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Cover photo by Nathan Jacob

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MISSION STATEMENT

The Emory Undergraduate Medical Review (EUMR) publishes a semesterly journal that features faculty and student-authored articles on cutting-edge medical issues. Our interdisciplinary articles span various clinical fields and are peer reviewed by medical professionals from more than a dozen leading academic institutions, including Emory University, Yale University and the Mayo Clinic.

In addition to our publication, EUMR hosts various medically-related events on campus, including collaborations with the School of Medicine. Our projects have been featured by Emory's News Center and have caught the attention of President Sterk.

LETTER FROM THE EDITOR

Dear Reader,

The publication of this journal issue marks the end of the year 2020, and the end of a second semester lost to the pandemic. The state of the world remains largely interrupted. We, as students, have endured another semester of "Zoom University" and those who were able to step onto campus found it muted and vacant. We know what "unprecedented" means now, and see it defined in the masks on strangers' faces, bottles of hand sanitizer and the droning video calls that stand in for education. At this point, we are no stranger to uncertainty and change, yet our adjustment does not equate to an acceptance of what has become the new normal.

In a year where time seemed to stagnate, we collectively mourned the college experience we never had, of the wasted opportunities and lost communities never built in the first place. It makes us question if we've done enough and made satisfactory progress towards some end or goal. Yet, we hope this first installation of the seventh EUMR volume testifies to our carrying on, despite the myriad challenges, and the accomplishments achieved in the face of adversity.

We would like to thank our talented editorial board for, once again, making possible another issue. In particular, we would like to congratulate our new members for their first publication — we hope to meet you all in person someday!

Many thanks to the members of our advisory board who continue to mentor and guide us. Your efforts do not go unnoticed and your invaluable input helps shape the content we put out.

We look forward to working with everyone again in the new year, hopefully accompanied by changes of the positive kind. With that being said, we hope you enjoy the first issue of our seventh volume.

Cordially,

Daisy Li & Nathan Jacob
Editors-in-Chief
EUMR 2020-2021

DNA nanotechnology: Drug delivery system

LAURA PAULE
Staff Writer

Deoxyribonucleic acid (DNA) is widely known as the carrier of genetic information in living cells, coding for genes that can be transcribed into mRNA, and then translated into proteins. Scientific innovations have broadened the uses of DNA, employing it as an engineering material in the creation of nanostructures. The scale applicable to nanotechnology is often cited as 1-100 nanometers, which is small enough to avoid harming healthy cells upon introduction of nanostructures into living organisms.

These artificial nucleic acid arrangements are enabled by the strict complementary base pairing rules of DNA (Chi, 2020). The four nucleobases of DNA are adenine, thymine, cytosine and guanine. Formation of correctly matched base pairs is favored, meaning that DNA will try to maximize these interactions (A with T, and C with G). This is coupled with the energetically-favored hydrophobic effect, which allows for the aggregation of the non-polar regions of DNA, while excluding water molecules. Using this rationale, scientists can selectively assemble stable structures such as two- and three-dimensional crystal lattices and other arbitrary shapes (Seeman, 1999). This article aims to portray the different methods by which DNA nanostructures are created, as well as to dig deeper into the development of a DNA-based drug delivery system that has the potential to surpass current delivery systems.

Scientific innovations have broadened the uses of DNA, employing it as an engineering material in the creation of nanostructures.

The process of generating a sequence of nucleic acids that will associate into a desired conformation is known as nucleic acid design. Scientists have used DNA for self-assembly of a wide variety of nanostructures, ranging from simple to complex structures. Not only are DNA nanostructures favorable because of their base pairing abilities, but also because they are capable of being pre-programmed for rapid assembly within hours, integrating thousands of DNA components into complex architectures (Wyss Institute, n.d.).

There are multiple ways in which these structures are developed, including tile-based bottom-up assembly and origami assembly (Hu et al., 2019). Tile-based bottom-up assembly consists of creating tiles (the base of the structure) from which the remaining structure is built up. The simplest tile created consists of an immobile structure of DNA containing a Holliday junction (junction at which homologous DNA strands exchange genetic material during genetic recombi-

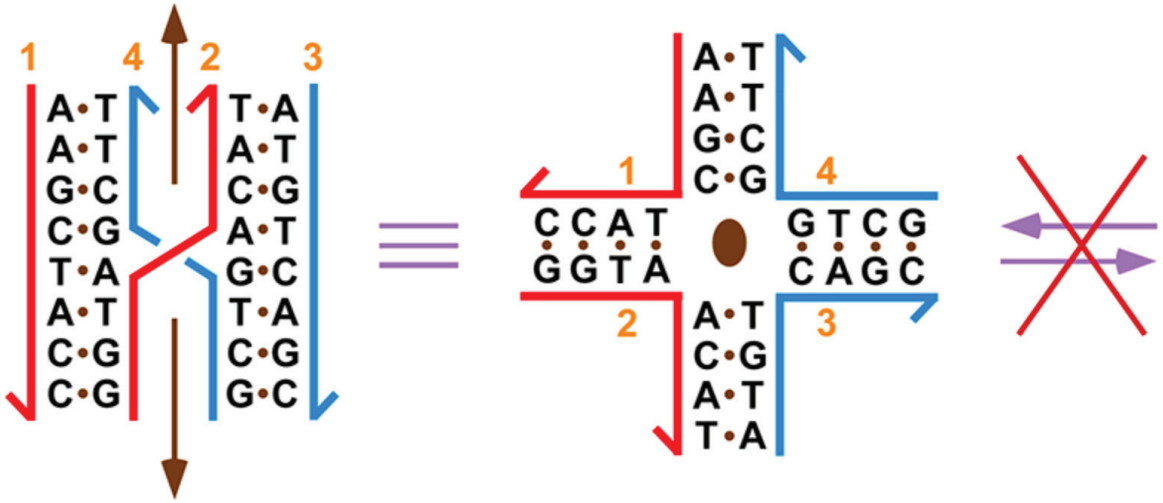

Figure 1. This figure shows the Holliday junctions used to form DNA nanostructures. Image from Hu 2019.

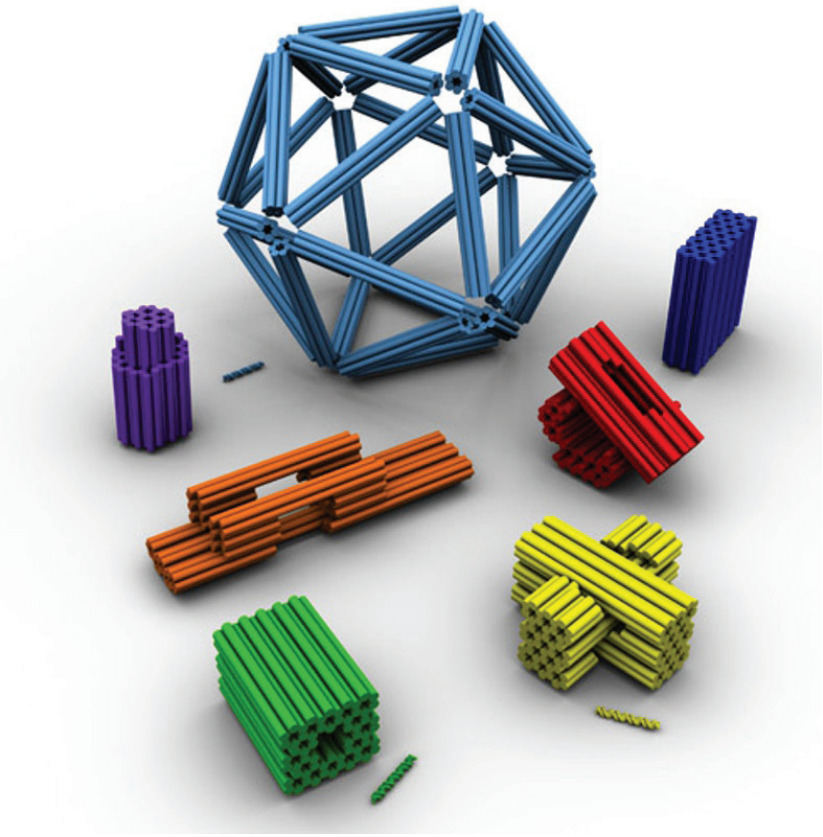

Figure 2. These are examples of nanoscale three-dimensional shapes, where each cylinder represents one double helix, 2 nm in diameter. Image from Wyss 2020.

nation). DNA origami uses one long single strand of DNA as a 'scaffold,' which is manipulated to form lattices with short DNA strands designed with computer softwares (Wyss Institute, n.d.). Through the use of strategies like the ones mentioned, a variety of dynamic structures have been created, including transmembrane channel structures and valves that control gated transport of materials across a phospholipid bilayer. However, one of the most novel aspects of this technology is its potential as a drug delivery system into organisms.

As a means of improving medication, scientists have worked to discover and create sophisticated systems for drug delivery. These innovations seek to produce high targeting selectivity and reduction of side effects in individuals (Gardner, 1985). Some of the best-known drug-delivery systems created thus far include natural systems such as viruses, synthetic organic systems such as cationic dendritic polymers, and synthetic inorganic systems such as gold nanoparticles (Hu et al., 2019). These systems contain drug molecules by chemical linkage, encapsulation or physical absorption. Although very effective, there are limitations or risks associated with each of these systems.

For example, natural virus-based delivery systems have inherent safety issues, including the insertion of viral DNA into the host genome (Somiya, 2017), mutagenesis, cytopathic effects (structural changes in host cells that are caused by viral invasion), and random insertion sites. In addition, viruses can only deliver small fragments of DNA into cells (Hu et al., 2019), increasing the need for the development of an improved method of drug delivery with higher loading capacity and lower immunogenicity (ability of a foreign substance to provoke an immune response) (Keles, 2016). A downside of dendritic polymers is that their cationic surfaces are cytotoxic, which increases immune toxicity (Lingala & Ghany, 2016). Many of the inorganic systems also contain toxic materials and are difficult to degrade. Due to the limitations discussed above, DNA nanotechnology-based delivery systems are being studied and tested as a potential solution to these problems.

In order to create an effective drug delivery system based on DNA nanotechnology, scientists consider primary and secondary targeting of these structures. Primary targeting consists of directing the drug and nanostructure towards the desired organ, while secondary targeting involves specificity towards the desired cells within the organs (Hu et al., 2019). Due to the highly modifiable nature of DNA, unique structures can be

However, one of the most novel aspects of this technology is its potential as a drug delivery system into organisms.

created that target very specific organs within the body.

For example, particles with size less than 15 nm can be directed to the brain, as they can bypass the blood-brain barrier (Enochs, 1999). Nanoparticles targeting the lymph are designed so that they can bind to receptors in leukocytes. These particles are more readily taken up by leukocytes if the surface of the particle is negatively charged (Fidler, 1986). Nanoparticles smaller than 100 nm can be directed towards the liver, while large inhaled particles with low density are likely to be retained in the lungs (Sadauskas et al., 2007). It is clear that by making minor modifications in nanostructures more efficiency can be achieved in targeting desired organs.

Secondary targeting of these structures involves several methods, including endocytosis and channel proteins located in the plasma membrane. For example, clathrin is a cytosolic molecule that makes coated vesicles. Ligands in drug carriers are recognized by receptors in the plasma membrane, which ultimately leads to the formation of clathrin-coated vesicles in the cytosol engulfing the nanocarriers (Céline M. Dubéa, 2012). Caveolae-mediated endocytosis uses caveolae instead of clathrin. Caveolae is a cholesterol and sphingolipid-rich invagination in the plasma membrane. Upon receptor binding, caveolae vesicles can move within the cytoplasm to different cell compartments, while avoiding degradation of the nanostructures before they arrive at the desired location (Peters et al., 2003). Caveola vesicles can carry particles less than 80 nm in diameter, while clathrin vesicles can carry particles greater than 100 nm. Artificial channels that form pores in the membranes can also be created with DNA origami, allowing certain ions to move into the cell cytoplasm for specific targeting (Hu et al., 2019).

The use of DNA nanotechnology to create structures for drug delivery holds great promise for curing inherited and acquired diseases.

The use of DNA nanotechnology to create structures for drug delivery holds great promise for curing inherited and acquired diseases. Some of these include cancer, neurological disorders, AIDS and cardiovascular diseases (Keles et al., 2016). In fact, potent anticancer drug molecules have been successfully loaded on DNA nanostructures to increase cell uptake efficiency (Hu et al., 2019). DNA can be precisely engineered with controllable shape, size, function and surface chemistry to be directed towards specific organs and specific cells. Although this approach would solve many of the issues inherent in current delivery systems, it is important to also note the drawbacks. This technique often leads to less than 100% yield of the desired product due to mis-assembly or mis-folding. Also, the structure must be specified through local interactions, which

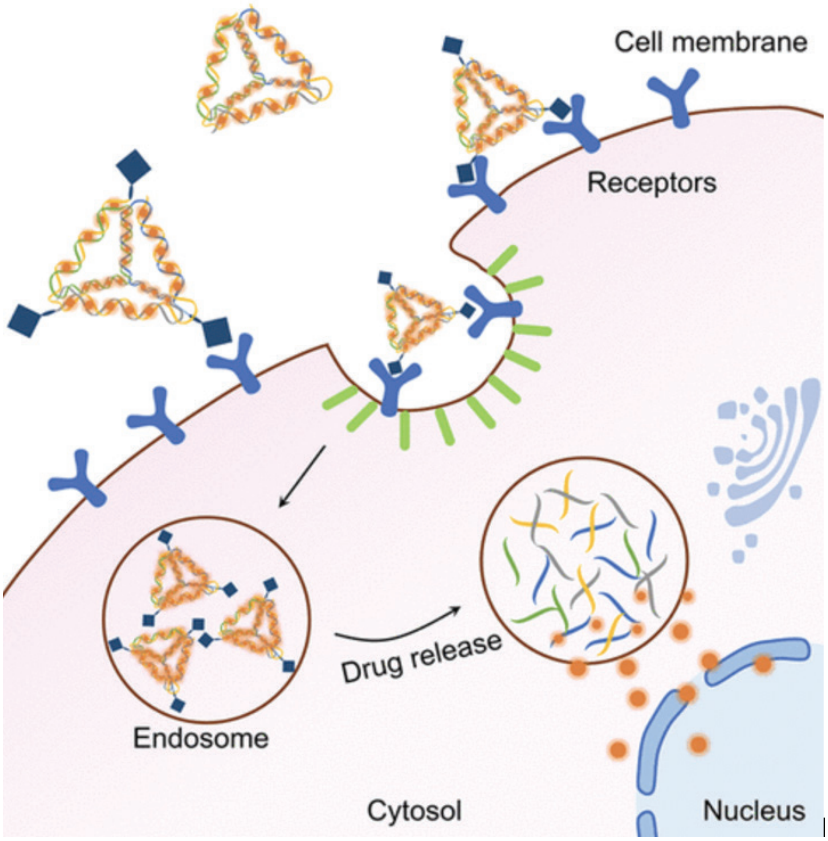

Figure 3. This image shows the mechanism by which DNA nanostructures interact with cells for effective drug delivery. Image from Hu 2019.

requires many unique building blocks so that sufficient information becomes available, which can often be very expensive. DNA nanotechnology is a field in progress, and scientists will continue to optimize the creation of these nanostructures to develop the ultimate drug delivery system in the human body. ❧

AUTHOR BIO

Laura Paule is a third year in the college double majoring in Biology and Spanish & Portuguese. The hobby she could never give up is playing chess.

