain the link, we must look at the shape which defines the golden ratio, the golden rectangle. This is a rectangle which has side lengths such that it can be split into a square and a second, smaller golden rectangle, as shown in Figure 2:

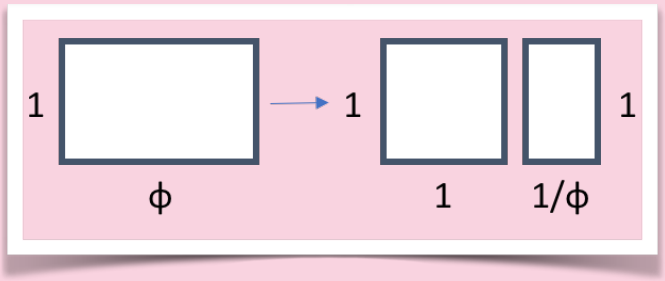


Figure 2

Figure 2 demonstrates that φ = 1 + 1/φ, or, with a little rearranging:

$\phi \hat{} 2=\phi+1$ Eqn 1

This equation is quadratic, so it has two solutions, which I will call φ and φc.

$\phi=(1+\sqrt{5})/2 \quad \phi\_c=(1-\sqrt{5})/2$

The second solution, which is negative, is known as the golden ratio conjugate. Many people choose to ignore the golden ratio conjugate, as it is negative. This is a bit harsh on the golden ratio conjugate, as it is extremely important – watch out for it later!

To make the link between the Fibonacci

numbers clear, we need to calculate the powers of the golden ratio. Equation 1 allows us to simplify the powers.

Power	Working	Result
φ0	1	
φ1	φ	
φ2	φ+1	
φ3	φ(φ2) = φ(φ+1) = φ2 + φ	2φ + 1
φ4	φ(φ3) = φ(2φ+1) = 2φ2 + φ	3φ + 2
φ5	φ(φ4) = φ(3φ+2) = 3φ2 + 2φ	5φ + 3
φ6	φ(φ5) = φ(5φ+3) = 5φ2 + 3φ	8φ + 5
…	…	
φn	F(n) φ + F(n-1)	

With a bit of working out, we see that raising the golden ratio to the power of n gives an expression for the nth and n-1th terms in the Fibonacci sequence. Take some time to try this: it is quite satisfying.

Now we have explained the link between Fibonacci and the golden ratio, but where did that graph come from? This is where the golden ratio conjugate comes in handy. As equation 1 also applies to the golden ratio conjugate, we can write equations 2 and 3:

$$F(n)\phi+F(n-1)=\phi^n \quad \text{Eqn 2}$$

$$F(n)\,\phi\_C+F(n-1)=\llbracket\phi\_C\rrbracket\ ^n \quad \text{Eqn 3}$$

Subtracting equation 3 from equation 2 gives:

$$F(n)\ \llbracket(\phi-\phi\rrbracket\ \_C)=\phi^n-\ \llbracket\phi\_C\rrbracket\ ^n \quad \text{Eqn 4}$$

$$F(n)=(\phi^n-\ \llbracket\phi\_C\rrbracket\ ^n)/\ \llbracket\phi-\phi\rrbracket\ \_C \quad \text{Eqn 5}$$

Equation 5 gives an expression for the nth Fibonacci number. This equation is known as Binet's formula, after Jacques Phillipe Marie Binet (1786 – 1856), although this formula was known for at least a century before Binet. As n increases, the golden ratio conjugate term, which is a negative fraction, gets smaller and smaller until it tends to zero (so you can ignore it if n is high enough – sorry, golden ratio conjugate!). This means that for high enough Fibonacci numbers, you can just multiply the previous term by the golden ratio.

I would like you to take some time to appreciate how crazy Binet's formula is – using the golden ratio (an irrational number) to build a set of integers seems like it shouldn't work, but it does. Finally, let's get back to the graph in Figure 1. What is going on there? Well, Binet's formula has another interesting property. If you ignore n being a whole number for a second and plug in a fraction (such as n = ½), Binet's formula returns complex numbers, because you are trying to find the root of a negative number. Complex numbers have two parts: a real part and an imaginary part. The real part is a number of the sort that you are most familiar with, whereas the imaginary part is a factor of the square root of -1. I personally don't like calling them 'imaginary,' as these numbers are used in many real applications, from electrical engineering to communications, but that is just my opinion.

