Leicester Grammar School's

YOUNG SCIENTISTS journal

How we got to the moon?

An article investigating the rockets and technology used to get humans onto the moon

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ISSUE 6 LENT TERM 2019

A Message from the Team:

“With this being our sixth issue, it marks a change in the editorial team for our school’s Young Scientist Journal (YSJ) as the previous year 12 team have taken over from the departing year 13s as they have embarked on the next stage of their education. We would like to take this opportunity to thank both Maria and Prab for not only introducing our school to the YSJ initiative and instilling its philosophy, but for also guiding us through this transition. Despite this change in leadership, there is still great continuity in our aims; we strive to incorporate participation from pupils of all ages and we definitely encourage scientific passion and curiosity to shine through in our issues. We truly believe that our pupils’ scientific minds are something special and should be celebrated in abundance through the YSJ. Looking forward to the future, in addition to the termly issues, we would also like to expand the YSJ community in our school possibly by the introduction of an inaugural competition involving pupils being given the opportunity to present their ideas or topics of interest to a panel of judges with interactive voting by the audience. However, we are in the early stages and so are open to any suggestions; after all this is a magazine by the pupils, for the pupils! This issue sees the topics of the moon landings, gene therapy and cardia arrest in sport (to name a few) being discussed.

A reminder to all budding scientists throughout the school of all ages that any input, whether that be writing an article or helping designing the layout of the magazine, is much appreciated and valued. If you would like to get involved then please don’t hesitate to contact lgsyoungscientists@gmail.com or alternatively come to one of our meetings on Thursday break-times (specific details are read out in daily notices).

We would like to acknowledge the following for their contribution:

The LGS Editorial Team:

Marcus Teo / Zain Girach — Chief Editors

Writers:

Oscar Schwabe

Joey England

Tejas Easwar

Keshen Pathmanathan

Mohamed Hassouna

Zain Girach

Harroop Bola

Teachers:

Mr Reeves

Dr Griffin

Articles in this issue:

Who are We?

We are a collection of Leicester Grammar School students who have come together to produce a variety of pieces of writing about the world of STEM. As a school, we have become a hub for the Young Scientists Journal, an international peer-review written and edited entirely by young people.

Contact Us

Anyone interested in joining the YSJ to help to write, edit and publish is more than welcome to meet us at our meetings during lunchtimes (specific details will be in the daily notices). We welcome submissions from all year groups on any scientifically-related topic; so come along to a meeting or email us at:

lgsyoungscientists@gmail.com

See more of the Young Scientists Journal at:

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Are Sodium Ion batteries the future?

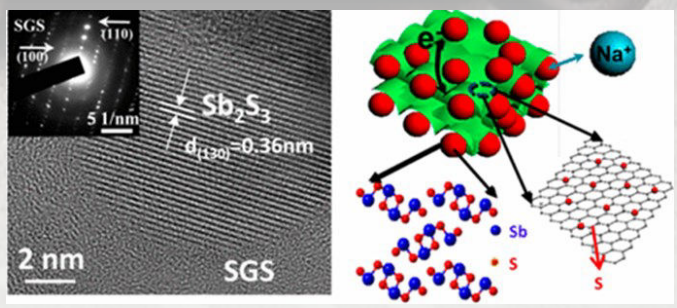
Oscar Schwabe discusses the use of a possible future energy source

Lithium ion batteries have become essential to most of the gadgets in everyday life. They also appear to be essential in efforts to minimise CO_2 emissions; in electric vehicles and storing energy from renewable sources when it is not available. Bloomberg reports that electric car production is set to increase to more than thirty times current levels by 2030 and many countries including the UK have said that they will ban sales of petrol and diesel vehicles by 2040. It is clear that demand for lithium is only going to increase.

However lithium is expensive, at over $20,000 per ton and resources are not unlimited. The U.S. Geological Survey estimates that there are around 39.5 million tons of lithium that could viably be extracted in the future. Current usage is 37,000 tons per year but at the rate that demand will increase, some estimates suggest that this lithium could only last for 50 years. There is lithium in seawater but it is at such low concentration that its extraction is very energy intensive. Sodium however, is far more abundant and could provide a solution.

A battery works, in simple terms, by storing electrons at the sodium cathode and then during discharging these travel to the anode. The limitation of sodium ion batteries is the performance of the anode because it has been difficult to make a battery that retains capacity over many charge-recharge cycles.

Graphite is used in lithium ion batteries but this doesn't work for sodium ions. A paper published in ACSNano by Meilin Liu, Chenghao Yang and colleagues, suggests that they have found a material for the anode that performs better retaining 83% capacity over 900 cycles. They material used was "nanostructured Sb_2S_3 on sulphur-doped graphene sheets."



There is research into many other options too, and as yet sodium ion batteries are not commercially available. But it is clear that there is potential and given the amount of research going on and the obvious necessity for low cost large capacity batteries, it seems likely that sodium ion batteries are not far off.

Oscar Schwabe

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How We Got To The Moon

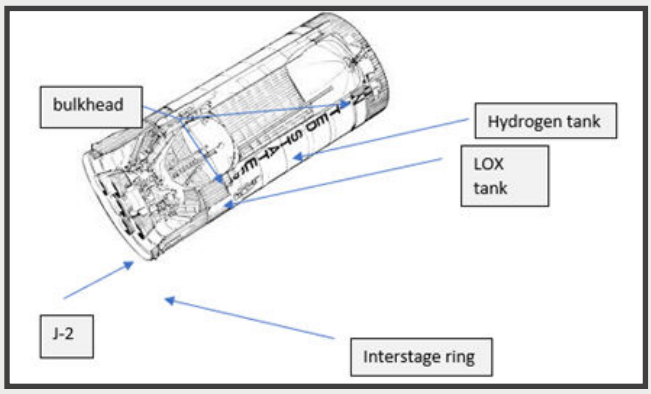
Joey England looks into the rockets and technology used to get humans onto the moon

The moon landings. We're all familiar with Neil Armstrong's first steps on the desolate lunar surface from the lunar lander and his historic words, but how did we get there?