Edited by Lauren Flamenbaum, Alex Sandberg and Dr. Mohammed Shahait

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Organ-on-a-chip: A microfluidics simulation of organ physiology

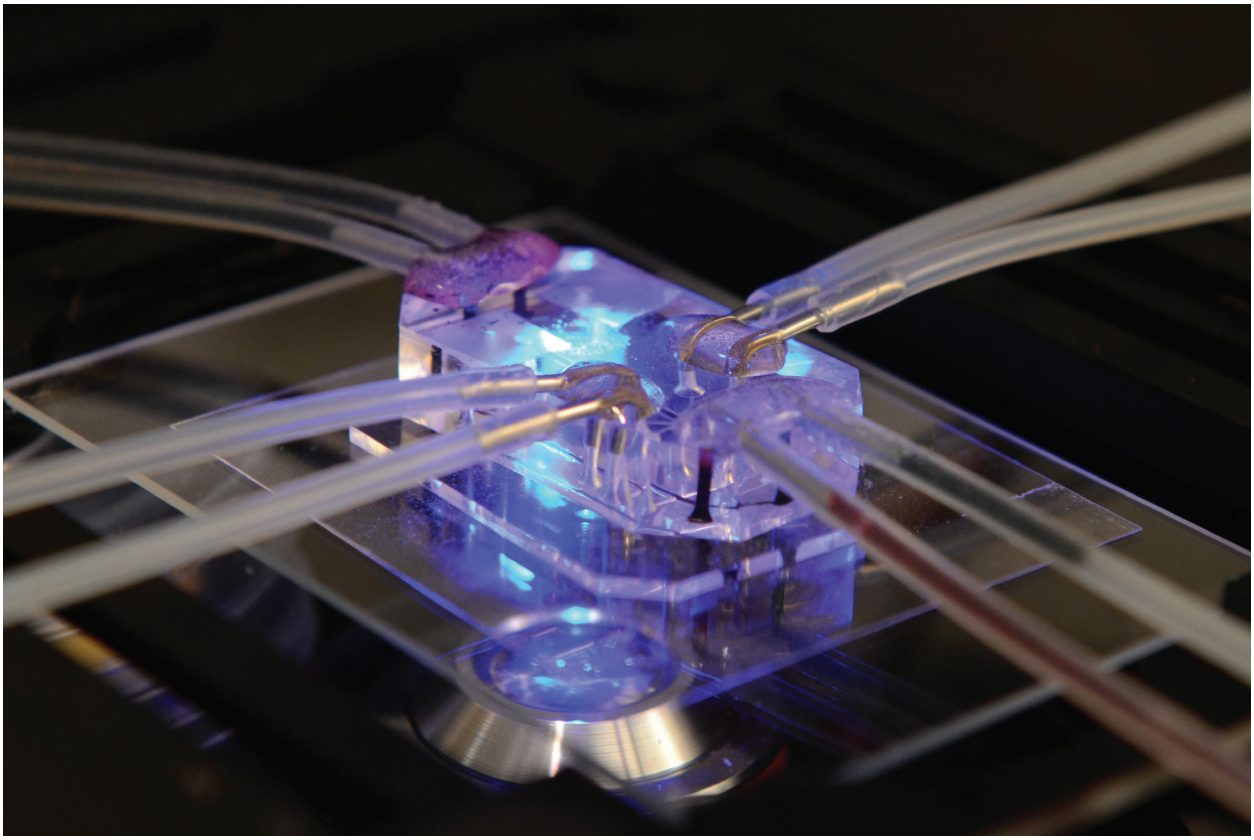

Figure 1. A "lung-on-a-chip": The chip, positioned here atop a microscope, is connected at microfluidic channel inlets and outlets to vacuum and flow channels to simulate the physiological behavior of the organ. Image from Wyss Institute/Design Museum 2013.

ANIRUDH RAGHAVAN
Staff Writer

Today's pharmaceutical industry faces an immense hurdle with regard to the inefficiency associated with drug discovery and development. In a recent study published in JAMA Network, Wouters et al. estimated that the median research and development cost per FDA approved therapeutic drug or biological agent was $985 million, after accounting for expenditures associated with failed clinical trials. In light of the growing necessity to model human diseases in vitro to accelerate drug development and to improve clinical predictions of drug efficacy and safety in humans, microfluidic cell culture devices —"Organ-on-a-Chip (OOAC)"— have proven to be promising in their adaptive design flexibility, precise experimental control over molecular-scale properties, and their ability to mimic the physiological conditions of organs (Fig. 1). Organs-on-chips are fabricated using soft photolithographic etching, a form of the lithographic etching used in manufacturing computer microprocessors. The chip itself is roughly the size of a AA battery and consists of an optically clear, rubber-like polymer with hollow 3D microfluidic chambers that function as adhesive islands for human organ-specific cell populations in a sea of culture media, providing a tunable microenvironment (Fig. 2). The result is a virtually living, experimentally manipulatable cross-section of human organs. However, the technology is still in its infancy — OOACs are not yet robust and reliable enough to satisfy regulatory guidelines for clinical drug testing, and the technology's scalability in cap-

...[it is] estimated that the median research and development cost per FDA approved therapeutic drug or biological agent was $985 million...

turing whole-organ and multi-organ function remains questionable. Nevertheless, the prospect of simulating organ function on a microdevice warrants discussion of its design process and applications, as well as thoughtful debate regarding its potential points of merit and demerit.

Designing an OOAC culture system involves closely reflecting in vivo intracellular and extracellular environments. The first component required in a microfluidics system is a dynamic culturing system to mimic the supply of nutrients and the removal of waste materials from cells. This is accomplished using a technique termed "micro-pump perfusion" (Wu et al., 2020). In addition to this, micro-pump perfusion also exerts both the fluid shear stress and the mechanical stress needed for proper cell differentiation and mechanotransduction, wherein cells activate signaling pathways in response to mechanical stimuli to mediate tissue development. The second component required is a method for maintaining microfluidic biochemical concentration gradients. The mode of flow of fluids within an OOAC is laminar - this means that fluid flow is orderly and stable with particles close to micro-tube surfaces moving in straight, parallel trajectories. This is significant since the experimenter can manipulate micro-tube geometry and flow velocity with ease and can set up desired concentration gradients without needing to compensate for irregular fluctuations in flow. The third component in the system is living tissue, and the fourth component is a means to capture, assess, and quantify data from living tissue. The precise positions of individual cells within tissue must be controlled to replicate the cell heterogeneity observed in functioning organs. In OOACs, this can be accomplished by 3D printing which creates complex, hydrogel-based, biocompatible scaffolds. With respect to data collection and analysis, researchers describe using embedded microsensors and automated confocal imaging techniques to analyze variant cell phenotypes, either induced by pathophysiological conditions or by drug molecules, with improved detail and accuracy compared to standard microscopic techniques (Peel et al., 2019; Basiji et al., 2007).

given the increasing cellular complexity...with macro-scale 3D culture systems, it is easier to conduct high-resolution imaging to visualize cellular processes in OOACs

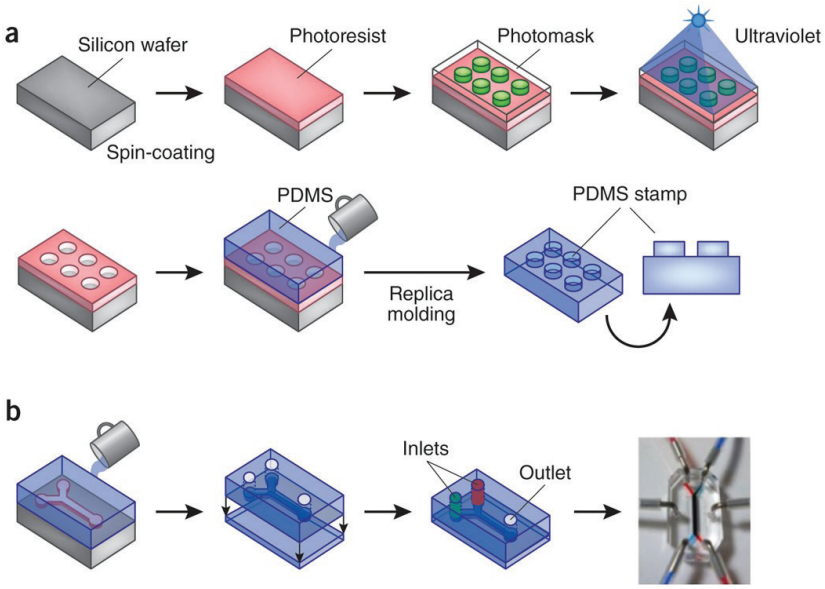

Figure 2. The original fabrication method for microfluidic chips. Panel (a) describes the photolithography process of etching the microscale pattern onto the silicon chip, and the replica molding technique of using liquid polymer to create a polymer "stamp" bearing an etched photoresist pattern which can be used for microcontact printing of extracellular matrix (ECM) molecules onto any substrate. Panel (b) depicts a single-channel microfluidic chip consisting of two inlets, a single main channel, and one outlet. Image from Bhatia & Ingber 2014.

Once the OOAC has been designed, how is it used for drug synthesis and development? In recent years, multiple research groups have utilized OOACs to study drug ADMET properties (Adsorption, Distribution, Metabolism, Elimination and Toxicity) of drug molecules and to create pharmacokinetic models to track drug trajectory through the human body. Specifically, livers-on-chips and liver-kidney microfluidic chips have been used extensively to illustrate the ADMET properties of certain anticancer drugs (Fig. 3), and the results have been noteworthy.

One study employs the use of livers-on-chips to study how the liver metabolizes the anti-

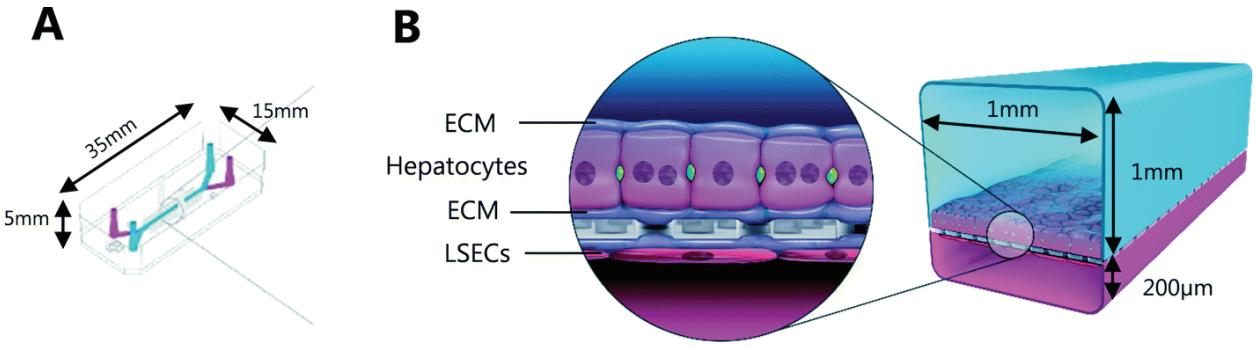

Figure 3. (A) Dimensions of a typical liver-on-a-chip; (B) Microfluidic cell-channel interface, incorporating a layer of hepatocytes held within extracellular matrices, and a layer of liver sinusoidal endothelial cells (LSEC) which emulates the blood capillaries of the liver. Image from Peel et al. 2019.

cancer prodrug flutamide into the drug hydroxyflutamide (a prodrug is an pharmacologically inactive compound which is metabolized by the body into its active form) and analyzes any potential hepatotoxicity. Researchers used a hepatocellular cancer cell line within microfluidic biochips to metabolize flutamide and reported dysfunctions in both mitochondrial function and glucose homeostasis (Choucha-Snouber et al., 2013). Extracellular glucose consumption and citric acid cycle activity was markedly lower compared to their controls, leading to increased lactate production and amino acid metabolism. Further, there was a constitutively high energy demand in the liver cells in the OOAC; the greater oxidative stress could not be alleviated due to decreased glutathione levels that resulted from increased metabolism of several amino acids (Choucha-Snouber et al., 2013). Since glutathione is an important antioxidant, reduced levels is a classic hepatotoxic signature reflecting [or leading to] a buildup of potentially DNA-damaging reactive oxygen species (ROS). All the aforementioned effects were consistent with previous literature and patient data from clinical trials, demonstrating the capability of livers-on-chips for studying drug metabolism. In another study conducted by the same research group, the metabolic effects of the chemotherapeutic prodrug ifosfamide (which is metabolized in the liver to become the active drug isophosphoramide mustard) were analyzed using a microfluidic liver-kidney chip, and this time the liver was modeled using both the hepatocellular cancer cell line and a human liver stem cell line to test nephrotoxicity. The authors noted that the nephrotoxic metabolite chloroacetaldehyde, which results from ifosfamide metabolism, was only produced by the stem cell line and not by the liver cancer cell line (Choucha-Snouber et al., 2013). This finding coincides with previous literature as well - ifosfamide treatment does have a direct nephrotoxic effect (it causes direct tubular injury) in testicular cancer patients who have normal liver function (Nissim et al., 2006); however, ifosfamide is ineffective in treating hepatocellular carcinoma (Lin et al., 1993). Thus, this study demonstrates the power of OOACs to simulate cell selection and illustrates the ability of OOACs to model organ-organ interactions (Bhatia & Ingber, 2014).

Specifically, studies on the predictive capability of animal models have shown a poor correlation between data derived from animals and human patient outcomes

As with any 3D culturing system, OOACs have distinctive advantages and disadvantages. Macro-scale cell culturing systems generate more cell and tissue mass than microfluidic chips, which is advantageous when performing drug screening with analytical techniques such as mass spectrometry. Microfluidic chip fabrication requires micro-engineering expertise (Bhatia & Ingber, 2014) and is relatively cost-ineffective for use in personalized or precision medicine. There is also a substantial disadvantage of OOACs in terms of the material used for cell patterning, which is often poly dimethylsiloxane (PDMS): PDMS has been implicated in the absorption of small hydrophobic molecules and is highly perme-

able to certain gases, which can adversely affect certain drug concentrations and pharmacological effects (Shay, 2017). Additionally, due to the microscale nature of the chip, it is difficult to uniformly seed microfluidic channels and protect the system against microbial contamination (Bhatia & Ingber, 2014). Animal models have also proven to be more accurate than OOACs in recreating certain highly complex organ systems such as the endocrine, immune and nervous systems (Esch et al., 2015). Nevertheless, microfluidic culture systems offer many merits: given the increasing cellular complexity and functionality of the organ or organ system with macro-scale 3D culture systems, it is easier to conduct high-resolution imaging to visualize cellular processes in OOACs (Bhatia & Ingber, 2014). The ability to manipulate fluid flow in microchannels allows for long-term modeling of pathophysiological responses, such as those described previously, which is difficult to accomplish in other 3D culture systems. Fluid flow also recreates interactions between circulating cells and other physiologically relevant components such as immune cells, blood cells, and tumor cells (Bhatia & Ingber, 2014). The ability to change the vascular composition of microchannels, and the ability to modify how each cell interacts with the extracellular matrix allows for the creation of a truly dynamic microenvironment.

Given the current regulatory requirements for drug approval, the organ-on-a-chip technology may represent a financially efficient, in addition to temporally efficient, alternative to traditional research and development processes such as animal testing. It has been reported that the OOAC technology can potentially reduce the average total pharmaceutical research & development cost by 10–26% (Franzen et al., 2019). Some researchers have suggested the use of OOACs in modeling certain rare diseases and pediatric diseases, for which research is limited by the lack of appropriate in vitro modeling approaches, low patient availability, and small patient population. OOACs also show great translational accuracy from in vitro research to clinical research in comparison to animal testing models (Shay, 2017). Although animal studies can mimic whole-organismal physiology, their scientific validity and translatability to humans are increasingly being questioned (Esch et al., 2015). Specifically, studies on the predictive capability of animal models have shown a poor correlation between data derived from animals and human patient outcomes, due to substantial interspecies differences in key disease pathways and gene expression profiles (Esch et al., 2015). Despite its limitations, the OOAC model has proven to be quite robust in assessing the pharmacokinetics of drug compounds and possesses remarkable potential for improving the modern drug development process. ❧

AUTHOR BIO

Anirudh Raghavan is a third year in the college double majoring in Chemistry and Biology. He can read, write and converse in four different Indian languages.