To find the real and imaginary parts, we start by noting that:

$$\phi - \phi_C = \sqrt{5} \quad \text{Eqn 6}$$
$$\phi_C = -1/\phi = -\phi^{-1} \quad \text{Eqn 7}$$

Thus, Binet's formula can be re-written as

$$F(n) = (\phi^n - [\![\phi^{-n}\,(-1)^n)/\sqrt{5} \quad \text{Eqn 8}$$

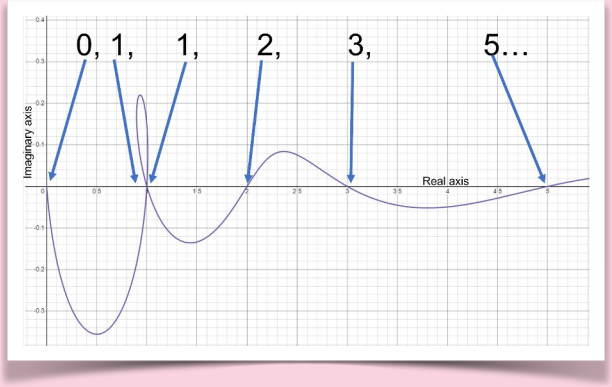
Using the handy fact that $(-1)^n = \cos(n\pi) + i\sin(n\pi)$, we see that:

$$F(n) = (\phi^n - \phi^{-n}\,(\,[\![\cos([\![n\pi) + i\sin([\![(n\pi))]\!]\,]\!]\,)/\sqrt{5} \quad \text{Eqn 9}$$

We can now break the function down into real and imaginary parts: Real part:

$$\mathrm{Re}(F(n)) = (\phi^n - \phi^{-n}\,[\![\cos([\![n\pi)]\!]\,)/\sqrt{5} \quad \text{Eqn 10}$$
$$\mathrm{Im}(F(n)) = (-\phi^{-n}\sin(n\pi))/\sqrt{5} \quad \text{Eqn 11}$$

We can now obtain the graph by plotting the real part on the horizontal axis and the imaginary part on the vertical axis (Figure 3). And the points where n is an integer give the Fibonacci numbers, which lie on the real axis.



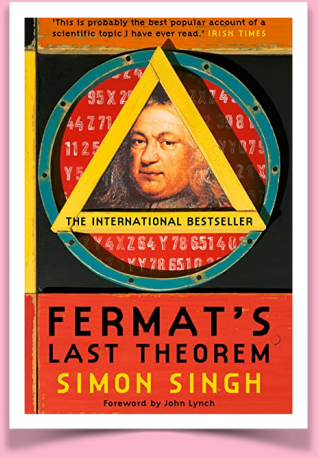
If you are interested, I have made an interactive graph on Desmos to explore further. The link is https://www.desmos.com/calculator/dpv3uzzty0. This will allow you to explore other sequences such as the Lucas and Pell numbers, and calculate some other metallic ratios.

MORE MATHS?

Fermat's Last Theorem - Simon Singh

Annie Jakes-McKay

A gripping story written by a journalist encapsulating the journey Andrew Wiles took to prove the theorem, interviewing various experts. It was fascinating to see different perspectives of the theorem. I would say that it contains a lot of complex maths language so I think it's suitable for GCSE and up!