The rocket that lifted the three astronauts and the Apollo spacecraft was the mighty Saturn V, a 110m long gargantuan weighing 2.97 million kg which could carry 118 tons to low earth orbit and produced 35,100KN of thrust at launch. Compare that to today's most powerful rocket, the SpaceX Falcon heavy, which comes in at 70m, 1.42 million kg and can carry 24.75 tons into low earth orbit and produce 25,000KN of thrust at launch. Big difference. So, what made this rocket so good and how did it work?

The Saturn V was a three-stage rocket, meaning that there were three main parts, the S-1C or first stage powered by five Rocketdyne F-1 engines, the most powerful single combustion chamber engine ever, this produced 35,100KN of thrust; the S-II or second stage, powered by five smaller J-2 engines, also made by Rocketdyne, produced 5,141KN of thrust and the S-IVB or third stage powered by one J-2 engine, made 1,033.1KN of thrust. On top of this, there was the Apollo spacecraft made up of the 2-stage lunar excursion module, the service module, and the command module topped off by the launch escape system.

The S-1C was the largest part, coming in at nearly half the entire height of the rocket. It weighed 2290 tons and produced 35,100KN of thrust. It would burn for 168 seconds and get the Saturn V into space. It used RP-1 and LOX in the F-1 engines (RP-1 is a refined type of kerosene and LOX is liquid oxygen and they were kept in huge tanks with LOX at the top and RP-1 at the bottom). The LOX tank feed line tunnel (pipe to combustion chamber) went through the RP-1 tank as they couldn't put it around it because the RP-1 tank produces stability for the rocket. It burned for 2 minutes and 42 seconds.



The S-II (second stage) was powered by 5 less powerful J-2 engines which were HydroLOX fuelled (HydroLOX is when you use hydrogen as fuel and oxygen as an oxidiser). These are kept at cryogenic temperatures for optimum performance and the common bulkhead tanks are stabilised by small helium tanks.

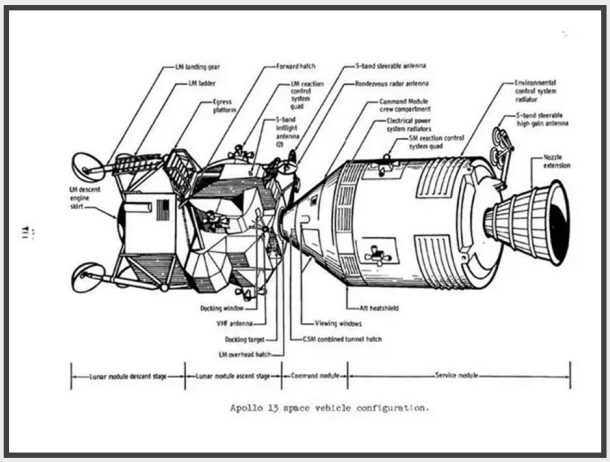
It was used to get it up to height for the

circularisation burn to get into orbit and burned for 7 and a half minutes.

The S-IVC was the third stage, which orbited around the earth at a height of 118 miles (190km). This was called a parking orbit as the rocket couldn't stay there for long because, although being above the Karman line (the boundary of space at 100km), there was still a few air molecules, only oxygen and nitrogen.

This stage also carried out the trans-lunar injection burn to get it on a course to the moon, I'll talk more on that later. It shuts off from the orbit burn 11 minutes 39 seconds into the flight but doesn't detach as it still has to carry out the injection. It is the most important stage and is powered by a single J-2 engine and uses a bulkhead fuel tank.

On top of this, there was the Apollo spacecraft (shown below) which captured itself in Lunar orbit, landed on the moon and came home. It was made of the 2-stage lunar module, the command module and the service module.



Apollo 13 space vehicle configuration.

So, how did it get to the moon? This huge rocket lifted off of launch complex 39A at cape Canaveral Florida and took 12 seconds to clear the launch tower. The three astronauts felt up to four Gs as they were crushed into their seats. At 2 minutes 42 seconds and 67 kilometres, explosive bolts fired, the first stage detached, the interstage ring detached and the second stage ignited. This is called staging, it allows you to get rid of empty fuel tanks and change to a more suitable engine for the conditions that the rocket is in. The second stage fired boosting it until the apoapsis (highest point) at 118km. Here the launch escape system was jettisoned (the big tower at the top of the rocket). The S-II was now out of fuel at 9:12 so the S-IV fired and put the spacecraft into a parking orbit. Orbiting is just falling with so much horizontal velocity that the spacecraft misses the force that is pulling you in. This didn't detach yet though, as after around 2 hours in orbit, it carried out the trans-lunar injection burn. The trans-lunar injection is where the 3rd stage is fired up for a few minutes to get it on route to the moon, in such a way so if the capture fails, they will be flung back to earth around the moon. After that, the S-IV was out of fuel and it was time for some docking! The shell around the LM (lunar module) deployed and the command and service module turn 180 degrees to face the LM and dock before disconnecting the 3rd stage. This now went into a slow roll to stop one side being 500 degrees cooler than the other. It does this until it reaches the dark side of the moon where the engine fires retrograde to get into orbit of the moon.

Alright, now the spacecraft is captured in moon orbit. Now, 2 people got into the LM, the LM disconnected and the toughest bit of the whole mission came to life, landing. It is essential to land on the surface of the moon. After burning retrograde (opposite of the way to get to orbit or the way you are going) and the spacecraft is going straight down aided by the reaction control system or RCS. Now small

burns are carried out to softly reach the surface. After that they got out, and did some stuff until it was time to go. The ascent stage disconnected and the engine fired, this engine could only be fired once ever and that was to get humans off the moon. The ascent stage must launch at the correct time as to dock with the service module.