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Placed by Vivian Huang

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Genomic predictors enhancing sports injury prevention

NICHOLAS RYU
Staff Writer

Between 2011 and 2014, there have been a recorded 8.6 million sports related injuries in the United States according to the CDC (Sheu, Chen, and Hedgaard, 2016). Most of these injuries tend to be sprains and strains of muscles, ligaments, and tendons (Stanford Children's Health). Understanding the prevalence of injuries in sports requires a multifactorial explanation of modifiable and non-modifiable risk factors, including the type of sport being played, environmental factors, fatigue, overtraining, and genetics. Noticeably, genetics is a highly individualized factor in sports etiology that cannot be prevented. Genetic variation can affect certain structural characteristics of the human body, which consequently may influence a person's risk for injury. Multiple studies have shown the stabilizing or destabilizing effects that some gene variants have on joint structure and their correlation to particular sports injuries. The prevention of injuries caused by predispositions to certain genetic variations is difficult to address given current technology and ethical standards, because we can only treat the symptoms instead of directly addressing the underlying genetic cause. By determining genes that code for structural phenotypes and understanding how these gene variants influence body structure, we can make important advances to improve the predictive power and prevention of acute sports injury.

Genetic variation can affect certain structural characteristics of the human body, which consequently may influence a person's risk for injury.

First and foremost, it is important to clarify how genetics affect structure, including a

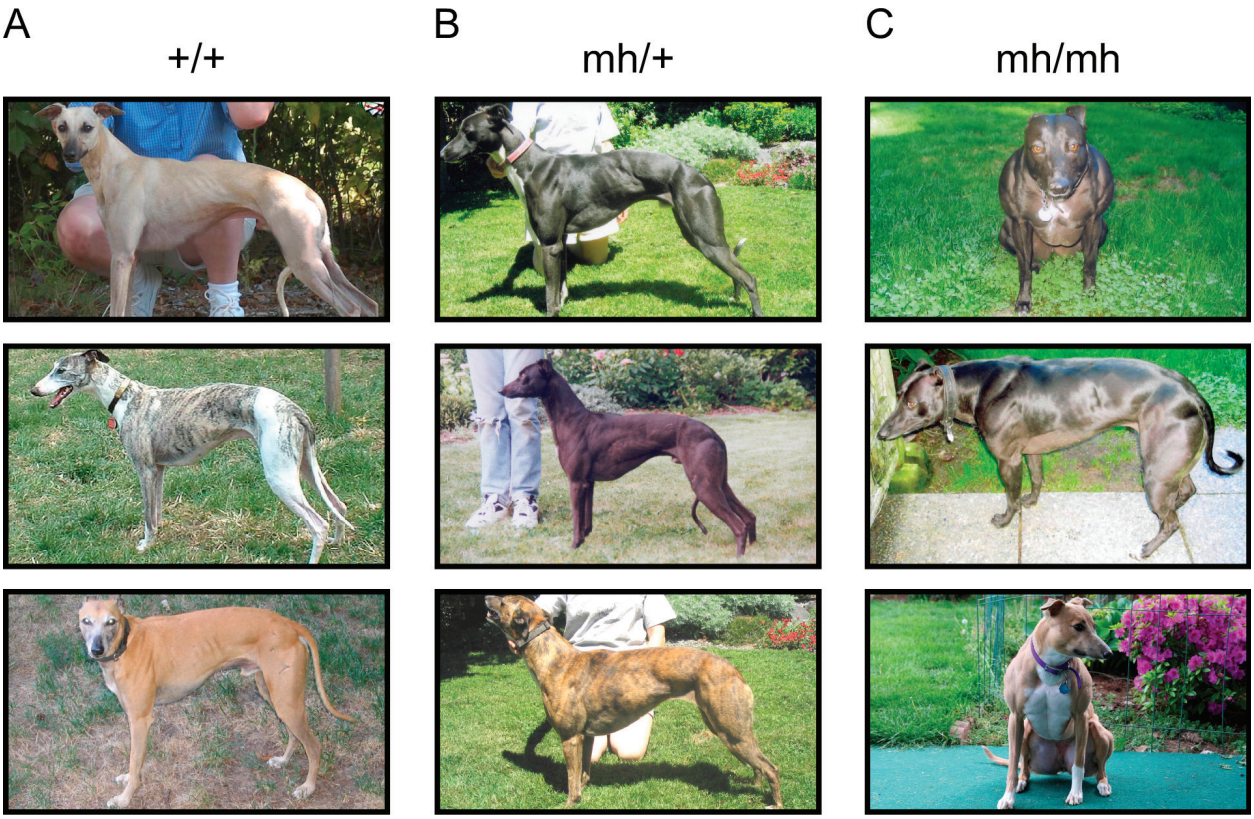

Figure 1. The whippet on the far left has the wildtype alleles (+/+) with no MSTN gene mutation, the one in the middle has one MSTN allele making it slightly more muscular (mh/+), and the far right is homozygous for the MSTN gene mutation (mh/mh) completely deregulating muscle growth inhibitors. Image from Mosher et.al, 2007.

person's appearance and physical makeup. The human genome contains all of the information we need to build and maintain life, and determines what we will look like and how we will function. The power of genetics and their influence over our body is often taken for granted, but it is primarily our genetic makeup that determines our body's phenotypical structure. However, genes are not created equal because they vary from person to person. In regards to anatomical structure, each person has different genetics and are therefore built differently. Two examples that highlight the effects of genetic variation on different corresponding phenotypes are the myostatin gene in muscle growth and collagen genes in Ehlers-Danlos syndrome.

Each gene is on a different chromosomal position and codes for specific structures in the body, with their own stabilizing or destabilizing effects in joints.

In a study that examined the genome of heterozygote racing dogs, researchers found that a mutation in the myostatin gene (MSTN) produced dogs more fit for racing (Mosher et.al, 2007). These dogs were faster and had more muscle mass than the homozygous wildtype dogs who did not have the mutation (Mosher et.al, 2007). Figure 1 below illustrates this difference between whippet muscular phenotypes. The data collected in this study shows how a single point mutation in a gene has the potential to drastically alter muscle generation and structural phenotypes. Another study by Verbrugge et al. manipulated genes in mice and identified 47 genes, including the MSTN gene mutation, related to muscle hypertrophy (2018). These 47 genes were either expressed or suppressed throughout experimentation. This study further shows that different gene expression patterns can have drastic results on phenotype. This concept is not just present in muscle growth but in all structures of the body.

Ehlers-Danlos syndrome is a heritable connective tissue disorder caused by mutations in the genes coding for collagen structure and stability: COL5A1, COL5A2, and COL51A (Malfait et.al, 2007). The syndrome is characterized by joint hypermobility and stretchy skin due to the presence of more elastic collagen fibers in the skin. More common and less extreme examples of collagen differences can be found in those who have simple joint hypermobility, formally called hypermobility syndrome (HMS). HMS is similar to Ehlers-Danlos syndrome and is caused by similar genetic mutations affecting collagen structure phenotypes; however, HMS phenotypes exhibit collagen elasticity only in joints and on a less severe level (Malfait et.al, 2006). Both Ehlers-Danlos syndrome and HMS showcase the genetic potential for connective tissue variability in individuals.

The myostatin gene mutations in muscles and collagen gene variants leading to Ehlers-Danlos syndrome and HMS demonstrate how genes are integrally related to body structure, and that each individual has the potential to be structurally different due to genetic variations. With the myostatin gene mutations, being able to generate more muscle than normal may have a beneficial effect in improved joint support and a reduced risk of injury, while in Ehlers-Danlos syndrome and HMS, having stretchy collagen may increase the risk of injury due to joint instability. Since genes can either have a stabilizing or destabilizing effect on the anatomical structure, it is import-

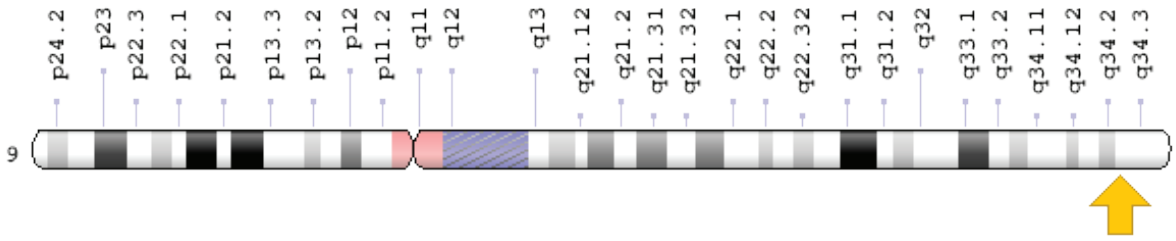

Figure 2. The arrow is pointing to the location of gene COL5A1 on the chromosome, variations of this gene are associated with protein expressions correlated with Ehlers-Danlos syndrome and HMS leading to joint instability. Image from MedlinePlus Genetics.

ant to determine which genes are associated with greater risk of orthopedic injury and their corresponding phenotypic changes. Determining these unknowns would prove to be a beneficial addition to sports etiology as it will provide athletes, trainers, and sports medicine specialists with more accurate predictions and the foresight necessary to prevent potential injuries.

McCabe and Collins published a recent study highlighting how genetics can predict injuries in soccer players (2018). Their goal was to identify genes that could be associated with ankle and knee injuries, which are under constant stress in soccer and therefore, are more likely to be injured. Players in the sample population were genetically tested and then the number of ankle or knee injuries during the season was recorded for each person. Based on the genetic analysis of those players, researchers found that allelic variants in genes GDF5, AMPD1, COL5A1, and IGF2 were correlated with injury (McCabe and Collins, 2018). Each gene is on a different chromosomal position and codes for specific structures in the body, with their own stabilizing or destabilizing effects in joints. Results from the study have shown that different allelic variants of the aforementioned genes result in different protein expression rates that correlate with increased rates of ankle and knee injuries in the soccer player sample group (McCabe and Collins, 2018). The data collected in this study identifying these specific genes lays the foundations for future studies to identify the specific mechanisms that allow these variants to cause structural instability. From there, researchers can then develop treatments and training regimens that serve to alleviate the structural instability.

Figure 3. Utilizing exercises to strengthen muscles around the joint and developing the correct movement fundamentals in sports decreases one's inherent risk to sustaining an injury. Here, the forward step-down as demonstrated in HEP2Go is a great exercise for developing balance as well as strengthening the muscles around the knee. Image from Hep2Go 2012.

...having genetic information allows for the prescription of...therapies that can...directly compensate for potential genetic destabilizing effects and reduce risk to injury.

It would be wise to conduct more studies similar to McCabe's and Collins's for different sports, in order to identify more genes that contribute to athlete injury risk. By building a database, it opens the gates for future research and opportunities for injury prevention.

Progress continues to be made on the research front, but the information and data already collected leaves medical professionals, trainers, and athletes at a bit of a standstill, since there is no way to directly change an athlete's genetic makeup. A pilot study by Goodlin et al. was successful in performing genetic testing on athletes and prescribing appropriate training regimens as therapy (2015). For example, 3 athletes in the sample group had genetic variants that put them more at risk for Achilles tendinopathy, and therefore, altered training regimens and therapy were prescribed to mitigate this risk. Analyses and training prescriptions were given to other

athletes with predispositions for other acute sports injuries. Eight out of the twelve athletes were ultimately recommended for new training regimens based on their genetic assessments. As a result, the rates of sustaining an injury in the sample population decreased from 71% in the previous season to 33% in the new season (Goodlin et.al 2015).

Although a promising advancement, the use of genetic testing for injury prevention has limitations, including unequal access to testing, ethical questions, and confounding variables that require more studies to be performed before the practice can be broadly implemented. In regards to accessibility, genomic sequencing is still a relatively expensive procedure, with each sequence costing the consumer up to $1000 (Wetterstrand, 2020). Although the price has fallen since its introduction into the scientific community, genomic sequencing is an expensive test that most non-professional or amateur athletes may not be willing to pay. In addition, generating a genetic database may lead to societal concerns over the collection and use of private health information. There are currently no federal health regulations in place that dictate how collected genetic data can be used. Therefore, it is important to define these regulations before implementing widespread genetic testing for injury prevention (Goodlin et.al, 2015). Lastly, there are some experimental design flaws that arose in recent studies, including small sample sizes (most studies generally ranging between 10-20 participants) which decreases the validity of the studies due to potential sampling errors. More importantly, the probability of sustaining an injury is the most frequently used metric without accounting for other variables. This can lead to misguided correlations and assumptions that genetics are the dominant cause for injuries. Going back to the fundamentals of sports etiology, sustaining an injury is due to a combination of factors, such as external variables like weather or freak accidents involving other players. It is important to try to mitigate these external variables in order to draw stronger correlations between genetics and injury risk. By doing so, it will not only increase the validity of the study, but also crystallize the effects and correlations surrounding genetic variants.

Employing genetic testing can yield intriguing correlations regarding the way genetics affects injury risk. In this emerging field, more studies that utilize a larger athlete sample size are needed to support the validity of the data already collected. The collection of genetic information should not be used to discourage individuals from playing certain sports or activities, but rather as a baseline that athletes can use to identify weaknesses that can be offset with the right training regimen, diet, and lifestyle choices. Given greater accessibility, improved ethicality, and refined data collection methods, the role of genetics in sports etiology has the potential to provide crucial information that can transform the field of sports injury prevention. ❧

AUTHOR BIO

Nicholas Ryu is a third year in the college majoring in Anthropology & Human Biology with a minor in Predictive Health. This recent quarantine has allowed him to develop an interest in cooking and often enjoys making east asian flavors he grew up eating with his family.

Edited by Aditya Jhaveri, Luisa Taverna and Dr. Sarah Blanton

Placed by Carissa Wu

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The role of diet in mediating Alzheimer's disease risk

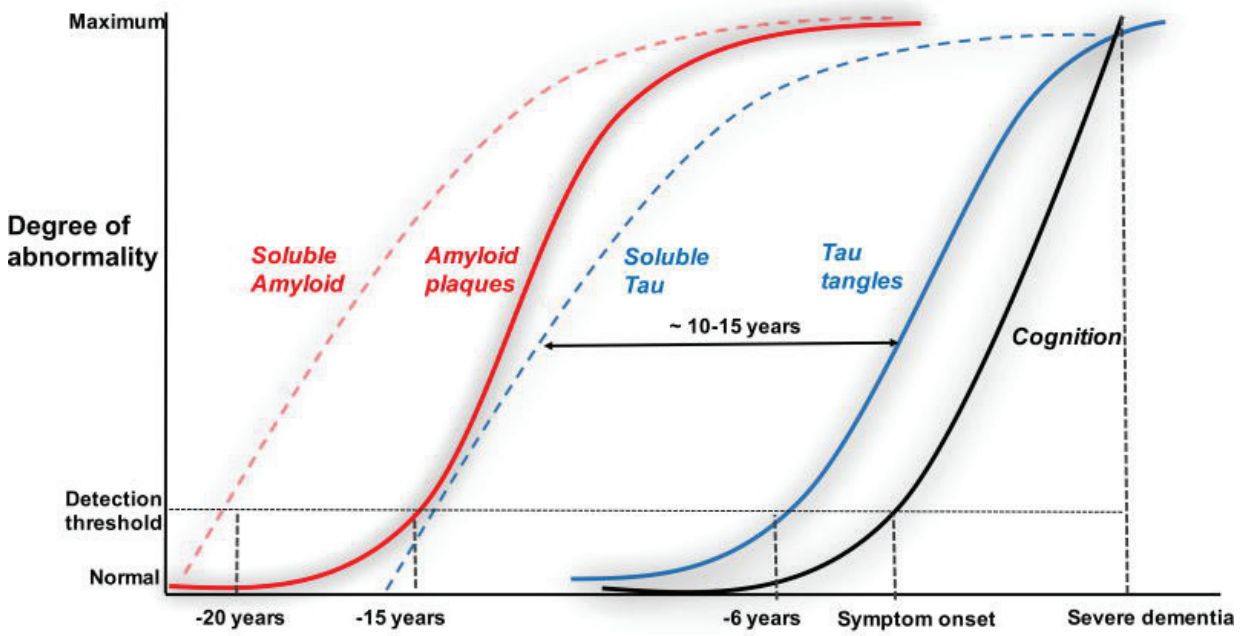

Figure 1. Amyloid plaques begin building in the brain up to 15-20 years before any symptoms of AD are observed. These symptoms typically begin during the increase in tau tangles in the brain. Image from McDade 2018.