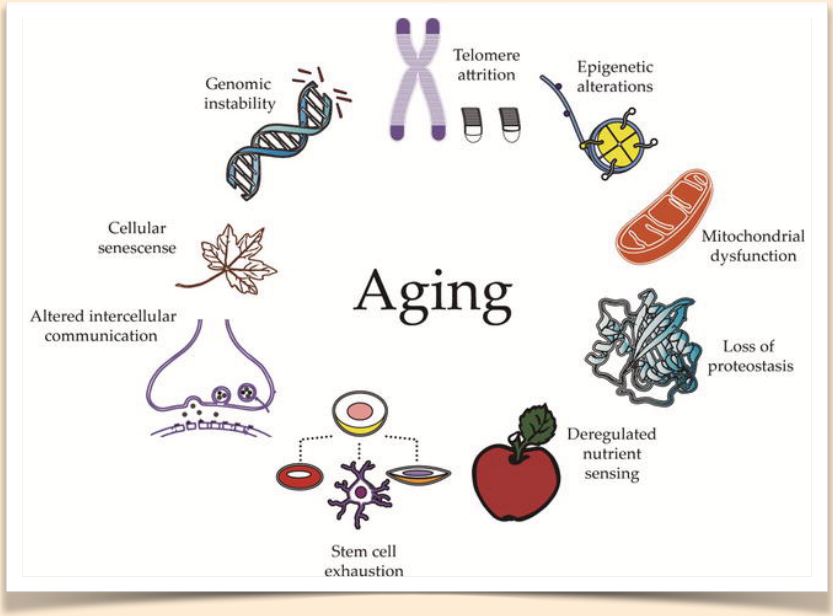


Is Ageing a Disease?

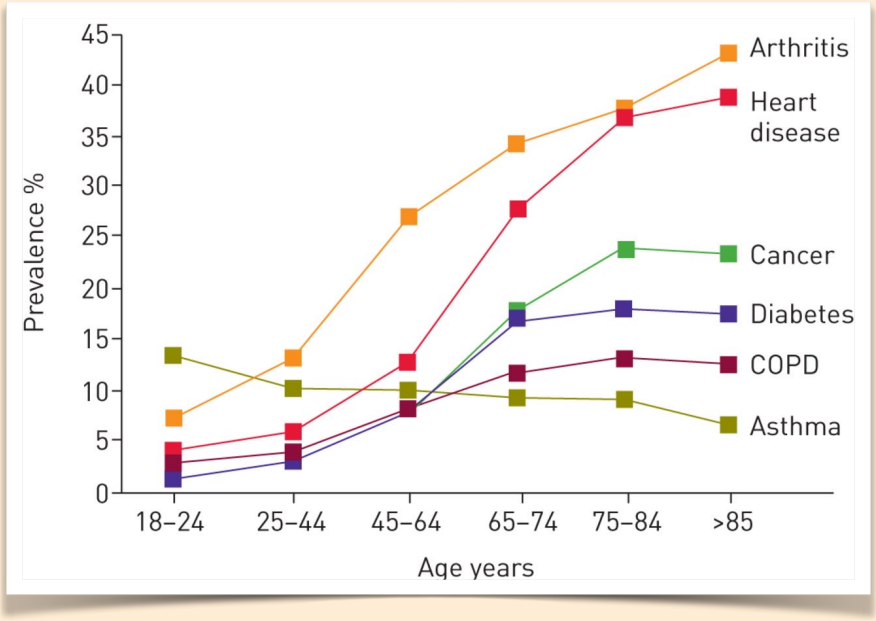
Reham Abdelmagid

This has been an ongoing debate for many years; the question recently came to light when the WHO had a plan to replace their diagnosis of “senility” with “old age”, as it was more of a broad category. There are many conflicting opinions, and I will cover different viewpoints in this article.

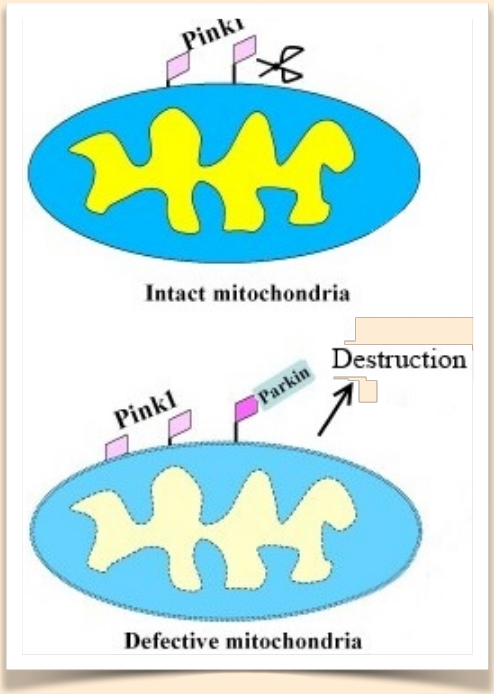
As you become older, you are usually more susceptible to getting chronic diseases and your body starts to slowly stop producing cells. So, why is this happening? Despite making good lifestyle choices at a young age, such as maintaining a good diet and exercising regularly, your body will continue to get weaker as you become older. Ageing is the decline of function with time, according to Simon Melov, a professor at the Buck Institute for Research on Ageing.