So, now to get home. After re-docking, they did the trans-Earth injection. To do this, first they scrapped the lunar module and crashed it into the moon, then, they went to the same place that they did the capture burn and burned prograde (to go faster not slow down). This got them on course to hit Earth's atmosphere and land. They were now near the Karman line; jettisoned the service module and entered the atmosphere. As they entered the atmosphere, they rubbed against air molecules and this caused friction which soon heated up so much that plasma was created.

Eventually they cooled down and at 2 miles parachutes opened, splashdown in the ocean occured and they were picked up by an aircraft carrier.

Joey England

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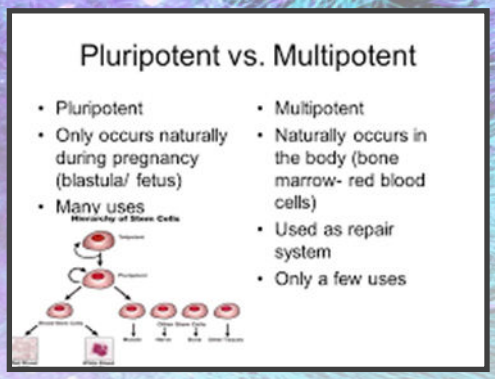
Like water into wine: Somatic cells into pluripotent stem cells

Tejas Easwar takes a look into induced pluripotent stem cells

Just over ten years ago, Shinya Yamanaka, a Japanese scientist announced to the world that he had succeeded in generating iPSCs. Since then he has received a Nobel Prize and global fame for his work. In this article, I will be finding out just exactly what he had discovered and what his research entailed.



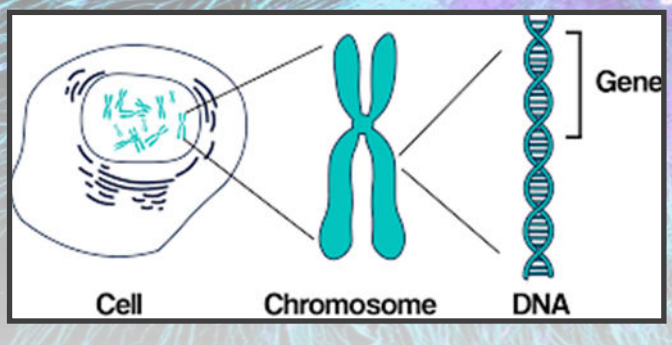
In the human body we have trillions of cells, most of which carry out specific functions and cannot be changed into other types of cells (we call these somatic cells). However, dotted all around our bodies, from our brain to our bones, we have special cells known as the 'stem' cell. These stem cells are different and unique compared to the rest. They can differentiate and change into many different types of cells whilst perpetually renewing. There are two categories of stem cells in our bodies: Pluripotent (embryonic) stem cells and multipotent stem cells. Pluripotent stem cells are capable of giving rise to several different cell types, whilst multipotent stem cells are capable of giving rise to more specific cell types.

Blood stem cells that form into blood cells and muscle stem cells that form into muscle cells are all examples of multipotent stem cells. Multipotent stem cells can only differentiate into certain cells according to their location in their body and the biochemical surroundings that influence them. However, just after fertilisation, when we were just mere specks in our mothers' wombs, nearly all the cells of our body were embryonic stem cells (ESCs). With time, these cells become more specialised and lose their pluripotent abilities. Human ESCs cannot only differentiate into every cell that we are made up of, but they can divide without limit. This potential makes them extremely useful for research into the functions of the human body, drug testing and discovery, and as a source for transplantation in medicine.

Despite their medical potential, human ESCs face several ethical controversies regarding the destruction of embryos. An alternative is needed, Shinya Yamanaka may have found it.

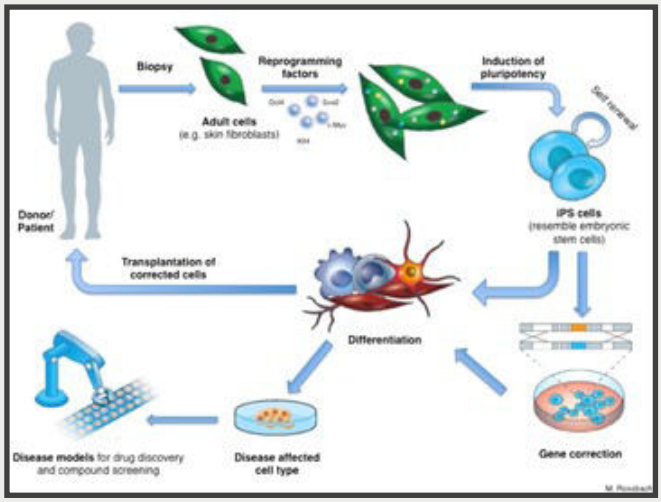
Yamanaka had been able to change a normal adult 'somatic' cell back into the state of

pluripotency that can be found in an embryonic stem cell. In the nucleus of every cell in our body are 23 pairs of chromosomes that can make up every different cell. Each chromosome consists of long strands of DNA. The DNA is divided up into sections or genes that code for specific proteins. Specific combinations of these proteins give specialised cells their unique identity.



Every cell in our body carries the same genes. However, in skin cells, only the genes that code for skin proteins are turned on – the active areas are unwound; the rest of the genes are turned off – they are tightly wrapped away. Yamanaka wondered if the same proteins that kept an ESC pluripotent, could be used to reprogram the specialised identity of a reprogrammed cell. At first, Yamanaka came up with a list of over a hundred possible proteins involved with pluripotency. He was not sure if these proteins worked alone or in conjunction with each other, meaning a possible of over one million variations. Using a computer program, Yamanaka was able to identify 24 likely possibilities. The team of scientists at the Kyoto University in Japan had further narrowed down to just four factors; they continued by infecting somatic skin cells from adult mice with a virus intended to introduce four certain genes responsible: Oct3/4, Sox2, Klf4 and c-Myc. These factors normally only act together in ESCs. What happened next is not yet fully understood, however, scientists think that the chromosomes unwind and allow certain Yamanaka's factors to attach to the genes allowing embryonic stem cell proteins to be synthesised. Yamanaka's factors can overwhelm the skin cell into thinking it is in embryonic conditions. With further replications by mitosis, this cell becomes ever more like an ESC, until they are indistinguishable. In this state, this cell can produce any cell in the body. The scientists originally used a virus to insert the genes. However, this was a problem as using viruses can often cause mutations in the cell, leading to tumour formation.