LARISA KOYEN
Staff Writer

While improvements in U.S.A. sewage systems, housing, and education during the 19th century led to a 32-year increase in life expectancy, they also introduced unpredictable health problems that have the power to change the identity of a person (Mather & Scommegna, 2016). The most common of these diseases is dementia, caused by Alzheimer's Disease (AD) 60-80% of the time. Until the interaction among the environment, diet, and genotypic predispositions towards AD are understood, treatments and prevention for this debilitating disease will continue to be insufficient.

Since amyloid plaques, which are associated with AD progression, can begin building up in the brain up to 20 years before symptoms begin, some therapies attempt to increase the number of years lived between these two events (Sanders, 2020). A healthy diet and lifestyle continues to be recommended for all, regardless of genetic predispositions for illness or current health conditions, It is worth exploring whether the genetic and environmental predispositions that put individuals at higher risk for developing AD can be offset by the consumption of certain foods.

There are certain genetic and environmental factors linked to predisposal to AD. While aging and AD rate are strongly positively related, it is unlikely that normal aging is the sole factor involved in AD development. Brain tissue atrophies much faster than normal in those with AD (Eid, Mhatre & Richardson, 2019). Other common signs of AD are loss of brain tissue, decreased memory, and decline in cognitive functioning, which are typically associated with the build-up of amyloid plaques in the brain. There is not enough evidence to establish a causal relationship between amyloid plaques and AD. Furthermore, amyloid plaques are also found in smaller amounts in the brains of healthy humans, which further

...amyloid plaques are also found in smaller amounts in the brains of healthy humans, which further complicates research on better understanding the pathology.

complicates research on better understanding the pathology. Nevertheless, Alzheimer's treatments typically address the build-up of these insoluble amyloid plaques and neurofibrillary tau tangles in the brain.

The inability thus far to determine if plaques are a cause or effect of AD has led scientists to look to other potential links. One of the more promising of these hypotheses implicates the most common bacteria in gum disease, *Porphyromonas gingivalis*, for the worsening of cognitive decline. This bacteria is found in the brain of AD patients in the same areas as amyloid plaques and, on its own, leads to neural damage in healthy mice (Mackenzie, 2019). Mutations during DNA replication is another possible explanation for the development of AD. These can occur as a result of exposure to mutagens which can cause expression of normally inactive genes. In addition to these aspects of the environment that may play a role in AD etiology, there is also strong evidence that diet is key to the story.

...plant-based diets and caloric restriction, but not malnutrition, can decrease rates of general neurodegeneration.

Since the discovery of Alzheimer's Disease in 1906, the scientific community has been closely examining the possible protective effects of specific foods and nutrients against the development of the disease. For example, plant-based diets and caloric restriction, but not malnutrition, can decrease rates of general neurodegeneration. On the other hand, high red meat and processed sugar intake are associated with a higher level of cognitive decline.

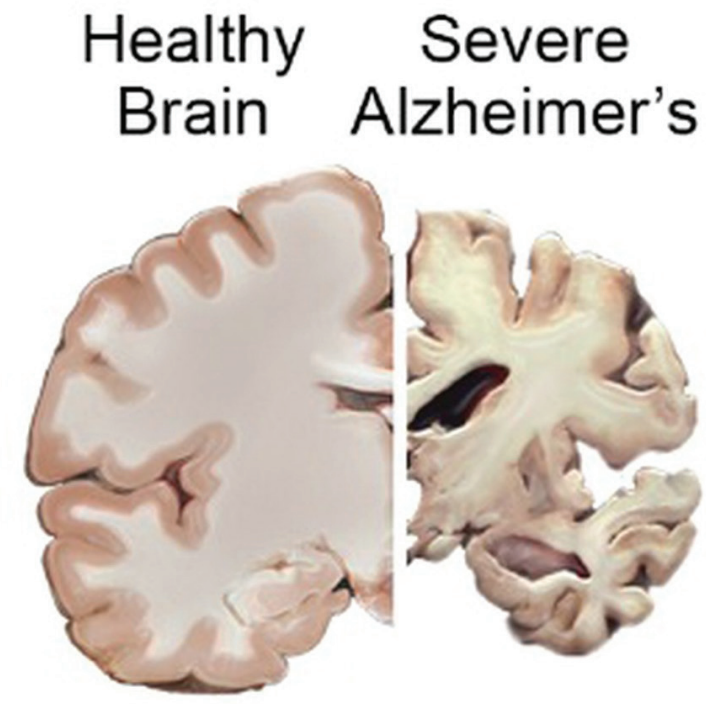

Figure 2. The brains of most AD patients show extreme shrinkage of the cerebral cortex and the hippocampus, leading to severely enlarged ventricles. This is the end result of neural damage. Image from NIH National Institute on Aging 2019.

Even more, the addition of a single ingredient such as turmeric to a diet in mice was shown to benefit spatial memory and neuronal function, whereas single nutrient deficiencies in phytonutrients, vitamins B and D, and minerals such as iron and magnesium are also associated with a lower levels of cognitive impairment and higher rates of AD (Pistollato, 2018).

In addition, the omega-3 fatty acids found at high levels in fish and nuts also help prevent the degeneration of neural tissue. Omega-3 fatty acid consumption increases the efficacy of microglial cells in preventing the tau aggregates associated with AD the amount of microglial cells that are put in the anti-inflammatory phase instead of the inflammatory phase and control the amount of receptors on the surface of microglial cells. Both of these biochemical responses have the power to decrease the spread of tau protein since AD is characterized by the prolonged inflammatory state of microglial cells, which promotes the hyperphosphorylated tau aggregates (Desale & Chinnathambi, 2020).

Some argue that eating turmeric and fish every week won't save someone from developing AD and that diet should be approached in a more holistic manner. One example of this approach is the Mediteranean diet, which consists mainly of fruits, vegetables, whole-grains, minimal meat and dairy consumption, and no processed

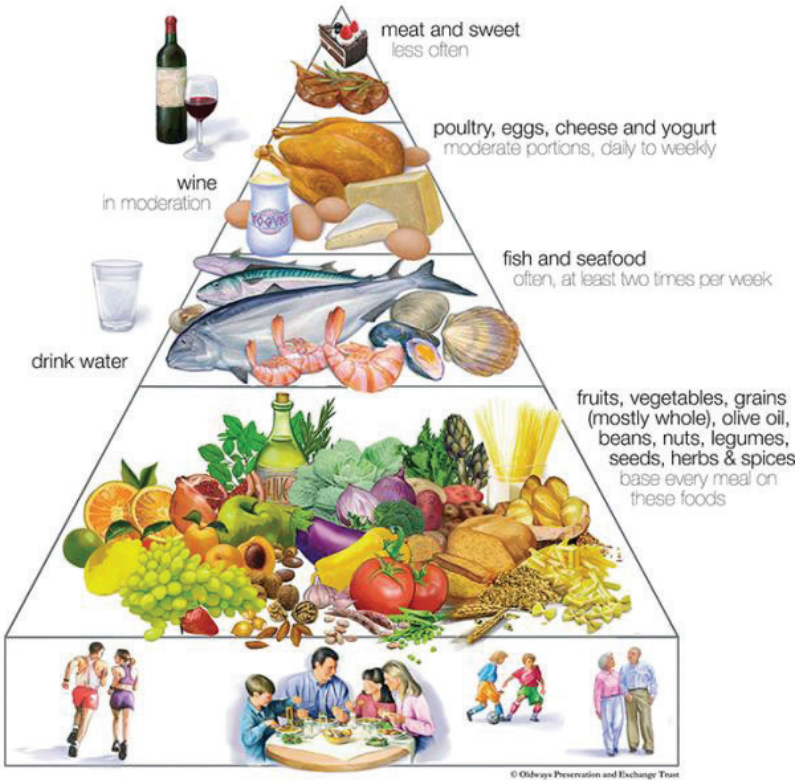

Figure 3. The Mediteranean diet focuses on plant-based foods, ranging from whole grains to fruits and vegetables. Image from Oldways Preservation and Exchange Trust 2016.

food. The unsaturated fatty acids, antioxidants, folates and vitamins E and B12 in this diet have been shown to slow cognitive decline. Consuming these nutrients could potentially aid in the prevention of developing Alzheimer's Disease (Solfrizzi et al., 2014).

How much, if at all, can genetic risk factors for developing AD be overcome by a diet high in plant-based foods and unsaturated fatty acids? While scientists have not yet gathered sufficient evidence to provide a direct link between certain foods or lifestyle modifications with a reduced rate of AD, it is clear that a combination of healthy food consumption, exercise, and reduction of anxiety can at least moderate genetic risks. The great variation in how the disease presents itself strongly suggests that environmental factors play a role in the development of the disease. However, environmental factors cannot, on their own, explain the progression of the illness, just as no single genetic mutation can.

The historically and significantly lower-than-average dementia prevalence in Greece, where the Mediterranen diet is commonly consumed also is consistent with the importance of food choice in relation to AD

But the interaction between genotype and environment provides a clear basis for differences among AD phenotypes. In a longitudinal study where 75-year old patients with a gene that gave them an increased risk for developing AD were assessed for symptoms of dementia, those who exercised regularly showed decreased symptoms after the four and a half year follow-up ("2018 Alzheimer's," 2018).

The historically and significantly lower-than-average dementia prevalence in Greece, where the Mediterranen diet is commonly consumed also is consistent with the importance of food choice in relation to AD (Kosmidis, et. al., 2018). As there are many known, and likely unknown, genetic unmodifiable factors increasing the chances of developing this disease, eating some nuts and vegetables is a viable option. There are certainly modifiable environmental and unmodifiable genetic factors that can increase chances of developing AD. However, diet is one of the modifiable factors. Individuals hold more power over their long-term health than many might think. ❧

AUTHOR BIO

Larisa Koyen is a fourth year in the college majoring in Biology. And interesting fact about her is that she has never broken a bone in my body.

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Placed by Anshruta Dhanashekar

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Fact to fiction: Children's storybooks as a catalyst for agency among pediatric patients

SARINA ADELINE
Staff Writer

Figure 1. A diagram of the SPIKES clinical model for delivering difficult news to patients. Image from The Wall Street Journal 2015.

You click your pen. You don't have anything to write down, but you want to seem as though you do for the sake of the mother, who is looking at you as if you have all the answers. You are nervous: sweaty armpits, hot breath, and a quiet burn behind your nose. Knowing the answers doesn't mean you know how to *deliver* the answers. The lab results gaze back up at you cruelly, unabashedly. You wonder if she will cry when you tell her she has sickle cell anemia. She doesn't cry when you read her the blood counts from her lab results. She doesn't sniffle when you tell her that she likely inherited one sickle cell gene from her mom and one gene for beta thalassemia from her dad. She picks her cuticles while you tell her that there are two types of beta thalassemia: "0" and "+." She doesn't even blink when you tell her that many of her red blood cells are shaped like crescent moons. It isn't until you mention blindness that she looks up. But how will she paint? All she wants is to be an artist. Her face crumples. This is the worst part. You tell her she is brave, but she gets up from the examination table and runs to her mom. She cries for a long time. You have to move onto the next patient, so you apologize. You want to cry, too, but instead you click your pen a couple more times, write down the name of a specialist for a referral, and excuse yourself. You've sat through a couple of webinars about compassion based care—and you do care—but knowing what you know, it's hard to speak the same language as a little girl who wants to paint.

...it's hard to speak the same language as a little girl who wants to paint.

With the pressure to provide both accurate information and compassionate care, what is a physician to do in a situation like this?

Delivering bad news is a challenging responsibility for the physician. Balancing scientific accuracy and emotional competence, the doctor walks on a high-wire, requiring precision, accuracy, and empathy. Patients prefer to receive difficult news in person, with the physician's undivided attention and "in clear, easy-to-understand language with adequate time for questions" (Berkey et al., 2018). Skillful delivery of life-altering or difficult news is essential to the patient's understanding of their health as well as their ability to care for themselves. In other words, a

physician's ability to communicate with patients, especially in regards to medical diagnoses, impacts a patient's agency. A framework to guide doctors through presenting potentially distressing information to patients and their families in an organized manner does exist, known by the acronym "SPIKES" (Kaplan, 2010). The acronym stands for the following: setting, perception, invitation or information, knowledge, empathy, and summarize or strategize. The sequence is designed to remind doctors not just to consider the patient's feelings, but to acknowledge and validate them while delivering critical information.

The SPIKES model aligns well with the goals of compassion based care, in which doctors practice a "form of cognitive and emotional perspective taking" (Fernando, 2016) that empowers physicians to better understand and alleviate suffering. By delivering difficult news and an action plan, doctors provide patients with a sense of control, a greater ability to tolerate pain, and in some cases, the capacity to recover from illness (Ha & Longnecker, 2010). However, the SPIKES framework requires the patient to be in a position to process the information given. A variety of factors could inhibit a patient's understanding of medical information, including cognitive development, education level, and access to information. For a pediatric patient, patient-doctor communication is an act of translation. A great responsibility rests on the doctor: to find a common language that is developmentally appropriate yet accurate. Dr. Rita Charon, a professor at Columbia University who pioneered the field of Narrative Medicine, emphasizes the importance of patient narratives in the collaboration between doctor and patient (2001). After all, narratives "provide the means by which people organize and relate the important experiences in their lives" (Russell, 1988).

A story can serve as a proxy for an emotional experience by placing a character in a situation that might resonate with the reader.

Narratives shape our lives. Beginning in infancy, the entertainment we consume, whether films or fairy tales, exists in various narrative forms. In one study, the ability of kindergarteners to understand and communicate through narratives appeared to be a predictor of reading comprehension and school achievement later in life (Demir, 2014). This suggests that narratives are not only common; they are integral to human development. The field of Narrative Medicine provides a unique conceptual lens through which to approach information. Its humanities-centric ideology stands in sharp contrast to the hard sciences and fact-based analytical approach to evidence that doctors must learn in order to thrive in the medical world (Zaharias, 2018).

Understanding the significance of narratives becomes vital in the context of breaking difficult news to a patient. Though a doctor may understand a diagnosis through blood counts and gene mutations, a patient understands it through how those symptoms manifest themselves and impact daily life. Communicating medical information to any patient is challenging, but the pediatric patient presents an added layer of complexity. While doctors train to work in the arena of the analytical, the nuance and complexity of scientific communication with pediatric patients warrants the humanitarian touch of an unlikely academic partner: fiction.

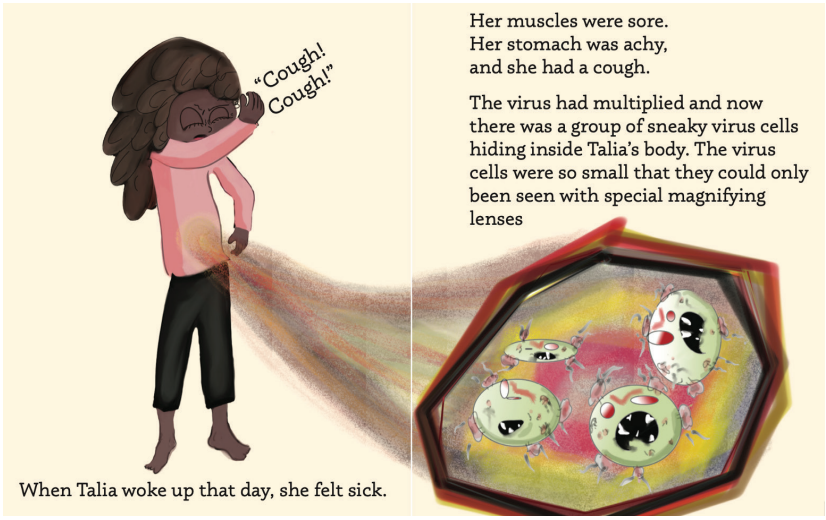

Figure 2. The spread (above) depicts one of the opening scenes from a fictional story about a girl who contracts a viral infection. The book, Talia and the Tiny T Cells, is authored by Jacqueline Palmer and illustrated by Matthew Taylor (2020).