The definition of disease itself has changed a lot in the medical field. The medical definition is any abnormality of bodily structure or function, apart from physical injuries (Marcovitch, 2009). Therefore, according to this definition, then ageing is a disease. However, many researchers suggest that considering ageing a disease, alludes to the fact that it is preventable. Despite this, in this present day, the ageing process is inevitable. Labelling ageing as a disease would be harmful especially in our current society that is obsessed with youth. This can have a detrimental effect as it creates an unhealthy mindset; the fact that the person is old means that they expect illness. This implies that since ageing is a disease, people should not improve their lifestyle by incorporating a healthy diet and regular exercise. Indisputably, getting older does make it more likely for diseases to develop, but we should not encourage this problematic approach to ageing. This would be counterproductive and instead scientists should aim to research the process of age-related cellular deterioration.



Intrinsic ageing occurs in all humans. This process is when cells begin this degenerating process as it enters senescence (the cells become older). The cells in our body start to perform cell division less and cells are replaced at a slower pace. This in turn means that organs cannot function as well as it relies on cells being renewed. Your body doesn't work as well and can develop diseases more easily; indicating that ageing is a risk factor for developing diseases. Although recognising that ageing is a disease is controversial, there are some researchers who acknowledge the advantages of this. According to David Sinclair, professor at Harvard Medical School, by not recognising that ageing is a disease, it slows down the development of potential cures of life-threatening diseases. The director of UCLA's Ageing centre, Ming Guo, is researching ageing reversal approaches and her team showed that it could remove nearly 95% of damaged mitochondria in fruit flies. This shows promising progress in the potential reversal of ageing. Looking into the ageing process in depth means that we can potentially find causes for diseases, and it will likely prolong the lifespan of many people.



So, is ageing a disease? I believe that the best antidote to ageing is maintaining a healthy diet and regular exercise in the end. Nevertheless, our healthcare system should recognise that ageing is the underlying cause of many chronic diseases in our elderly population. Recognising this can allow for more progress in tackling chronic diseases such as cancer.

How Do We Know Medications Are Safe to Take?

Daisy Hart

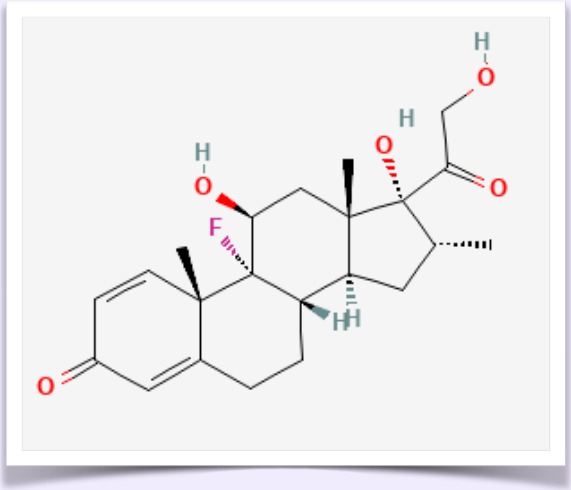
When we are unwell we visit our doctor or the pharmacy and are prescribed medication that the majority of people have full confidence they will be safe and effective for the condition that we have sought help for. Doctors ask routinely about allergies (e.g. penicillin) but otherwise there is an assumed trust that these medications on balance have much greater benefit than risk of unwanted side effects. Most medications have some occurrence of side effects in a minority of people, most of which are likely to be minor but occasionally can be more serious. The British National Formulary (BNF) is a regularly updated reference book listing all available medicines and their known potential side effects. The BNF is used routinely by prescribers: doctors, nurse prescribers & pharmacists. They use the side effect detail to inform their patients of what to expect when starting a new medicine. Why do we have trust in the medications that we are prescribed? The answer is that there is a thorough, structured process that ensures that new medicines are carefully tested in clinical trials, from the design point to the production point making sure they are both safe and effective.