Over the course of the following year, many scientists had confirmed the results and had improved the reprogramming method. During the next six months, Yamanaka and James Thomson, an American developmental biologist, had successfully shown the same technology was possible in human cells. Yamanaka could not only change skin cells, but he was able to turn any differentiated cell into an iPSC.



Advantages over ESCs:

Unlike ESCS, induced pluripotent stem cells do not pose any ethical concerns, since they are not derived from embryos. However, having said that, iPSCs still pose concerns as it is possible to form male or female gametes and thus form an offspring from somatic cells.

In addition, iPSCs can be generated from individual patients, so the genetic information can be identical to the patient. If we can then transplant these cells, they will not be recognised by the patient's immune system. The stem cell can then differentiate into a heart cell, brain cell, insulin-producing cell etc. without the risk of transplant rejection. The problem with using ESCs is that they are are often dissimilar to the recipients' cells.

Why aren't iPSCs currently being used in hospitals worldwide?

The major setback currently is safety. The time taken for the iPSC to differentiate is long and as a consequence tumour formation is possible. iPSCs have not yet been used in clinical practice and the only clinical trial has now been suspended.

Where the future lies: -

iPSCs have potential for transplant treatment and cell replacement after injuries and trauma. They can differentiate into the cells that have been lost. IPSCs also have the potential of being used as a research tool to investigate the efficacy of certain drugs on the human cells. Treatments for neurological diseases such as Parkinson's or Alzheimer's Disease can be trialled on iPSCs.

Tejas Easwar

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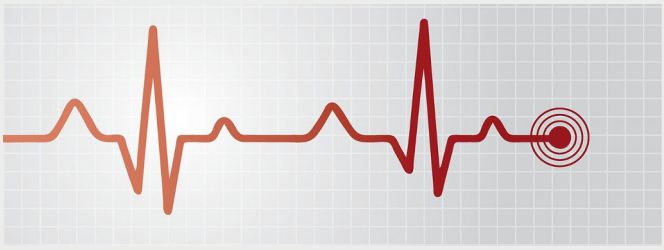
Reducing the impact of sudden cardiac death in athletes

Keshen Pathmanathan discusses the issue of cardiac arrests in sport

Sport unquestionably brings benefits to ones health; yet, perhaps paradoxically, the same vigorous physical activity which yields these great benefits is also able to momentarily increase the risk of an acute cardiac event occurring (Schmied & Borjesson, 2013). This is the case with respect to sudden cardiac death, a condition in which a person who has no previously fatal condition, dies both unexpectedly and naturally from a cardiac cause within a brief period of time, usually within one hour of the first onset of symptoms. Frequently, such rapid deaths are put down to the heart beating with an abnormal rhythm (cardiac arrhythmia), but following the emergence of implantable cardioverter-defibrillators (ICDs) with monitoring capabilities, it has become recognised that classifying deaths based solely on clinical circumstances can be deceptive, and often impossible. This is due to the fact that approximately 40% of sudden cardiac deaths are not seen. It is only with the aid of an electrocardiogram (ECG) or a ventricular electrogram recorded by an implanted device at the time of death that conclusions about an arrhythmia can be drawn. The indicators present between the initial appearance of symptoms and the full development of the condition are often nonspecific, and even symptoms that signpost ischemia (chest pain), a tachyarrhythmia (fast and irregular heartbeat), or congestive heart failure (shortness of breath) cannot be regarded as definitive. Thus, attempting to classify sudden cardiac deaths into cardiac and arrhythmic mortality is often a futile activity.



The reasoning behind measures considered and taken to prevent sudden cardiac death in athletes is largely centred on the premise that most people who suffer a fatal cardiac arrest have an underlying, frequently unknown, cardiovascular disorder, which significantly increases their risk of sudden cardiac death. Cardiovascular disorders are actually more common than one might think, with as many as 1 in 300 athletes assumed to have an underlying disorder. Through cardiovascular screening, the intention is to pick out athletes whom are at an increased risk of sudden cardiac death; this often occurs in conjunction with identifying athletes with abnormally high blood pressure and both work towards preventing cardiovascular events in the future (Schmied & Borjesson, 2013).

Although in the majority of athletes the 'athlete's heart' is easily identifiable from cardiac pathology, there exists a subset of athletes in which exercise induces significant electrophysiological changes, which may overlap with presentations of cardiac disease. Certain sports, particularly those that contain a substantial amount of isometric exercise, can lead to left ventricular hypertrophy. In this case, the thickness of the left ventricle wall (12 -14mm) is in the same range as would be classified mild hypertrophic cardiomyopathy. These examples of the 'athlete's heart' presenting in a similar manner as a pathological heart highlight why it is vital that cardiac screening is analysed by cardiologists who are trained and have the experience to understand the cardiovascular changes that take place in athletes, and so are able to recognise an 'athlete's heart' (Wasfy, Hutter, & Weiner, 2016).

Recent studies have also illustrated that sport in itself may not only lead to the development of the 'athlete's heart', but may also cause the development of a cardiac abnormality. The example of cyclists has been used, as there have

been cases where their right ventricle has experienced changes like those seen in an individual with arrhythmogenic right ventricular cardiomyopathy (an inherited disease of the heart muscle caused by genetic defects that causes an arrhythmia) in a condition known as 'exercise-induced ARVC' (LaGerche, Burns, & Mooney, 2012).