Children's literature offers one of the most powerful tools for cultivating empathy among children (Kucirkova, 2019), and it makes use of narratives to present information in a way that is accessible and palatable to pediatric patients. Fiction has the capacity to accommodate a variety of subjects, serving as a medium through which to begin a dialogue. For example, a fiction story might represent a young girl with a diagnosis of sickle cell anemia navigating the triumphs and adversities of life with a medical condition. A story can serve as a proxy for an emotional experience by placing a character in a situation that might resonate with the reader. Specialists from other disciplines, including many educators, have already begun to harness the power of narrative.

Emory University's Center for Contemplative Science and Compassion-Based Ethics developed a curriculum to promote social, emotional, and ethical learning in the classroom. Using fictional stories as tools in the classroom provides a framework for elementary students to puzzle through and problem solve in difficult scenarios, as well as build valuable skills, such as practicing kindness (2019). Processing challenges through a narrative removes the emotional stakes of experiencing adversity oneself, and it provides a sense of solidarity and comfort to those who may have *already* experienced a similar situation. *Talia and the Tiny T Cells*, a forthcoming book, uses the fictional story of a young girl who contracts a viral infection to introduce some basic concepts of immunology (Palmer & Taylor, 2020).

Figure 3. These book pages show a fictional character's recovery from a viral infection. From Talia and the Tiny T Cells by Jacqueline Palmer and Matthew Taylor (2020).

The storybook anthropomorphizes pathogens as well as T cells inside Talia's body, telling the journey of her recovery while presenting the pathways of viral infection and immune response in a format that is accessible to a young patient.

The book reassures a child reader that the human body contains defense mechanisms against infection, so that the story delivers both scientific information and a sense of security. Talia's story approximates some of the complex processes that might occur in a pediatric patient's body, allowing a young patient to not only to comprehend illness, but to cultivate a sense of optimism, courage, and curiosity. The narrative format, which is communicated both through visual and written storytelling, provides an excellent tool for discussing illness while avoiding the immediacy that accompanies a discussion of one's own body.

...fiction offers an overlooked tool for physicians when they are considering how to help a pediatric patient process difficult medical news.

Such a resource would greatly enhance a doctor's interaction with a pediatric patient, providing a narrative framework through which to convey information as well as cultivate a sense of hope. Most importantly, increasing the accessibility of medical information by placing it in a familiar format gives young patients a greater understanding of their bodies and health. This understanding empowers the patient, giving even young patients the agency to contribute to conversations about their wellness. Although doctors are well-equipped with scientific and medical information, knowing facts alone may not be sufficient to provide adequate care, particularly in an emotionally fraught situation. Fiction provides a potential mode of delivery for distressing information that is familiar and comprehensible.

Greater collaboration be-

tween fiction writers and medical professionals could revolutionize patient-doctor conversations, just as Compassion Based Care completely altered the medical field's view of the role of empathy in healthcare. While scientific fact is an essential pillar of medicine, fiction offers an overlooked tool for physicians when they are considering how to help a pediatric patient process difficult medical news. ❧

AUTHOR BIO

Sarina Adeline is a third year in the college majoring in Creative Writing. She once had an aquaponics shrimp farm in her dining room.

Edited by Lizzy Wagman, Bushra Rahman and Dr. Laura Otis

Placed by Henry Mangalapalli

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Assessment of meat analogs as a major future food source

AIDAN SPRADLIN
Staff Writer

As the human population grows, we find ourselves asking the fundamental question of who and *what* will feed all these people. While agriculture and livestock continue to be the primary sources of sustenance for the population, they have significant environmental and human health consequences. Meat analogs— products that simulate the chemical, nutritional, aesthetic, and organoleptic qualities of food— became widely popular in the late 2010s. By inspecting the quality and impacts of meat analogs, we can explore their potential role in the modern market.

The future of meat analogs depends on the future population's demand for them. In a 2019 assessment, the United Nations predicted a global population of 8.5 billion people by the year 2030 (Desa, 2019). Similarly, the demand for food will increase in the near future by as much as 100% by 2030 (UNFPA, 2008; Valin et al., 2014). Additionally, GDP and wealth, especially in developing countries, will increase. Considering the positive correlation between a nation's GDP and meat consumption, demand for meat will increase at a similar rate (Vranken, et al., 2014; Steinfeld, et al., 2006).

Not only does livestock occupy approximately 30% of ice-free land and 8% of freshwater, but it also produces an estimated 18% of greenhouse gases...

Secondly, meat substitutes have the potential to address the globally growing plea for environmentally conscious practices. "Global warming" describes a physical change in the Earth's environment due to the depletion of the ozone and the rise of green-

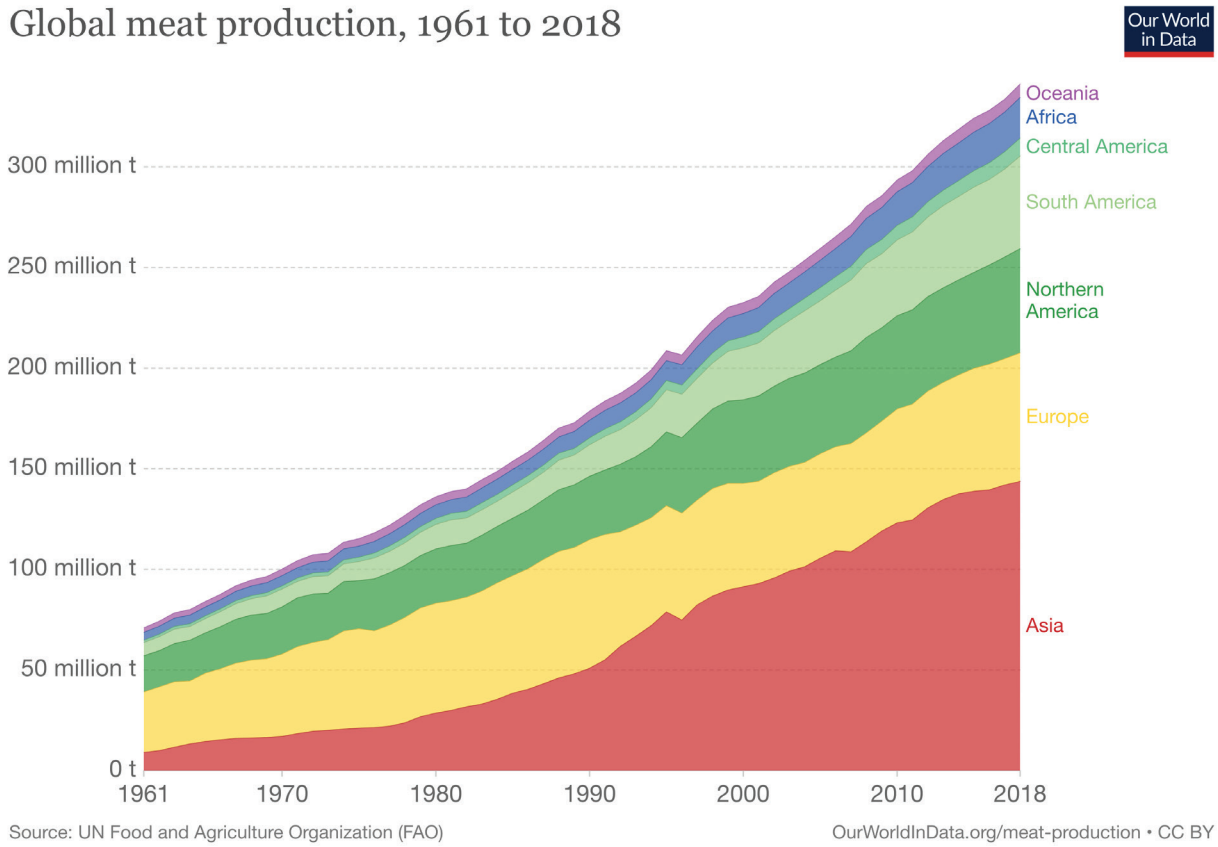

Figure 1. Change in global meat consumption from 1961 until 2018. Image from Ritchie 2017.

house gasses which trap heat in the Earth's atmosphere (IPCC, 2014). Not only does livestock occupy approximately 30% of ice-free land and 8% of freshwater, but it also produces an estimated 18% of greenhouse gases, notably more than the transportation sector (Tuomisto & Teixeira de Mattos, 2011). However, the environmental costs of meat production stretch far beyond greenhouse gas emissions.

Figure 2. Impossible burger made from plant based ingredients. Image from Impossible Foods 2018.

Agricultural practices have degraded the quality and biodiversity of ecosystems throughout the world. Many environmentally harmful crop production processes used today are largely due to demand from the meat industry. Deforestation, monocropping, nitrogen fertilization, water pollution, topsoil runoff, land degradation, and insecticide overuse are examples of production processes connected to the demands of meat production (McWilliams, 2009). Livestock requires large quantities of food and crop production must supply this demand, leading to unsustainable practices. While not all livestock inflicts the same damage on the environment, meat production as a whole is significantly more environmentally damaging than crop production (De Vries & de Boer, 2010).

While meat analogs have become popular lately, some such as soy-based tofu were produced as early as 965 CE

In addition to their environmental costs, both meat production and high meat diets pose health risks. Diets high in red meat (especially processed meat) are associated with higher total risk mortality, colorectal cancer, type 2 diabetes, and cardiovascular disease (Battaglia et al., 2015). Additionally, high non-therapeutic doses of antibiotics in livestock feed lead to antibiotic-resistant strains of MRSA, Salmonella, *E. Coli*, Campylobacter, and Enterococcus (Sayre, 2009). Given that bacterial and viral pandemics in humans typically begin with infection of other mammals, farms with concentrated livestock are quite literally a breeding ground for pathogens (Sebastian et al., 2009). If the meat industry continues to grow at its predicted rate, many of the related consequences will become more harmful to humanity as well as the environment.

New practices must be adopted before a rise in environmental and health impacts lead to further irreversible damage. Meat substitutes are an obvious alternative approach. While meat analogs have become popular lately, some such as soy-based tofu were produced as early as 965 CE (Shurtleff & Aoyagi, 2014). Wheat protein originated in 1301, yuba (a soy protein) in 1587, and tempeh in 1815 (Shurtleff & Aoyagi, 2014).

However, while the history of meat substitutes may be ancient, advances in modern science have just recently led to novel, and perhaps groundbreaking discoveries. In 2011, a biochemist at Stanford University studied meat analogs in an unusual way. Patrick O. Brown sought to construct analogs from the ground up that not only resembled meat, but also tasted similar and provided similar nutritional value, which he accomplished by examining and investigating the qualities of meat on a biochemical level (Liu, 2019; Simon, 2017).

What distinguishes Patrick O Brown's Impossible™ "Beef" from previous meat substitutes is the presence of a chemical compound called "heme" (Liu, 2019). Heme is found naturally in both plant and animal cells but is more concentrated in the latter; it is one of the main components that makes up the flavor profile of beef. Brown sought to concentrate heme from a plant-based

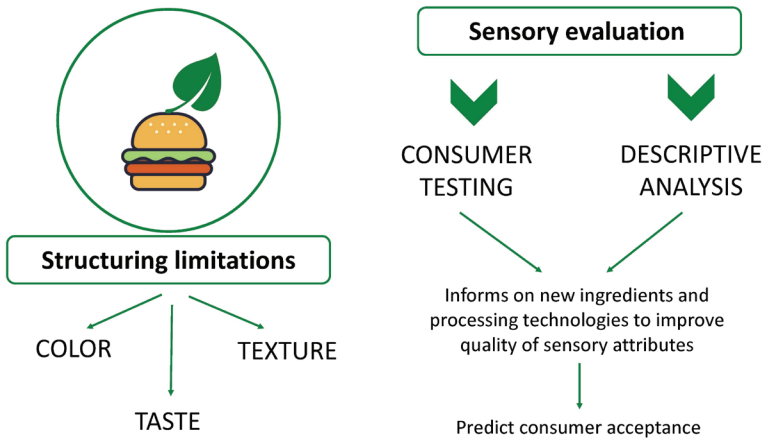

Figure 3. Processes involved in producing meat analogs. Image from Fiorentini 2020.

source, soy, in order to construct "beef" that tastes similar to cow meat. And although Impossible™ "Beef" is not a perfect analog, many people fail to distinguish it from actual beef (Simon, 2017).

While nearly perfecting the imitation of taste in meat substitutes is quite an accomplishment, how do the nutritional values of newly engineered meat analogs compare to those of meat? Macro and micronutrients include a broad range of molecules and elements needed by the human body to maintain homeostasis or more simply, stay healthy. All these macro and micronutrients can be derived from plant-based sources (Bohrer, 2019; Kumar et al., 2017). However, in order to get many of these same nutrients into a product that looks, tastes, and feels like meat, many of the ingredients are 'ultra-processed' (Monteiro et al., 2013).

Ultra-processed foods were first introduced in the 1980s (Monteiro et al., 2013). Many of the concerns about this category of food lie in the fact that most do not deliver needed nutrients (Bohrer, 2019). For example, in the case of proteins, processes such as heat treatment, high-pressure environments, pH changes, protein fractionation, enzymatic reactions, milling, and fermentation can influence the bioavailability of the amino acids in the food (Meade et al., 2005). While techniques exist that can produce a product high in protein and low in saturated fat, many of the meat substitution products available, such as the Impossible Burger, have high saturated fat content to make the product more similar to meat (Sun et al., 2020). Additional concerns regarding the processing of meat analogs simply lie in the lack of knowledge about long-term effects of these ultra-processed foods on the body.

...although Impossible™ "Beef" is not a perfect analog, many people fail to distinguish it from actual beef

Scientific advances in recent years have revealed new ways to produce meat substitutes. Considering the environmental and human health disadvantages associated with meat production, meat analogs that could replace this market are becoming more attractive. However, there are concerns surrounding the level of processing used to construct these analogs as well as the nutritional values of current products. Still, with future research, development, and newly found technology, meat analogs appear to provide a viable alternative to meat products. ❧

AUTHOR BIO

Aidan Spradlin is a third year in the college majoring in Chemistry and minoring in Physics. Fun fact: he can cook minute rice in 59 seconds.

Edited by Andy Chen, Lauren Flamenbaum and Dr. Arri Eisen

Placed by Albert Liu

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The vitamin fad

MUSKAN DUBEY
Staff Writer

Figure 1. Vitamins play a paramount role in maintaining a healthy metabolism but overconsumption of vitamins can lead to deleterious symptoms. Image from Kate Whitely n.d.

It isn't unusual for Americans to start their mornings by taking vitamins. A poll conducted by the American Osteopathic Association (AOA) revealed that 86% of Americans take some variation of vitamins or supplements, but only 21% of vitamin users actually experience vitamin deficiency (AOA, 2019). So why the discrepancy? These statistics reveal a critical aspect about our current "health culture". Most people simply do not realize that given an adequate diet, vitamins provide little to no additional benefits. Rather, the excessive intake of vitamins has been correlated with digestive distress, nausea, vomiting, and even muscle weakness (Hathcock, 1982). The major driving force of this increase in supplement consumption is our cultural environment and the pharmaceutical industry. Ultimately, while our modern culture has completely re-shaped our understanding of vitamins and created an attachment on these supplements, the efficacy of vitamins is, in fact, widely contested in the scientific community.

Astonishingly, the products of several multivitamin companies contain almost four times the recommended international unit dosage of Vitamin A.

Vitamins pose several adverse effects to the human body that oftentimes go unnoticed or are completely disregarded. Several studies have linked vitamin intake with symptoms of toxicity. For example, humans have a limited ability in effectively metabolizing Vitamin A, so excessive intake of Vitamin A can overburden intracellular binding proteins, leading to cell membrane lysis (Bender, 2018). The lysis of cells can lead to symptoms of toxicity such as hypercalcemia, ataxia, and hepatomegaly (Bender, 2018). This wide array of symptoms is characterized by the disruption of calcium homeostasis, central nervous system function, and liver physiology respectively (Bender, 2018). The disturbance of multiple organ systems is especially concerning, given that the general population is uninformed of these complications. However, even after learning about these detrimental effects, some staunch believers in vitamins still may not be alarmed because these symptoms are only associated with "excessive" Vitamin A intake. How could they get poisoned taking the recommended amounts printed on the outside of vitamin bottles? Astonishingly, the products of several multivitamin companies contain almost four times the recommended international unit dosage of Vitamin A. The recommended dosage of Vitamin A for an adult is 2700 IU, and certain vitamin companies contain a dosage of 10,000 IU (Seachrist, 1995). This immoderate quantity of Vitamin A not only poses a

tremendous risk to adults, but has also been associated with neonatal malformations of the face, head, nervous system, thymus, and heart of fetuses when pregnant women take these vitamins (Seachrist, 1995). In a longitudinal study conducted from 1984 to 1987, researchers reported that "1 in 57 infants of mothers who took the vitamins with excessive dosage suffered birth defects as a result of the supplementation" (Seachrist, 1995).