There are four stages to a clinical trial during the process of a new drug approval. Phase I involves a small number of healthy volunteers and allows analysis of the side effects of the new treatment (e.g. does it raise blood pressure or cause nausea?). Phase II continues to use a small number of people but they tend to have the condition that the medication is aiming to treat, so the effectiveness of the drug can be tested and the correct dosage can be calculated. Phase III is a longer trial with even more people (generally hundreds or thousands) who are usually randomly selected to receive treatment and sometimes a placebo is used. The purpose of this stage is to assess how well the treatment works over a period of time in a population big enough to represent the wider community. The final phase IV of a clinical trial occurs once the medicine has been approved by the drug regulatory authority to gather information about the effectiveness of the medicine within various populations in the real world setting. This also allows surveillance for any long-term side effects of the drug, particularly looking out for any rare side effects that may not have occurred in the earlier trial phases examining smaller numbers of patients. This clear procedure allows for thorough analysis of new medicines before public use (or in the very early stages of use) to ensure the benefit is far greater than any possible side effects.

There are a variety of different processes for medicine approval in different countries, but they all follow the same

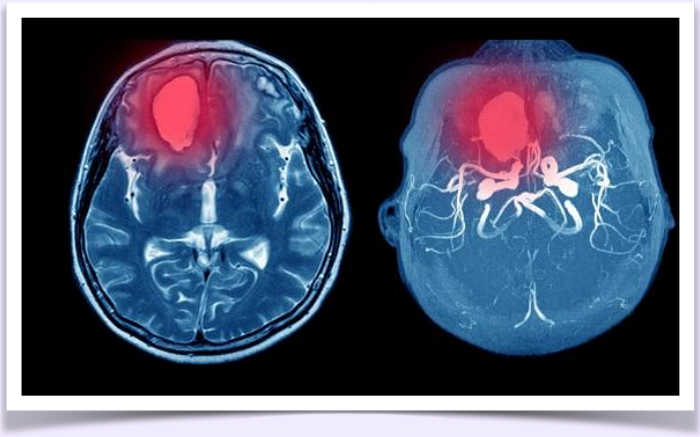
fundamental process of the described trial designs to provide data that supports a medicine being approved for general use. However, the organisation that approves the new medicine will vary. In the U.S the FDA (food and drug administration) oversees the drug approval process whereas in the EU, the EMA (European Medicines Agency) takes on this role. The UK left the EMA in 2020 after the decision to leave the EU was made and now has a new system with the MHRA (medicines and healthcare products regulatory agency) being responsible for approving or rejecting new products.

The NIHR (national institute for health and care research) is responsible for the funding and delivery of research that improves peoples' health and well-being in the National Health Service (NHS). The NIHR have contributed to numerous successful clinical trials that have resulted in discoveries that have positively impacted countless lives worldwide. For example, they helped deliver pioneering trials for the severe bleeding disorders, haemophilia A & B, with the imminent approval of use of gene therapy for these conditions. Additionally, the NIHR played a major role in COVID-19 research, recruiting over a million people to help, and supporting the RECOVERY trial which was the world's largest clinical trial into treatments for COVID-19. The RECOVERY trial was led by Oxford university but supported by the NIHR and had 40,000 participants across 185 trial sites in the NHS. Researchers found that the inexpensive steroid called dexamethasone lowered the mortality rate



among COVID patients receiving breathing support in hospitals. This discovery reduced death rates by up to one third and consequently is estimated to have saved one million lives globally by March 2021. This clinical trial was immensely successful and amplifies the global importance of such trials - to understand a disease and how to find medicines to treat it . Another recent success in clinical trials was the development of the COVID-19 vaccinations. However, because of the acceleration of the trialling and approval of the vaccination during the pandemic, it created a level of scepticism and hesitation within a subgroup of the public, often circulating stories/conspiracy theories on social media. The creation of the vaccination became a global focus due to the devastating effect of the first COVID wave and therefore the major funding and global teamwork enabled the high speed process that would not normally have

been possible for other medicines. However, this speed of development uncovered doubt within some communities, leading to an anti-vaccination (anti-vax) movement. In addition to the hesitation around the speed at which this complex scientific research took place, further doubt was created around the AstraZeneca vaccine due to the vast media coverage around the extremely rare complications (VITT – vaccine induced thrombotic thrombocytopenia). Areas of the public



believed that this complication should have been predicted or picked up on sooner, however because of how rare this complication was (there were 260 VITT cases in the UK after 30.8 million administered AZ vaccine doses) this wasn't possible which unfortunately fuelled the scepticism and reluctance further. The vast numbers of people involved in the vaccination trial programme ensured that just because the complex research was completed in a short time frame, it was equally safe to if it had been completed over a number of years. Again, this uncovered the necessity for a structured drug approval process as, in the case of a pandemic, when an immediate new vaccination is needed, a structured process allows for the procedure to be accelerated without vital safety measures being omitted. The detection of the rare VITT complication demonstrated how the ongoing surveillance for and reporting of expected and unexpected side effects for medicines is important. This is called pharmacovigilance.