The occurrence and causes of sudden cardiac death show great variation with respect to age, gender, race and type of sport of the athlete. Thus, a blanket preparticipation screening protocol for all athletes may not be the best option. Moreover, the incidence of sudden cardiac in athletes, despite being the primary medical cause of death in athletes, is not particularly high; the incidence is in the range of 1:40,000 to 1:80,000 (Harmon, Drezner, Wilson, & Sharma, 2014), and this significantly trails heart disease, which has an incidence of 1:519 in the USA, and cancer, with an incidence of 1:549 in the USA. This is not being said to undermine the seriousness of the issue of sudden cardiac death in athletes; after all, each life has intrinsic and infinite value – value to which statistics do not do justice. However, the world of healthcare is innately utilitarian: healthcare, and this is particularly true with regards to the world of free healthcare, attempts to bring the 'greatest good to the greatest number', using the fewest resources. This is in line with the quality-adjusted life years approach that NICE takes when evaluating the best course of action. Taking into account this utilitarian approach, it would be hypocritical to expect all athletes to be screened prior to participation; it would simply not be the most cost effective way to utilise limited resources. However, a screening program targeted at high-risk populations would be a more practical and effective use of resources.

Tackling the issue of sudden cardiac arrest is one that involves many complexities. Ideally, preparticipation screening would be mandatory for all athletes. However, due to limited resources, this would be difficult to introduce. It is highly debated as to whether such a move would save sufficient enough lives to justify the high cost of widespread screening. What is indisputable is that all sporting venues, both at the elite and recreational level, should be prepared for dealing with a sudden cardiac arrest; they should have an emergency response plan, individuals trained in CPR and on-site defibrillators. These factors can contribute to a six times increase in survival from a sudden cardiac arrest (Rothmier & Drezner, 2009). This simply cannot be ignored.

Keshen Pathmanathan

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To what extent may we consider Electroconvulsive therapy as an effective treatment

Mohamed Hassouna discusses the controversial Electroconvulsiuve Therapy

Medicine and medical treatments have evolved a great amount over time. With new technology and discoveries, this has allowed researchers and scientists to develop a much better understanding of the human mind and body. However, many previous treatments are still in use today which has led to a great amount of discussion and debate regarding its place in modern medicine. ECT is a very sensitive topic which some could say as being a clash between experience and evidence; personal experiences contest scientific evidence which has meant that the ECT debate is a perplexing one.

Whilst certain people detest and oppose the usage of ECT, many people in the world rely on ECT to help them get through mental illnesses. In a talk performed by Sherwin Nuland (Nuland, 2001) he quotes 'I am a man who, almost 30 years ago had his life saved by two long course of electroshock therapy', he later goes on to explain his story and how he had no choice but to resort to ECT which eventually turned out to save him from his mental illness. This story is not an incredibly unique one however, many accounts follow a similar pattern.

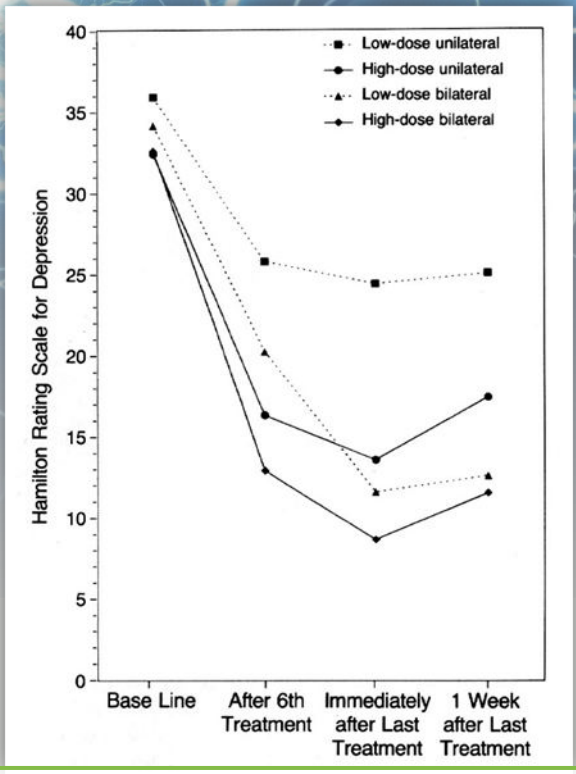
ECT is widely used in the world, with a reported 70 -80% success rate according to (Ministry Of Health, 2006) It was found in the years 2003-2005, ECT was considered the most effective treatment for short term treatment towards depression. The efficacy of ECT is supported by the research performed by Tew et al. (1999) where they mention that ECT allows for a positive response from groups of all ages however this study also suggests that ECT causes effects such as physical illness and cognitive impairment. One of the main benefits of ECT is that it can be used when anti-depressants and other mental health medications are unresponsive in the patient. Its referred as a 'last resort' throughout many pieces of research.

One of the positive effects found to be linked with ECT is the improvement in cognitive function for late-life depression. For those who have been found to have cognitive impairment whilst suffering from late-life depression, ECT has helped restore their cognitive function to an extent (to some level some patients have found that ECT has helped them regain some cognitive function). Quite Interestingly, an article written by Butter et.al (Butters, et al., 2000) claims that they witnessed an increase in cognitive function for those who responded successfully to ECT, 'successful depression treatment led to significantly improved cognitive functioning among elderly depressed patients with baseline cognitive impairment' (Butters, et al., 2000). They tested their initiation, preservation and conceptualisation and noted increases in all those sectors. Upon review of this article, it must be said that it is unsupported by other similar research. The article however mentions how a successful ECT may result in a more relaxed and focused mind from the effects of not being depressed. This would therefore mean an increase in cognitive function may be related to not being depressed rather than ECT itself. Butters et al. later goes on to explain how impairment in cognitive function results from structural damage to the prefrontal cortex or the subcortical structures. They also mention how one of the causes of weakened cognitive functions relates to the central nervous system (CNS), the

CNS is particularly vulnerable to depression therefore if the effects of depression are removed it would allow the patient to regain a certain level of their cognitive function.