A similar conclusion can be drawn with regards to Vitamin D toxicity. In fact, research has shown that Vitamin D toxicity in infants can occur in doses as low as 50 µg/day. Exceeding the recommended dose can lead to high blood pressure, calcinosis, contraction of blood vessels, and hypercalcemia (Bender, 2018). Furthermore, these multivitamin products may also be composed of minerals such as magnesium, potassium, and zinc. Such minerals, in large doses, have been shown to cause increased urination, irregular heart rate, and muscle weakness (Hamishehkar, 2006). Additionally, several supplements in the modern market contain more than fifty percent fillers, which are inactive ingredients added to drugs to allow for easier handling and measuring. These fillers are synthetic and consist of artificial coloring, hydrogenated oils, lead, mercury, PCBs, magnesium silicate, and titanium dioxide (PR Newswire, 2016). Research has demonstrated the role of these fillers in causing adverse effects such as cancers and cognitive impairments.

Despite the literature on vitamin supplements, the FDA has placed little to no regulation on the manufacturing process of vitamin supplements. Pharmaceutical drug products are administered to a high standard of regulation for efficacy by the FDA, but such provisions are lacking during FDA's approval process of dietary supplements. An actuality, there are little to no provisions on vitamins before they are brought to the hands of consumers (FDA, 2020). Much of FDA funding does not go towards regulating the composition and efficacy of vitamins, but rather towards routine monitoring of the vitamins already available in the market (FDA, 2020). This is also why the FDA receives consumer inquiries about the validity of claims made by the vitamin companies, as well as claims of adverse effects upon ingesting certain vitamins. The FDA's sole attempt at informing the public about the potential danger of vitamins is requiring vitamin companies to print disclaimers. These disclaimers warn that, "this product does not diagnose, treat, or prevent any disease" (FDA, 2020). Therefore, consumers need to be more vigilant and

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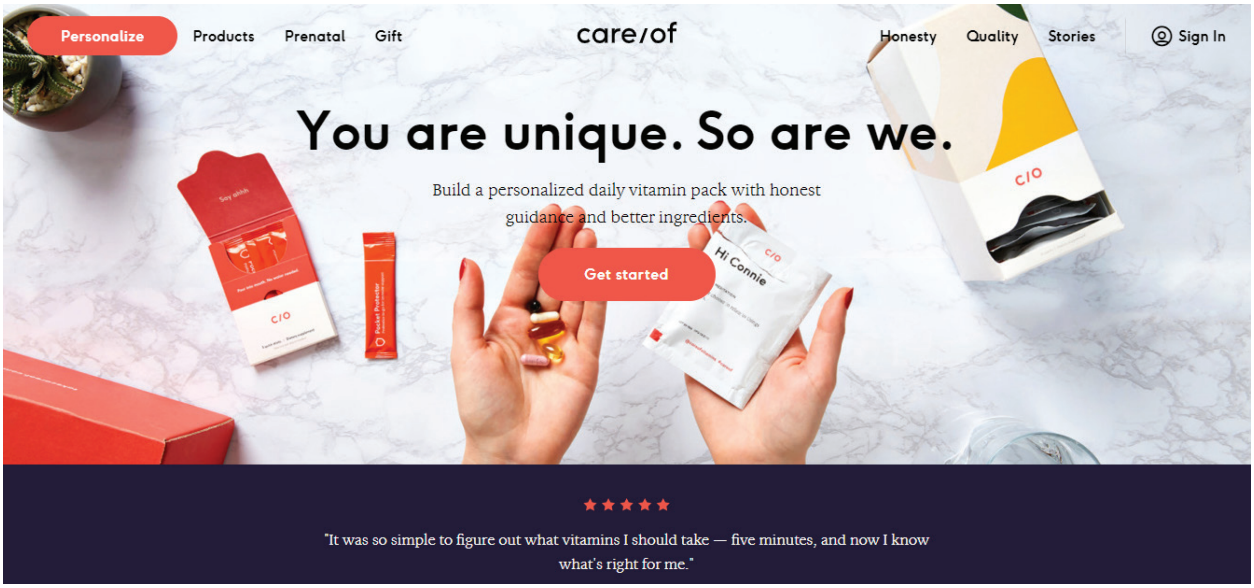


Figure 2. Online vitamin companies, like Care/of, have utilized personalized marketing schemes to gain consumers. Image from Care/of 2020.

be on the lookout for vitamins that include a "seal of approval or certification by an independent organization" (Poll, 2019). This ensures that the product is composed of ingredients safe for human consumption.

Given the high level of vitamin consumption in Americans, researchers conducted a survey in 2019 asking American participants about the basis for their vitamin intake. The survey revealed that 61% of participants consume vitamins without a physician's recommendation, 13% of which choose their vitamins purely based on their packaging. Another 6% of the participants base their decisions on endorsements by celebrities and social media influencers (Poll, 2019). In today's technology-driven society, that statistic is not surprising considering the rise of social media-based vitamin companies like Rituals and Care/of, which boasts a "more personalized experience" with their vitamins (Robert, 2020). Using these marketing tactics, companies rack in major profit with smart advertising and targeted marketing to young female millennials who are the main users of social media platforms (Tiffany, 2019). Business outlets report that Bayer, a German multinational pharmaceutical powerhouse, recently seized 70% of the Careof's assets, reportedly valued at $225 million (Tan, 2020). Nowadays, vitamin intake has not increased due to necessity, but rather as a social phenomenon. This is concerning given that these social media influencers "provide assurance about the efficacy of vitamins that consumers do not receive from physicians or the Federal Drug Administration (FDA)" (McCabe, 2012).

What aspects of culture, other than social media, are shaping our desire for vitamins? Primarily, our society, today more than ever, has a greater obsession with wanting to live longer, healthier lives. This notion is most aptly captured by a quote from Dr. Wolpe of the Emory Center for Ethics, who says: "The quest to live forever, or to live for great expanses of time, has always been part of the human spirit" (Oaklander, 2017). It's true that the human ability for developing complex culture and technology allows us to buffer the selective processes of natural selection and has allowed for an increase in the average human lifespan (Rincon, 2019). Even though humans have started living longer lives, we are still bound by the aging process. The rate of senescence of human cells has not changed dramatically despite daily advances in modern medicine (Flatt, 2018). As an antidote to this aging process, some have turned to vitamins. Our vigor for consuming vitamins to supplement the longevity of our life is ill-founded and stems from a belief that vitamins pose no harm (Thomas, 2006). This mode of thinking is known as the "magical thinking" mentality, which is characterized by

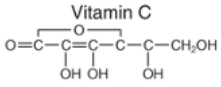
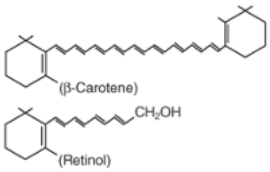
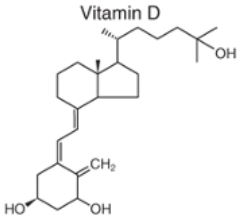
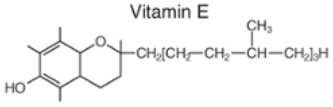
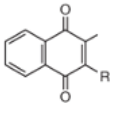
Vitamin	Active derivative or cofactor form	Principal function
Vitamin C 	Ascorbic acid and dehydroascorbic acid	Participation as a redox ion in many biologic oxidation and hydrogen transfer reactions
Vitamin A 	Retinol, retinaldehyde, and retinoic acid	Formation of rhodopsin (vision) and glycoproteins (epithelial cell function); also regulates gene transcription
Vitamin D 	1,25-Dihydroxyvitamin D	Maintenance of blood calcium and phosphorus levels; antiproliferative hormone
Vitamin E 	Tocopherols and tocotrienols	Antioxidants
Vitamin K 	Vitamin K hydroquinone	Cofactor for posttranslation carboxylation of many proteins including essential clotting factors

Figure 3. Vitamins are derived from different cofactors and serve varying purposes in regulating our overall metabolism. Image from Jameson 2018.

consumers who commit to vitamin usage without strong empirical data supporting its benefits (McCabe, 2012). In other words, these vitamin supplements are an "instrument of magic" that people take as an alternative to what they perceive as an uncertain healthcare system (McCabe, 2012). This lack of faith in the scientific community leads people to question the authority of physicians and health officials, and this uncertainty can spread from an individual to a social level (McCabe, 2012). One possible explanation for this inability to follow physicians' recommendations is a larger distrust in the healthcare system. A study investigating distrust towards institutionalized healthcare found a positive correlation between treatment discordance, which is an unwillingness to follow physician's advice, and healthcare distrust. Individuals with high levels of healthcare distrust were 22% more probable to claim treatment discordance than individuals with lower levels of distrust (Dean, 2017) . This also explains why 61% of the participants in the 2019 survey study ingest vitamins without proper prescription (Poll, 2019).

Given the dangers of excessive or unnecessary vitamin supplementation, the safest bet for consumers is to take vitamins only as needed. Experts advise that "the most prudent approach is to recommend a daily intake of fruits and vegetables as a likely source of essential nutrients" (Thomas, 2006). For most, it would be much safer to gain the nutritional benefits of vitamins by incorporating various fruits and vegetables into the diet. However, we must acknowledge that some people can have vitamin deficiencies due to a lack of access to fresh produce. Diagnosed vitamin deficiency is a serious problem that can cause scurvy, ricketts, beriberi, pellagra, and several other debilitating illnesses (Hathcock, 1982). Therefore, vitamin supplements can play a vital role in maintaining a person's overall health, because pathological imbalances in nutrients do exist.

Using these marketing tactics, companies rack in major profit with smart advertising and targeted marketing to young female millennials who are the main users of social media platforms

During these modern times, the vitamin industry has spearheaded a massive cultural change in our perception of health and overall well-being. Their tactical marketing campaigns capitalize on our desire for long-lasting health, leading to a culture of excessive vitamin consumption. As consumers, we need to become more mindful and critical of the claims made by Big Pharma and lean towards gaining much of our necessary vitamins from our diet. Furthermore, we should curtail our support of social-media vitamin brands which advertise personalized questionnaires and pills. Fundamentally speaking, the best way to live a long, healthy life is to eat nutritious food and practice a well-balanced lifestyle. ❧

AUTHOR BIO

Muskan Dubey is a third year in the college majoring in Neuroscience & Behavioral Biology and Astronomy. She is also fluent in three languages and currently learning a fourth!

Edited by Edward Xue, Andy Chen and Dr. Muhammad Azeem

Placed by Henry Mangalapalli

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An old treatment for a novel disease

Figure 1. Human serum retains an opaque yellow color, devoid of red blood cells. Image from Chinatopix 2020.

RICHARD LEE
Staff Writer

As new diseases arise and spread at a higher rate in today's interconnected society, it has become increasingly critical to quickly and effectively introduce treatments that combat these novel pathogens. Over 200,000 Americans have died from COVID-19 while the United States struggles to produce a vaccine and implement effective containment strategies (Rossen, 2020). Current treatments are limited; Remdesivir, originally synthesized for the Ebola virus, has been used more frequently on COVID-19 patients, while hydroxychloroquine, initially created to combat malaria and touted for a time as a possible therapeutic drug for COVID-19 infections, has now been warned by experts to be ineffective against the virus (Frediansyiah, 2020; Hashem, 2020). Instead, serum therapy, or the method of introducing neutralizing antibodies collected from recovered patients into the blood of sick patients, is an old medical practice that has shown promising results against the novel virus. As COVID-19 continues to threaten people's daily lives across the globe, serum therapy may assume an important role in remedying this pandemic. Being a proven and reliable method of alleviating numerous diseases in the past, serum therapy should be considered vital in mitigating COVID-19's impact until vaccines become widely available.

As COVID-19 continues to threaten people's daily lives across the globe, serum therapy may assume an important role in remedying this pandemic.

While vaccines stimulate our bodies' immune system to produce antibodies, serum therapy transfers antibodies from recovered individuals to current patients, giving them the biological tools to build a defense against the disease. Human blood is primarily made of cells and a liquid carrier called plasma. Within the plasma, serum — the aqueous portion — contains numerous proteins and peptides, including immunoglobulins that serve as antibodies when fighting infections (Psychogios, 2011). Scientists are able to transfuse serum from one patient to another. Once introduced, immunoglobulins from the serum recognize and bind to particular foreign molecules

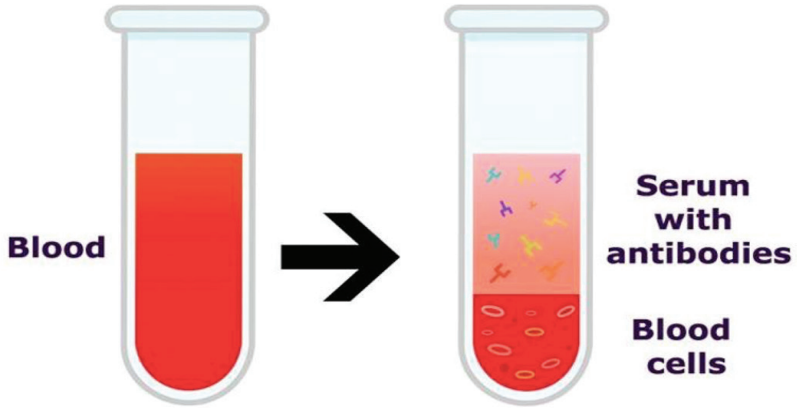

Figure 2. Human blood is made up of cells and serum-containing plasma. Image from Admin 2014.

called antigens, subsequently destroying them (Thermo Fisher, 2020). The advantage that serum therapy offers over vaccines, is the introduction of immediate, although temporary, immune effects without directly exposing the patient to the actual antigens. It bypasses the body's tedious process of developing antibodies and saves precious time to prevent further complications. Even though serum therapy has the advantage of rapid implementation, vaccines are still crucial to defeat a pandemic in the long run. In contrast to serum therapy, vaccines introduce antigens into the body that promote antibody production in the host cells. CD8 effector T cells and memory B cells crucial to adaptive immunity are recruited from a vaccine-induced T-cell memory pool and are important to boost plasma-cell numbers and serum-antibody concentrations for the next encounter with a virus, respectively (Burton, 2002, p. 709). Although nonpathogenic, the antigens in vaccines mediate cellular responses that simultaneously neutralize and memorize disease-causing agents. Proving an inactivated antigen's effectiveness in producing that adaptive immune response remains the challenge for any vaccine development. Adaptive immunity is also more elusive due to the extensive clinical trials necessary for vaccines to become FDA-approved. In the meantime, we can turn to serum therapy's existing application to battle illness.

Serum therapy has demonstrated its effectiveness against a plethora of diseases ranging from bacteria to viruses. The origin of this versatile treatment stems from a bacteria-based illness that has nearly been eradicated in today's world: diphtheria. Diphtheria is characterized by toxic infections caused by *Corynebacterium diphtheriae*. In the late 19th century, diphtheria was responsible for thousands of deaths worldwide (Cooper, 2002). German physiologist Emil von Behring first developed the diphtheria serum from a hyper-immune horse, which was distributed to different patients to boost their immunity. The serum later collected from recovered individuals contained the antitoxin against diphtheria. Physicians/researchers found that by transferring the recovered patients' serum to non-immunized humans and animals, the recipients experienced accelerated recovery, and even prevention of infection in some (Gluud, 2011). Due to its significant contribution to the fight against diphtheria, the first Nobel Prize in Physiology or Medicine was awarded to serum therapy (Nobel Media AB).