Despite how preventative this structured process can be to mistakes being made, there have been a few tragedies across history that have led to a revision of pharmacovigilance. The recent contaminated blood inquiry is an example of this. In the 1970-80s, people suffering from bleeding disorders were contaminated with HIV and hepatitis C through contaminated clotting factors during routine blood transfusions. This happened as a result of a blood donor shortage in the UK leading to blood being imported from the U.S. In order for the process to be kept cheap, blood was taken from prisoners, many of whom were drug addicts, meaning their blood was more likely to be infected. These risks were either not fully understood or potentially ignored by some leading clinicians and the government and this information wasn't shared with the patients receiving these American transfusions. At the time, people assumed that those suffering from haemophilia were also infected with AIDS which forced many to hide their condition

due to this stigma. Families were subject to abuse and forced out of jobs in extreme circumstances. 1243 people (including young children) were infected with HIV with fewer than 250 of those infected still being alive. Including complications of hepatitis C, it is thought 3,000 patients have died from this contaminated blood problem. In 2017, Theresa May launched an investigation and so far each victim has received an interim compensation of £100,000.

Another well known tragedy was with thalidomide. It took 5 years for the connection between thalidomide taken by those pregnant women and the impact it had on their children to be made. The drug was taken by pregnant women in the 1950s to treat morning sickness and was seen to be harmless, but it was discovered that the medication could harm the foetus by passing through the placental barrier if taken at a certain point during the pregnancy. Thalidomide was withdrawn in 1961 after 10,000 babies had been affected worldwide with around half having died within months of being born. One reason that the discovery of the damage took so long, was that the medicine was used with different names around the world, and the range of symptoms was wide. Symptoms varied from damage to limb formation and being born without arms or legs, to loss of eyesight and hearing and were commonly confused with some genetic conditions that affect upper and lower limbs.

In retrospect, there have clearly been a number of past drug approval decisions that have fallen below our current threshold of safety. This has allowed for adjustments to be made to refine the process to ensure that all precautions are taken and make the discovery and trial of new medicines as safe as possible.

FOR ASPIRING MEDICS:

The Good Nurse - Tati Lumb

I recently watched The Good Nurse on Netflix which I found gripping. It tells the true story of a Nurse hired in ICU who turns into a murderer by injecting insulin into saline bags. The saline bags are then given out to patients. They think he's killed over 400 people however he has only admitted to 20. He is currently serving three consecutive life sentences and I would recommend it to those over 15 as it is quite dark!

Telomeres and the Telomerase Complex

Miranda Barron

Chromosome breaks are surprisingly common. In fact, it has been estimated that double stranded breaks occur around 10-50 times a day per cell. Fortunately, most of the time this is not significant; DNA repair mechanisms efficiently pinpoint these breaks, re-joining broken chromosome ends in a matter of nanoseconds. However, issues begin to arise when two chromosomes break simultaneously. DNA repair machinery is relatively effective in targeting single breaks, immediately joining the two fragments of the chromosome. However, when two breaks occur at the same time, the ends of chromosomes may be joined up incorrectly if the repair machinery is unable to recognise which break happened on which chromosome. In these cases, hybrid chromosomes are formed which are then passed on to daughter cells during subsequent divisions. This is significant as the position (locus) of a gene within a chromosome is essential for determining its expression, or the rate at which protein is produced from it. When a gene is moved or rearranged to another locus, such as through incorrect chromosome repair, its expression may be altered. A prime example of a consequence of this is a condition called Burkitt's lymphoma, caused by the rearrangement of chromosomes 8 and 14. This can lead to a strong overexpression of the Myc gene which consequently triggers cells to aggressively proliferate.