On the other hand, Whilst ECT has provided hope and success for many patients, it has come under its fair share of criticism for its lack of legitimacy in terms of evidence-based reasoning; its adverse effects and consistent results. Previously, we have looked at positive ECT reports however not all ECT stories available are positive. An ECT story talked about by Dr Susan Cunliffe at the Kings College Maudsley (2018) describes ECT in a disturbing manner. She said '21 electric shocks were passed through my brain; I cannot use the phrase electroshock therapy because it caused life changing brain damage'. Such an impactful statement tests the supposed positives of ECT mentioned above; she later goes onto mention how she feels hurt by the alleged claims that ECT does not cause brain damage and cognitive dysfunctions.

As well as ECT having many adverse effects, the efficacy of its long term benefits also comes under a huge amount of scrutiny. Many different cases and accounts show the varying degree of long term success that ECT provides. An interesting article relating to the efficacy of ECT in the short term and long term comes from Sackeim et al. (1993). As presented in Graph 1, The Hamilton rating scale for depression does decrease to a substantial level after the 6th treatment. However, as we can interpret, one week after the last treatment, the scale already begins to decrease and this is within the first week after last treatment. We can interpret that the rating will increase as time goes on after the last treatment. This arises questions relating to whether there is a point in giving this medicine as the hospital will eventually see this patient again in the near future. This is an obvious concern; one aspect the patient must consider is that whether they are willing/able to come to hospital regularly to receive the electroshock therapy. A concern for the hospital is whether this method is economically efficient, it would cost the hospitals a great amount if they were to continue giving this treatment to a patient over a large period of time. This would mean that the budget for other sectors such as the anti-depressant pills will not receive as much funding.



Graph 1—Sackeim, et al., (1993) produce results on the effect of ECT on the Hamilton Rating Scale for depression

One area that has not been researched into too greatly is the idea that ECT produces a placebo response. Due to the lack of research in this area, it is hard to conclude whether this statement is true or false. Research provided by Read & Bentall (2010) suggest that ECT does provide a strong placebo effect. They were unable to produce this conclusion in years before this due to the fact that it was near impossible to replicate the shock effect on the patient without cause physical harm. The review quotes 'the fact that "rigorously defined endogenously depressed patients did exceptionally well with sham ECT, just as well as with real ECT.

This needs explaining because it is common wisdom that endogenous (melancholic) depressions are not supposed to be placebo responsive' (Sham ECT is the method of ECT which is used to research the placebo effect) If this research is validated in the future, it will lead to enormous concerns regarding the efficacy of ECT. If the patients are able to respond to 'Sham ECT' why would a patient undergo true ECT. It must be said that depression is not meant to be able to produce the placebo effect which then brings up the question of the legitimacy regarding the patients' depression. This is a strong argument against the use of ECT, this research paper would lead many to believe that the response from ECT is a placebo effect rather than a true outcome.

In conclusion, for me this indicates that ECT may not be eligible to be called a 'medical success'. Although ECT has provided many benefits for people overtime, its consistency constantly is under question. With many different journals and stories all suggesting different experiences. There are large amounts of people who have had their life changed in a positive way following ECT, I believe that to an extent ECT does hold a place in medicine, the reason I believe this is linked to the fact that ECT is not the direct response to those who suffer from major depressive disorder. The initial response involves prescribing anti-depressant pills or suggesting therapy, ECT is used as a last resort which for me is one more option for the patient if all else fails. Not all patients respond to the initial treatments, they can then look into other solutions, none of which they are 'obliged' to take. Those who do wish to undergo ECT will have all the risks and hazards of this therapy explained to them and if they are content with the possible outcomes, then in my opinion there is little reason to deny them the use of ECT.

Mohamed Hassouna

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Gene Therapy and Blindness

Zain Girach discusses the possible use of gene therapy to solve choroideremia

The rate of the advancements of gene therapy makes it one of the most exciting, talked-about specialties in the medical and pharmaceutical worlds. Great pioneers are pushing the boundaries of what gene therapy can achieve, and now there is a realistic possibility that it can cure the incurable cause of blindness by a disease called choroideremia.

The reason why ophthalmic pharmaceutical companies have majorly focused on gene therapy is due to its nature and potential as it is ideally suited for curing inherited, monogenic retinal diseases. The eye is best suited for addressing monogenetic diseases, since it is a small compartment, thereby requiring small doses only, which in turn leads to fewer side effects and lesser chance for immune reactions against the gene therapy. The eye also has approximately 250 causes of blindness, and that have been characterized genetically, and are amenable for gene therapy—with choroideremia being a common cause. The eye is also a compartmentalized organ, having tight junctions with a significant blood-ocular barrier that minimizes the chances of an immune reaction against the gene therapy. The recent invention of ocular imaging systems, such as optical coherence tomography (OCT), facilitates cross-sectional views of the retina, that allow direct visualization of where any gene therapy is inserted, and also allows a way to gauge any effect of the gene therapy. All these significant benefits of exploring gene therapy in the eye have led to a world of opportunities for potential cures for inherited diseases, particularly choroideremia.

Choroideremia is an inherited disease that affects 1 in 50,000 people and causes 4% of all blindness cases. Victims face a life knowing that someday they will lose their sight, and consequently this affects their lifestyle as often they are not able to obtain driving licenses, or participate in activities or work where sharp eyesight is needed. This not only decreases the quality of life for the victim, often leading to depression and mental health issues, but also hugely impacts the family. This is regularly evident in many cases as the loss of eyesight may lead to the primary earner in a household losing their job. Without a doubt, this has major financial and psychological repercussions on the family; a situation no family should have to endure, especially when choroideremia is not a disease self-inflicted by the patient. Although the disease effects different individuals with varying severity, the pictures below demonstrate the gradual progression of visual loss, from the tender age of 17, to approximately 55 when all vision is lost. Patients suffer night blindness when they are in their teenage years, followed by progressive visual field loss progression from the outside inwards. This progresses into their 20s and 30s, until they are left with a small area of central(tunnel) vision in their 50s, when even that small area of vision

disappears, and the patients are totally blind

Choroideremia itself is caused by a defect of the CHM gene, which has the function of providing instructions to produce Rab escort-proteins, found in the X chromosome, and therefore only affects males. This is the case as choroideremia is an X linked recessive mutation, so it manifests itself in XY chromosomes (i.e males), as a single mutation in only one copy of the gene in XX chromosomes (females), leading to females only being carriers. As a carrier, no significant effect of choroideremia is experienced, however potentially this can lead to small patches of cells dying in the retina, resulting in long-term visual impairment in the future. The nature of this mutation means the correct gene mutation must occur in both alleles in a female in order to have a significant effect.