Today, multiple branches of medicine are applying serum therapy to a range of contemporary medical challenges. Tuberculosis (TB), another severe bacterial lung infection, poses an imminent threat to people around the world due to its growing resistance to antibiotics. In an 1888 study of 412 TB-confirmed patients, oral treatments and injections of serum yielded clinical improvement in two-thirds of those human patients while the other third saw no change in clinical outcome (Glatman-Freedman, 1998). Even before antibiotics were invented, serum therapy displayed curative effects against tuberculosis, without inducing antibiotic resistance. Tuberculosis is not the only infection that can be targeted by the immune gamma globulins found in serum; the West Nile virus (WNV), a mosquito-induced virus capable of causing comas, vision loss,

Due to its significant contribution to the fight against diphtheria, the first Nobel Prize in Physiology or Medicine was awarded to serum therapy

and death, also responds to those same antibodies as demonstrated in mice. In a WNV study, mice were infected with the disease, and no mortality was observed in mice that received above a dose of 10 mg/kg (Engle, 2003). Even in the absence of an adaptive cellular immune response, serum provided an approximate 30-day protection period for mice against the WNV virus. While clinical trials of serum therapy for WNV have yet to confirm similar results in humans, the promise this treatment has shown *in vivo* is encouraging. The success of patient recovery across a multitude of studies and illnesses is not coincidental. Serum therapy promotes a temporary blockade against viral or bacterial attacks, and it can serve as a linchpin to a comprehensive treatment plan.

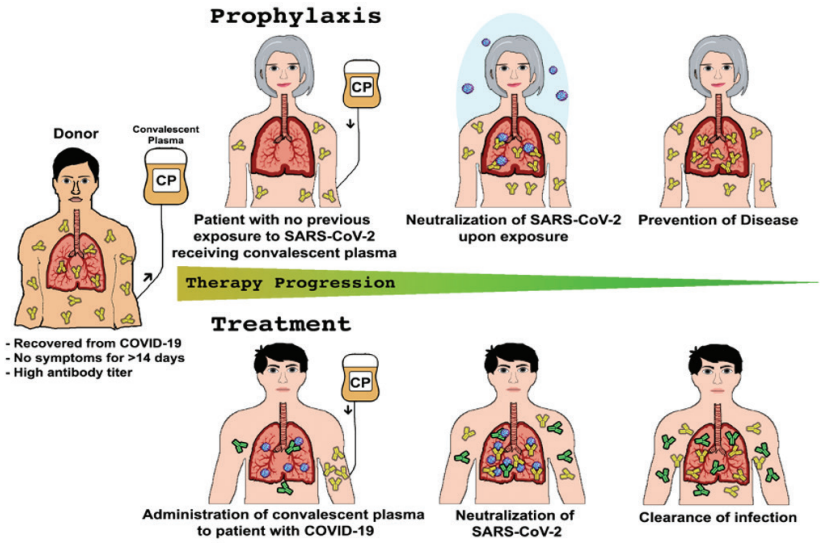

Figure 3. Serum therapy can prevent disease through prophylaxis or clear a patient of infections. Image from Montelongo-Jauregui 2020.

Operation Warp Speed is the United States' response to the COVID-19 pandemic, but it has struggled to sufficiently accelerate vaccine production before the end of 2020, leaving serum therapy as an increasingly attractive, if temporary, solution to the battle against COVID-19. Because of the high infection rate but relatively low mortality rate of COVID-19, researchers have successfully secured a wide pool of serum donors. The large sample size of donors globally has led to tightened protocols for treatments, where only plasma with high anti-SARS-CoV-2 titers — or concentrations — of immunoglobulins G and M (IgG and IgM) are used (Montelongo-Jauregui, 2020). When utilized in a clinical trial of ten patients, a single dose of convalescent plasma with high neutralizing antibody titers was well tolerated and led to improvements in COVID-19 clinical symptoms and the eventual disappearance of the virus in the blood for all patients (Duan, 2020). Knowing how serum therapy works against other diseases, immunoglobulins in the transferred serum would most likely attack COVID-19 viruses by binding to their surface and diminishing their affinity for human cell receptors. It is no surprise that this convalescent treatment results in a similar COVID-19 recovery rate analogous to the findings of the aforementioned diphtheria and West Nile virus studies. This treatment is most effective when implemented immediately following COVID-19 infection. A study of 86 patients in the Netherlands suggested that the use of convalescent plasma after 10 days of COVID-19 symptoms did not improve clinical outcomes, since those patients had already produced high levels of neutralizing antibodies themselves (Gharbharan, 2020). Additionally, while the use of convalescent plasma seems to relieve symptoms such as shortness of breath and fatigue in patients with moderate COVID-19 cases, this did not translate into a reduction in 28-day mortality or reverse the progression of disease severity in other patients (Agarwal, 2020). Therefore, more research is necessary to determine the specific interactions between serum therapy and the COVID-19 virus before we can generalize its benefits. As infection and mortality rates climb around the globe, numerous organizations are testing the promising initial findings of serum therapy. Even the FDA, which still has yet to declare an official COVID-19 treatment plan, recently pub-

...a single dose of convalescent plasma with high neutralizing antibody titers... led to improvements in COVID-19 clinical symptoms...

lished guidance recommending a minimum neutralizing antibody titer of 1:160 (Sheridan, 2020). Amid the current pandemic, serum therapy is, undoubtedly, gaining remarkable momentum. As official guidelines tighten and feasible vaccines are produced, the use of serum therapy in conjunction with other antivirals may lead to an optimal course of treatment for COVID-19.

Treating COVID-19 patients has presented profound challenges for researchers and healthcare workers alike. On top of growing uncertainties in regards to how the virus may mutate during the upcoming flu-season, the difficulty of determining an effective therapy for COVID-19 continues to challenge scientists who are grappling with this novel disease. While much remains unknown, one thing is certain: following its historical success in treating other diseases, serum therapy has also shown optimistic results in COVID-19 patients. Its implementation in 2020 has highlighted a common theme present throughout the field of science: capitalizing on the old to treat the new. ❧

AUTHOR BIO

Richard Lee is a second year in the college double majoring in Biology and English. He used to be left-handed, until his dad wrote with his right hand everyday for a year.

Edited by Helen Griffith, Edward Xue and Dr. Tyler Cymet

Placed by Alicia Yin

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The yin and yang of the century: Data science and medicine

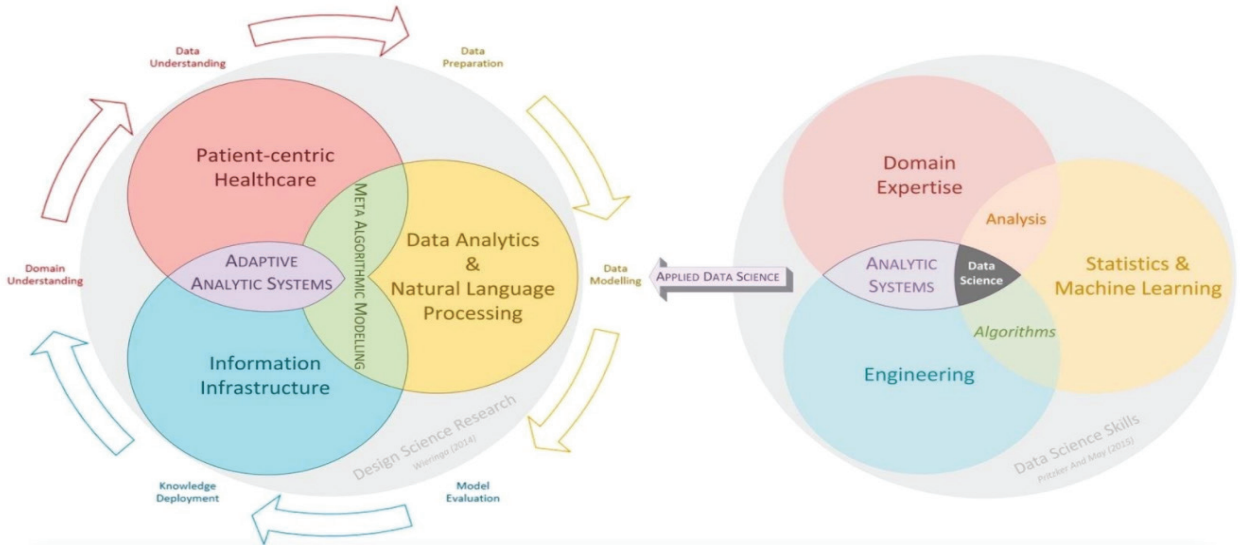

Figure 1. A visual on the combination of all different disciplines of data science and technology within healthcare. Image from Spruit & Lytras 2018.

JAI ARORA
Staff Writer

With the emergence of vast amounts of data in current times, there is a significant opportunity for improvement within the healthcare industry. Take this message from a doctor to his patient for example: "Hello Mr. Prescott, could you come to the hospital for a follow-up today? The device you are wearing has notified me that your blood pressure is higher than it has been in the last twelve months, and I would like to make sure that everything is okay." While it may sound far-fetched, this is in fact the future of medicine. Large amounts of data drives communication between patients and health professionals and among healthcare professionals themselves. Data science will not replace doctors' jobs but will rather supplement and inform their work. Doctors are already expected to be good at verbal/written communication and learning to analyze data would just be another added skill (Lerner et al., 2018).

An identified issue that could be mediated through data science is the lack of available physicians. As the number of people that need access to outpatient healthcare services increases, the number of physicians available is decreasing. Hospitals are predicted to be understaffed in the near future, which will affect hospital scheduling and wait times negatively. However, that is where data science comes in (Srinivas & Ravindran, 2018). A prominent concern that impacts scheduling is that a significant proportion of patients do not attend their appointments, which in turn has devastating financial effects on the healthcare system. The issue is that hospitals assume that the probability of patients missing their appointments is equal for all patients, which is not true. The electronic health record has a vast amount of data within it, but it is currently being underutilized. Data science has the ability to create a better way to schedule appointments. Firstly, all the data from the electronic health record and other sources should be gathered and cleaned so that missing values or incorrect information can be dealt with. Next, machine learning algorithms should be used to classify patients as either likely or unlikely to miss their appointment and the most effective algorithm should be chosen. Finally, based on the classification of a patient, a specific scheduling technique

Doctors are already expected to be good at verbal/written communication and learning to analyze data would just be another added skill.

should be assigned to each patient (Srinivas & Ravindran, 2018). There are two assumptions that must be made in order for predictive data analytics to work. The first assumption is that people are consistent in their behavior over time, which means that a patients' histories are a good indicator of their behavior and how likely they would be to miss an appointment. The second assumption is that the pattern of patients attending and missing their appointments makes a difference. The chances of patients missing their next appointment can either increase or decrease based on whether they made it to previous appointments (Harris et al., 2016). Identifying absent patients and predicting the number of missed appointments will significantly improve both the healthcare system and patient satisfaction. Currently, Columbia University uses predictive analytics to reduce wait times and the number of patients in their emergency room in a non-traditional manner. Instead of looking at when patients check out, Columbia looks at when patients check in to maximize the number of patients they see in a given period of time. If the predictive analytics show that more patients are likely to arrive than they can handle, then the hospital will consider sending patients to other hospitals to avoid unnecessarily long wait times (White, 2016).

Currently, Columbia University uses predictive analytics to reduce wait times and the number of patients in their emergency room in a non-traditional manner.

Additionally, diagnosing patients and choosing treatments is a crucial task, and the chances of a successful outcome can be improved through the use of predictive models that are specific to individuals rather than the entire population. Looking at patients' individual histories can be advantageous when diagnosing and sifting through treatment options because each person's body reacts differently. Being able to more accurately determine the best course of treatment would benefit both patients and health professionals. If patients are taken care of in the most personalized way possible, they are less likely to be re-admitted due to complications, which will save hospitals large amounts of money and time (Visweswaran et al., 2010). Furthermore, data science's

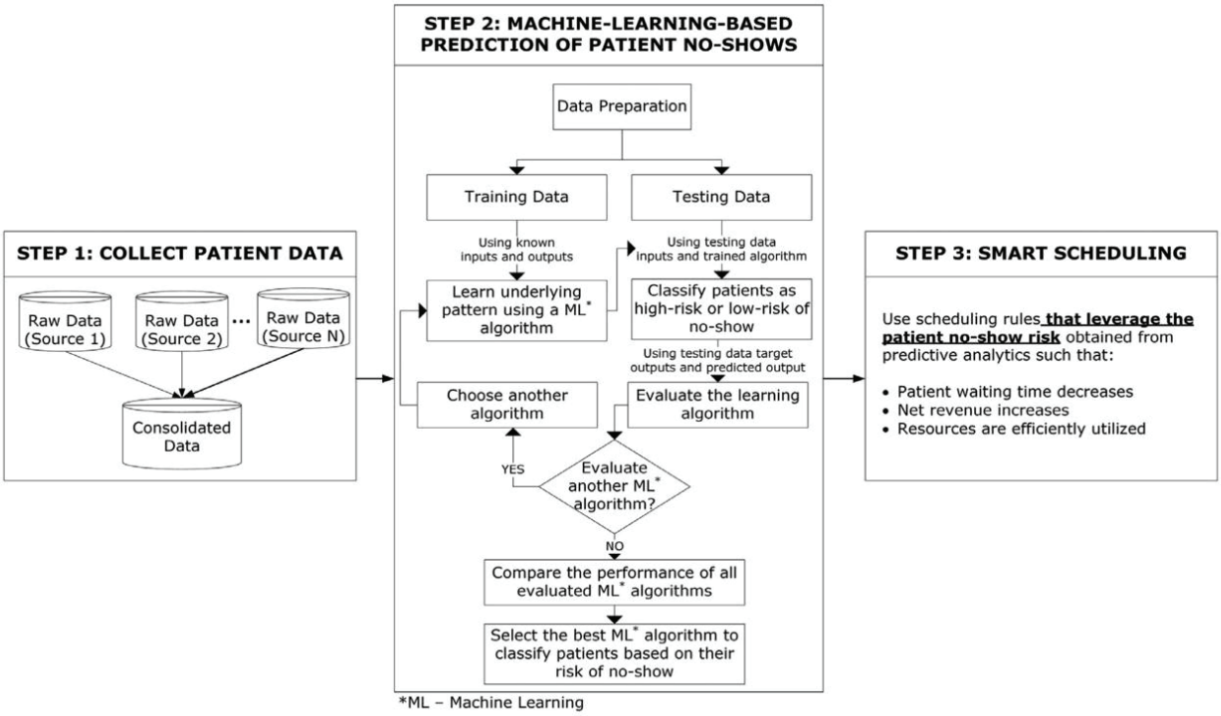

Figure 2. A diagram of the three steps on how data science can be used to schedule patient appointments within the healthcare system. Image from Srinivas & Ravindran 2018.

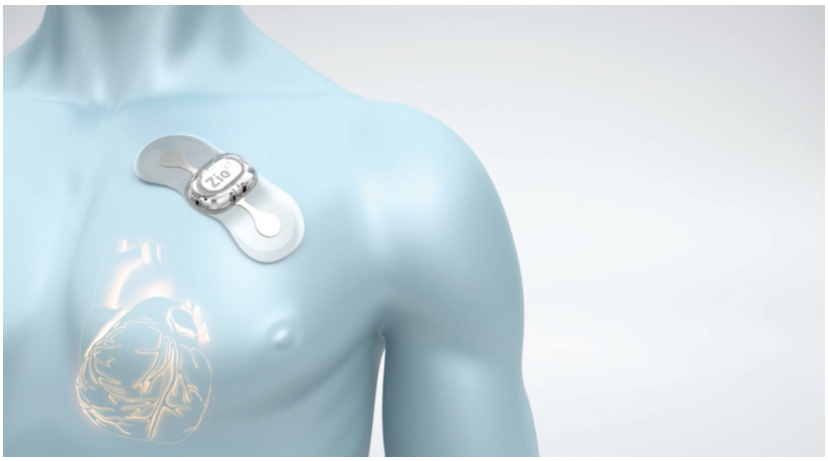

Figure 3. A picture of an ECG monitor patch. Image from Lovett 2018.

potential for diagnosing more efficiently does not stop within the walls of hospitals. Since there are so many individuals with chronic health conditions, it can become overwhelming for hospitals, which is why data and technology has been introduced to monitor patients remotely. People with chronic conditions can wear monitors that track their health and notify doctors of any changes in a more timely manner (Zheng et al., 2013). Some examples of devices include the ECG monitor patch and biofeedback breathing devices. The ECG monitor patch helps track patients' hearts, and more specifically, monitors their cardiac rhythms to make sure there is nothing irregular. Biofeedback breathing devices are used widely within different disciplines across medicine. They can help patients who suffer from physical health conditions such as asthma and hypertension, in addition to mental health conditions such as anxiety. An example of a biofeedback breathing device would be the StressEraser, which helps patients sync up their heart rate and breathing together (Zheng et al., 2013).