Fortunately, eukaryotes have evolved a system to prevent this, which involves long stretches of non-coding DNA. These sequences are referred to as telomeres, and are composed of a combination of repeating patterns of base pairs (TTAGGG) and a number of associated proteins that aid in maintaining their structural integrity. Essentially, telomeres act as markers for repair machinery to recognise chromosome ends, allowing them to be recognised and correctly joined together. Experiments using mouse models have demonstrated the importance of this process; mice with telomeres engineered out of their chromosomes almost always die in very early development as their repair machinery cannot recognise chromosome ends, resulting in normal chromosomes being joined together to form a slew of hybrids. This triggers a form of apoptosis (programmed cell death) due to the formation of extremely dysfunctional proteins.

Telomeres carry out another important function. With every cell division, the sequence of non-coding bases that makes up the telomere shortens as DNA copying systems cannot reach all the way to the end of each chromosome. Each time a cell divides, more of the telomere sequence is lost – an advantageous process that prevents the loss of important exon sequences. However, when telomeres

become critically short, cell senescence or apoptosis is triggered. To maintain a suitable length throughout cycles of division, our cells have evolved a system that involves adding new TTAGGG motifs back onto our telomeres in order to restore those that have been lost. This typically involves telomerase enzymes adding these sequences back onto chromosome ends, using a piece of RNA to act as a template for correct base addition. The activity of this restorative processes varies between different cell types; for example, cancer and stem cells often display high levels of telomere restoring activity, allowing them to rapidly proliferate and bypass senescence. In essence, our cellular systems will only maintain telomeres at a sufficient length so that we live long enough to reproduce, but not so long that we die an early death from cancer.

It comes without surprise that faults in this telomerase complex can lead to disease - whether that be through mutations in the genes encoding telomerase enzymes, RNA templates, or the structural proteins within the complex. In most cases, these mutations result in telomeres shortening at a faster rate than in healthy individuals, leading to symptoms that are associated with premature ageing. Interestingly, examining the effect of these mutations has allowed scientists to identify the causes of diseases previously considered idiopathic (having no known cause). Telomeric diseases often have an unusual pattern of inheritance, with the first affected generations often experiencing milder symptoms later in life, whilst subsequent generations, perhaps surprisingly, experience increasingly severe symptoms earlier in life. The symptoms appear to worsen over generations.

This can be explained by reduced or atypical activity of the processes that restore our telomeres. As previously mentioned, the telomerase complex is usually most active in germ cells. This is essential in evolutionary terms; long telomeres must be passed down to offspring to ensure that they live long enough to reproduce. However, in some families, mutations in genes encoding telomerase enzymes or accessory RNA factors may inhibit this enhanced activity in germ cells, hence each subsequent generation will inherit shorter chromosomes. As certain conditions only develop when telomeres reach a certain critical length, each successive generation may display different, and usually more severe diseases and symptoms. Whilst a grandparent may have relatively long telomeres and be asymptomatic, the following generation may inherit shorter sequences, and the third generation may inherit telomeres that are even shorter - enough to trigger conditions such as aplastic anaemia early in childhood.

Features

Medicine in the News

Laila Samarasinghe

Islamophobia in the NHS

Many Muslim healthcare professionals in the NHS are feeling marginalised and often forced to choose between their profession and faith. According to a survey in the Huffington Post two years ago, 81% of Muslim healthcare workers have experienced islamophobia or racism in the workplace and 57% feel it holds them back in their NHS career. This discrimination extends from medical school, where some Muslim students felt left out due to the huge drinking culture and continue to face it in the workplace. An example of this was when a female healthcare worker reported being asked by a doctor, "How can you be an intelligent woman and wear that [hijab] on your head?" This should be unacceptable today and it is the responsibility of people within the NHS to become more accepting of different people and their faiths and cultures.

(Source: the doctor. October 2022. BMA)

Vaping Myths

At King College London, scientists are encouraging people not to start vaping if they have not already. Many people believe it to be "safe" as public health messages are saying it has fewer health risks than smoking. Whilst it has been found that vaping nicotine is less harmful than smoking cigarettes for a short amount of time (evidence review commissioned by the government), this does not make it "risk free" at all. More studies are recommended for long term effects as we do not fully understand the health risks.