In Choroideremia, thereis a gene mutation of the CHM gene leading to reduced or no Rab escort protein-1 (REP-1) formation. REP-1 is vital to the retina's existence to clear the retina of toxic material by attaching them to Rab proteins which guides them to organelle membranes in the retina, where they can be removed. The Rab proteins, once bound to the surface of the organelle membranes, then permit intracellular trafficking, by allowing proteins and other substances to move within cells, and eliminate waste products in the retina. Therefore, when there are no escort proteins due to the CHM gene deficiency, the Rab proteins do not bind to the organelle membranes so intracellular trafficking does not take place. As a result, cells within the retina build up with toxic material and begin to die and thus atrophy (degeneration) of photoreceptors occurs. This eventually leads to blindness.

So how is gene therapy going to cure this?

Ever since Ludwig Mauthner first described choroideremia in 1872, extensive research has been carried out in order to find a cure. However, recently gene therapy has been considered as a viable solution. The theory behind it is that an adeno-associated virus (AAV) is used as a vector to carry the correct CHM gene into the retinal pigment epithelium (RPE) and photoreceptors once injected. With the correct CHM gene in place, a functional version of REP-1 protein is produced, which facilitates intracellular trafficking of waste products within the cells. As a result, the photoreceptor and RPE cells in the retina are able to survive, thereby blindness is prevented.

Zain Girach

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Pulse Oximetry: The Medical Physics on Your Fingertip

Harroop Bola investigates the use of pulse oximeters in Medicine

Background

Pulse oximeters measure the proportion of oxygenated haemoglobin in the blood in pulsating capillaries, most prominently used for the capillaries in the finger or ear. Pulse oximetry is a non-invasive method of measuring blood -oxygen saturation, using a medical instrument known as a pulse oximeter. The pulse oximeter is a clamp-like device which is usually placed on the ends of fingertips, toes and ears. Incorporated within the device are two different light emitting diodes (LEDs), which transmit light at varying wavelengths in the red light and infrared light end of the electromagnetic spectrum. Conventionally, the wavelengths transmitted by the LEDs are 660nm & 940nm for red and infrared light respectively. The proportion of wavelengths are then received by a photoreceptor which transmits the incident light waves as electrical impulses to a multiparameter patient monitor to produce a photoplethysmogram and an absorption spectrum.

Oxygen Saturation: Biological perspective

Haemoglobin is a conjugated globular protein molecule consisting of 574 amino acids, arranged in four polypeptide chains (2 alpha helices, & 2 beta-pleated sheets), which are held together by hydrogen bonds. Each chain is arranged around an iron containing haem group, this means that a haemoglobin molecule has the ability to bind onto four oxygen molecules, however there is no further or disulphide bonding between the chains. Therefore, these chains are weakly linked, allowing for conformational change of haemoglobin, once oxygen is bound onto the haem group, the shape of haemoglobin structurally changes. Once oxygen is associated to haemoglobin, the saturated molecule is referred as oxyhaemoglobin. In the lungs, oxygen binds onto haemoglobin (binds on the prophetic haem group) to form oxyhaemoglobin, this is because the affinity to oxygen is greater, since the partial pressure of oxygen is relatively high. This is a reversible reaction, as the oxyhaemoglobin dissociates the oxygen, breaking down into its component molecules, oxygen and haemoglobin. During cellular respiration, the partial pressure of blood oxygen decreases, and is comparatively low. Thus, the affinity to oxygen is reduced, leading to oxygen being readily lost to diffuse into respiring cells and satisfy the demand of oxygen.

$$Hb + 4O_2 \leftrightharpoons HbO_8$$

$$Haemoglobin + Oxygen \leftrightharpoons Oxyhaemoglobin$$

Oxygen saturation can therefore be monitored by evaluating the ratio of deoxyhaemoglobin and oxyhaemoglobin in the blood. The structural differences due to oxygen association results in varying absorptions of the different wavelengths of light. **[3][4]**

Function of Oximeter: Application of Physics

A pulse oximeter uses an electronic processor, and a pair of LEDs facing a photodiode though a translucent part of the patient's body. One LED emits red light (660nm), and the other emits infrared wavelengths of electromagnetic radiation (940nm). Depending on the oxygen saturation of haemoglobin, light absorption is significantly varying between oxygenated and deoxygenated haemoglobin. Oxyhaemoglobin absorbs a greater proportion of infrared light, thus enabling a high percentage of red light being transmitted across the translucent specimen, being received by the photoreceptor. Conversely, deoxyhaemoglobin enables a greater transmission of infrared light, absorbing a larger ratio of red light. There are other contributing factors involving the quantity of light absorption, these incudes, the length of the light path in the absorbing substance, and the concentration of the light absorbing material. Considering, the concentration of the light absorbing material, there is a seemingly proportional relationship between it and the absorption of light. A positive correlation is evident, when increasing the concentration of haemoglobin in the blood vessel, the light absorption consequently increases, whilst the diameter of the vessel is kept constant. This phenomenon can be explained using the Beer-Lambert law. **[5]**

Beer-Lambert law:

It is empirically found that when electromagnetic radiation passes through a sample of length L and molar concentrations [J] of the absorbing species, the transmitted and incident intensities, I and I_0 respectively are related by the Beer-Lambert law:

$$I = I_0 10^{-\varepsilon[J]L}$$

The quantity epsilon is called the molar absorption coefficient; this coefficient is dependent on the frequency and wavelength of the incident radiation and is at a maximum where the absorption is the most intense. E has dimensions of 1/ (concentration x length), expressed as $mol^{-1}dm^3cm^{-1}$, although in form of more conventional SI base units it is alternatively articulated as m^2mol^{-1} (Metre squared per mole). The latter units imply that the coefficient can be regarded as the cross-sectional area for absorption, resultantly as evident from the above expression, increasing the cross-sectional area of the molecule for absorption, the greater the ability to block the passage of incident radiation at a given frequency.