(Source: Private healthcare boom piles pressure on NHS GPs. The BMJ. 8 October edition)

Fewer Children getting vaccinated

Parents are being encouraged to make sure their children get all the vaccines they are eligible for. However, last year the 95% aim set by the WHO was not met, with only 89.2% of 24-month-old infants getting their MMR first dose. This can lead to an increase of preventable health problems.

(Source: Private healthcare boom piles pressure on NHS GPs. The BMJ. 8 October edition)

Cost of Living crisis

With prices rising, patients are cutting back on their use of paid-for medication to make it last longer and save on costs. This has been shown by a poll from the Asthma+Lung UK charity, which found that 1/6 of asthmatics were using their inhalers less so it would last for longer and 5% were getting one from someone who does not have to pay. The chair of the Royal College of General Practitioners said that the government needs to fight the “financial barriers that are restricting some patients' access to the medication.”

(Source: Private healthcare boom piles pressure on NHS GPs. The BMJ. 8 October edition)

Increased use of NHS talking therapies

From 2021-22, the number of people in England using NHS talking therapies has increased by 21.5% (in an NHS Digital report). This has helped people with mental health conditions such as anxiety and depression. Also, the number of patients completing the course for Improving Access to Psychological Therapies programme has increased by 4.6%.

(Source: Private healthcare boom piles pressure on NHS GPs. The BMJ. 8 October edition)

Discrimination in the NHS

A recent survey by the Black Equity Organisation has found that 3/4 of black people from 18 to 34 years old feel that they have been subject to prejudice by healthcare workers. This is especially seen in maternity care, where patients felt ignored and that their pain was dismissed by practitioners. Furthermore, black patients were less likely to be offered talking therapy and had more intrusive treatments.

(Source: Gareth Lacobucci. Private healthcare boom piles pressure on NHS GPs. The BMJ. 8 October edition)

Long waiting time for mental healthcare patients

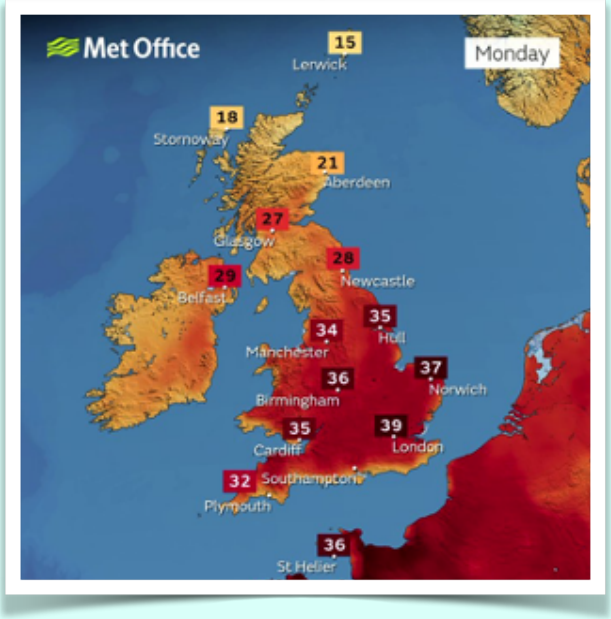
Close to 1/4 of mental healthcare patients have a waiting time of over 12 weeks to begin treatment according to the Royal College of Psychiatrists. In their poll of 535 British adults with a diagnosed mental illness, almost 80% went to emergency services or turned to a crisis line during the long wait between their first referral and the second appointment as they were not receiving enough support. This shows the need for more healthcare workers to improve the support as wait times are far too long.

(Source: Climate crisis: finding hope amid despair. The BMJ. 15 October edition)

Heatwave deaths over summer

From June to August this year, 2800 elderly people died during the heatwaves who would not have if not for the heat (according to the UK Health Security Agency). This shows that we must change our habits over summer to keep cool and stay safe as temperatures rise. This is especially applicable to the elderly and people with heart and lung conditions.

(Source: Climate crisis: finding hope amid despair. The BMJ. 15 October edition)



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Word Search
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Embryogenesis
Cholesterol
Computer
Transplant
Electron
Vaccine
Anastomosis
Trauma
Virus

Answers

Word Search

Embryogenesis	Cholesterol	Computer
Transplant	Electron	Vaccine
Anastomosis	Trauma	Virus

Thank you to all our contributors!

We look forward to handing over to the new team next term!

Under the Microscope

Issue 6 - Processes - December 2022

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