The change in intensity, dI, that occurs when electromagnetic radiation passes through one particular slice of sample is proportional to the thickness of the slice, the molar concentration of the absorber, J, and the intensity of incident radiation at that slice of the sample. Conclusively, it can be derived that $dIa[J]Idx$. The intensity is thus reduced by absorption, meaning that the change in intensity must be negative. K is the proportionality coefficient.

$$dI = -k[J]Idx$$
$$\frac{dI}{I} = -k[J]dx$$

(Expression applicable to each individual and successive slice)

In order to obtain the intensity that emerges from a sample of thickness L when the incident intensity on one face of the sample is I_0, one needs the sum of all successive changes. It can be assumed that the molar concentration of the absorbing species is uniform, and thus considered as a constant. Since a sum over an infinitesimally small increments is an integral, it proceeds that:

$$\int_{I0}^{I} \frac{dI}{I} = -k \int_0^L [J]dx = -k[J] \int_0^L dx$$

Therefore,

$$\ln\left(\frac{I}{I_0}\right) = -\varepsilon[J]L$$

The spectral characteristics of a sample can be reported as the transmittance, T, of the sample at a specific frequency.

$$T = \frac{I}{I_0}$$

Absorption, A: $$A = \log_{10}\frac{I_0}{I}$$

Thus, the two quantities can be associated by:

$$A = \varepsilon[J]L$$

(Product is the optical density of the sample) **[1][2]**

Therefore, assuming ε and L as constant, it can be followed than the absorption of the sample is directly proportional to the molar concentration. Thereby, increasing oxygen saturation, will increase the absorption of incident infrared light, reducing the resultant intensity of the electromagnetic radiation being received by the photoreceptor. Similarly, increasing the length of the blood capillary will consequently reduce the resultant intensity of radiation being transmitted across to the receiver. Processing units within the pulse oximeter incorporate in the Beer-Lambert method to determine the approximate absorbance ratio of each individual wavelength of transmitted light.

Infrared and Red light:

Pulse oximeters take advantage of the physical property between both oxyhaemoglobin and deoxyhaemoglobin regarding the absorption of specific wavelengths of light for each corresponding molecule. Deoxyhaemoglobin will absorb a greater proportion of red light, contrastingly, oxyhaemoglobin will absorb a higher proportion of infrared light. Evident from **Fig.1**, the comparative wavelength absorptions can be determined, concerning oxyhaemoglobin the ratio of red light: infrared light absorption is in favour towards the infrared end of the electromagnetic spectrum, as oppossed to the deoxyhaemoglobin spectrum. This physical property is integral for the analysis of blood oxygen saturation, with the assistance of the Beers-lambert law, the oximeter interprets the ratios of light being received and quantitatively processes this. Thus, the pulse oximeter can govern an approximation regarding the proportion of deoxyhaemoglobin: oxyhaemoglobin within the blood. A processed ratio favouring red light absorption is indicative of a higher level of deoxyhaemoglobin, conversely, a ratio tending towards infrared light, illustrates a higher concentration of oxyhaemoglobin.

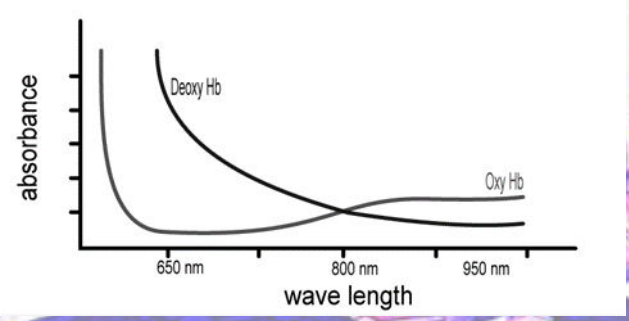

Figure 1: *Absorption spectrum of OxyHb & DeoxyHb, to their corresponding wavelengths.*

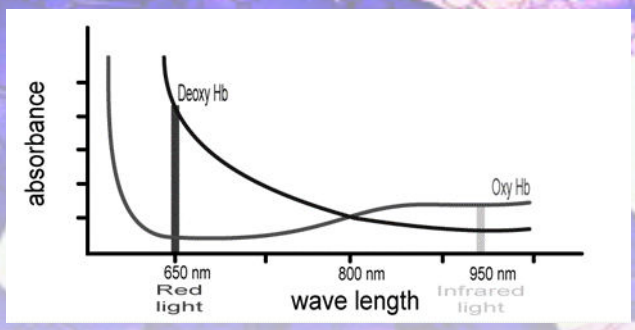

Figure 2*: The ratios of infrared and red light for each respective Hb type.*

Fig.2 represents the respective absorptions of each individual wavelength of light, this can be used to calibrate the pulse oximeter to calculate oxygenation saturation. With the oxyhaemoglobin graph being depicted at 100% oxygen saturation, whilst the deoxyhaemoglobin graph exclusively corresponding to 0% saturation. As a result, patient samples being processed by the oximeter, will result in an absorption spectrum being intermediately placed between the two standards. The typical oxygen saturation ranges between 80-89%, thus statistically significant fluctuations in oxygen saturation can be identified, and further processed to find a diagnosis of the condition, including hypoxia. **[5]**

Harroop Bola

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