To illustrate the positive impacts of data science on the healthcare industry, one must simply look at how data science is currently being used for limiting the spread of COVID-19, contact tracing, vaccine development, and overall in gaining a better understanding of the virus. If health professionals were able to collect good, dependable data, data scientists could analyze trends and patterns and help professionals within public health make decisions more efficiently and quickly to save more lives (Powell, 2020). An example of how data is being used is the app Covid Symptom Tracker, which was started by the Massachusetts General Hospital. Potential infected people are able to put in their symptoms and the app compiles symptom trends with this database. Because of this, the hospital was able to determine that loss of smell and taste is a good indicator of COVID-19 infection. On a larger scale, because of the pandemic, researchers in the United States have created the National COVID Cohort Collaborative - a database of everyone who has been tested for COVID-19 - and it has been an effective way for public health professionals to compile and analyze large amounts of COVID-19 data. A major obstacle of the dataset is that different hospital systems encode information differently, which is why researchers must be able to clean and merge the data so it can be interpreted (Yasinski, 2020). An example of a country that has made incredible use of large amounts of data in terms of contact tracing is Taiwan. Even though Taiwan has one of the closest ties to China due to workers commuting between China and Taiwan regularly, Taiwan was able to effectively manage the outbreak of COVID-19 and protect its citizens. This was primarily accomplished through online reporting of symptoms and through phone calls, which would place citizens within cate-

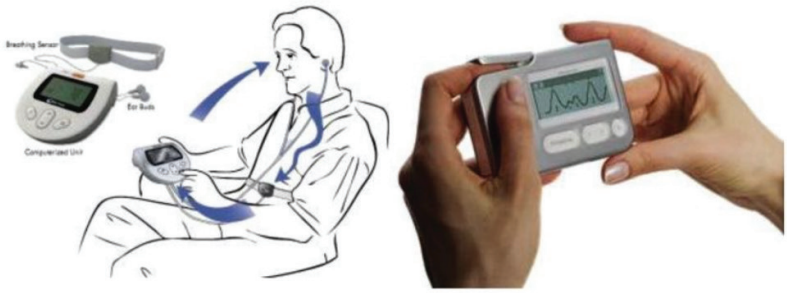

Figure 4. A picture of two biofeedback breathing devices: RESPeRATE (Left) & StressErase (Right). Image from Zheng, et al. 2013.

gories of high or low risk. During flights, if citizens were deemed to be at high risk due to the areas in which they have traveled or the symptoms they report, they would be mandated to quarantine and tracked using their phones to make sure that they do not break the quarantine mandate. Taiwan checked on their citizens under quarantine and gave them access to food and healthcare. If citizens were deemed low risk, they were given a pass to clear immigration faster when flying. By making use of the large amounts of public health data, Taiwan was able to keep the rate of COVID-19 infections low within the country (Wang et al., 2020). Nobody was prepared for a viral outbreak on a global level, which is why the data on COVID-19 is of low quality. Health professionals are busy saving people's lives, which is why they are not focused on collecting data, which makes sense; however, it can have negative effects for the future. While tracking people's movements during the pandemic could be seen as an invasion of privacy, it could just be the thing that stops an outbreak from occurring in communities (Powell, 2020).

Healthcare professionals have always had to be educated academically to the highest degree, but we are moving into times that will require them to be proficient in technology as well. Data science has the ability to change medicine for the better, and that is currently being proven during the COVID-19 pandemic. Samuel S. Wilks once said, "Statistical thinking will one day be as necessary for efficient citizenship as the ability to read and write!" Data science is a skill that is becoming integral within healthcare; however, everybody can benefit from data science regardless of the field they reside in. ❧

AUTHOR BIO

Jai Arora is a second year in the college majoring in Quantitative Sciences with a Concentration in Informatics. He is also a part of Emory Suri A-Capella.

Edited by Luisa Taverna, Vyas Muralidharan and Dr. Lynn O'Neill

Placed by Shreya Rana

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Antiviral potential of flavonoids in combating COVID-19

KRITHIKA SHRINIVAS
Staff Writer

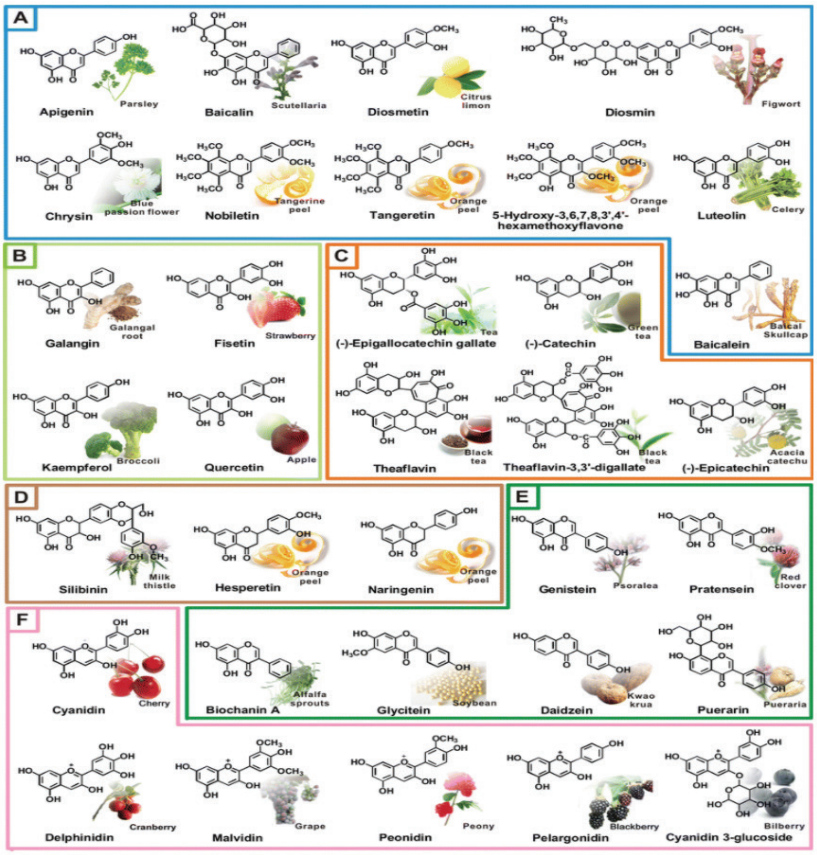

Figure 1. Table exhibiting types of flavonoids and the food sources they are found in. Image from Min-Hsiung Pan et. al. 2010.

While pharmaceutical companies across the globe rush to create a viable vaccine for the novel coronavirus, it is crucial that researchers also work towards developing an antiviral drug for COVID-19 in order to eliminate the possibility of this disease continuing to be as pervasive in our daily lives as influenza is each year. Flavonoids are polyphenolic compounds found in various plants such as fruits, vegetables, flowers, and leaves. They could be a key contender in the development of an antiviral drug for COVID-19 given their many unique therapeutic properties, being described as an antioxidant, antibacterial, antiviral, anti-inflammatory, and anticancer (Panche et al., 2016). Flavonoids have already proven to be remarkably useful in the development of vaccines for other viral diseases, such as HIV and Zika (Cataneo et al., 2019).

Throughout history, flavonoids have demonstrated biological properties with therapeutic applications, allowing them to treat various bacterial, viral, and inflammatory conditions (Zakaryan et al., 2017). While flavonoids can be found in natural sources such as fruits and vegetables, they can also be found in foods consumed regularly such as green tea, tofu, edamame, and chocolate. Flavonoids also regulate key cellular enzyme functions in the body, making them popular in the medicinal and pharmaceutical fields (Panche et al., 2016). For example, Indian Ayurvedic medicine heavily relies on the implementation of plants rich in flavonoids to treat a host of diseases. *Commiphora mukul*, or the Indian bdellium tree, for instance, increases one's white blood cell count to boost immunity and also protects against conditions such as the common cold and low cholesterol (Pandey et al., 2013). This is because the plant stimulates the maturation, differentiation, and activation processes used by white blood cells and enhances the process of leukocyte responses to activation signals (Haffor, 2009). Flavonoids such as Kaempferol are also present in the Hosta plantaginea, or fragrant plantain lily, a plant that is widely used in traditional Chinese herbal medicine. Kaempferol regulates inflammation in the body, which is why the flowers of this plant demonstrate potency in treating sore throats, lung heat, and toxic heat in Mongolia (He

Flavonoids...could be a key contender in the development of an antiviral drug for COVID-19...

et al., 2018).

Flavonoids have demonstrated efficacy in the past in the treatment of other viral diseases, making them a viable option to explore in the derivation of an antiviral drug for COVID-19. When exposed to DNA and RNA viruses, flavonoids have exhibited inhibitive properties such as preventing attachment of viruses to host cells. This curbs early state replication, blocks transcription and translation, and interferes with host factors necessary for infection (Lalani & Poh, 2020). Flavonoids have shown promise in *in vitro* studies for the potential treatment of Zika virus (ZIKV), a virus primarily transmitted through mosquito bites for which there is no antiviral treatment or vaccine to control its replication. The flavonoid naringenin (NAR) derived from plants including citrus fruits, tomatoes, cherries, grapefruits, and cocoa has displayed anti-inflammatory and analgesic properties when tested on ZIKV through *in vitro* means; these anti-viral properties were exhibited through the interaction of the phenol rings of flavonoids and viral proteins or mRNA (Cataneo et al., 2019). This interaction interferes with viral replication processes, preventing the virus from infecting other cells. This flavonoid was promising even when it was added to cultures 24 hours after the infection was present. It still displayed antiviral properties late into the life cycle of the virus, a testament to its strength. Furthermore, docking analyses conducted *in silico* show a strong affinity between NAR and ZIKV protease domain, further suggesting naringenin's potency in treating the Zika virus.

Flavonoids also regulate key cellular enzyme functions in the body, making them popular in the medicinal and pharmaceutical fields

Flavonoids have also shown promise in the treatment of HIV-1. The flavonoid baicalin (BA) is derived from *Scutellaria baicalensis*, commonly referred to as the Chinese Skullcap plant. Baicalin successfully blocked the replication of HIV-1 and HIV-1 entry into target cells early on when signs of infection were established (Li et al., 2002). Along with baicalin, the flavonoid myricetin, derived from plants such as Bellard's knotweed, also showed anti-HIV-1 properties, inhibiting 90% of HIV-1 BaL infection in TZM-bl cells, cell derivatives engineered with an HIV-1 based vector, when examined *in vitro* (Pardi et al., 2014).

In recent months, flavonoids have demonstrated potential in creating an effective antiviral for COVID-19. Flavonoids such as hesperetin, myricetin, Linebacker, and caflanone have demonstrated a high binding affinity with SARS-COV-2 spike proteins, helicase, and protease sites, causing a conformational change that inhibits the entry of the virus into the host cell, confirmed by *in vitro* and *in silico* studies (Ngwa et al., 2020). A docking analysis — a bioinformatic modeling technique that predicts how one molecule interacts with another to create a stable complex — was performed using ten flavonoids including Kaempferol, curcurmin, and pterostilbene compared against the SARS-COV-2 spike protein. This revealed that flavonoids demonstrated a higher affinity to the spike protein than hydroxychloroquine, a drug treatment proposed early on in the pandemic (Rane et al., 2020).

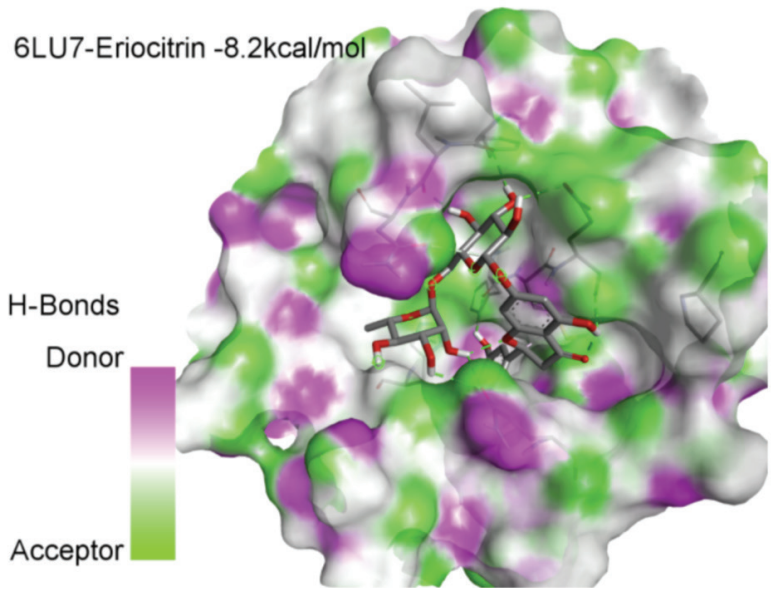

Figure 2. This visual provides an example of docking affinity in a molecule, demonstrating the high docking affinity between flavonoid Eriocitrin and the COVID main protease. Image from Shrinivas 2020.

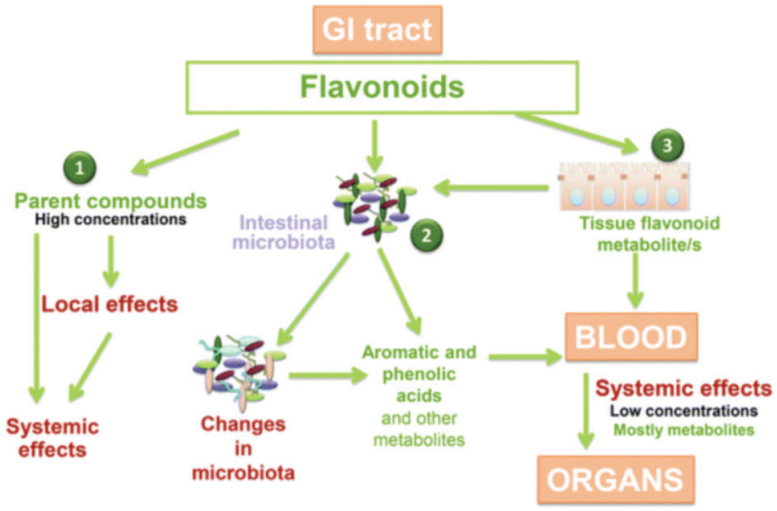

Figure 3. This visual demonstrates the positive effects of flavonoids on the human body Image from César Fraga et. al. 2019.

Furthermore, traditional Chinese medicine was thought to have a role in treating the symptoms of the virus; a treatment created containing twenty one plant-derived components known for their medicinal properties was administered to patients and showed 92% effectiveness in patients, reducing or keeping their clinical symptoms stable (Russo et al., 2020). 45% of this traditional Chinese medicine was composed of flavonoids. Based on these results, a strong argument can be made for flavonoids containing potential antiviral capacity that inhibits key factors responsible for the replication of the novel coronavirus.

Flavonoids are a strong contender for an antiviral COVID-19 treatment as they have demonstrated success in a broad spectrum of diseases including those closely linked to COVID-19 such as influenza. Furthermore, flavonoids are highly accessible in fruits, vegetables, and other plant based products which are already a part of human diets and can easily be derived from nature for pharmaceutical applications (Russo et al., 2020). Along with being a viable treatment option, flavonoids also exhibit preventative properties such as increasing one's white blood cell count to boost immunity, differentiating them from non-flavonoid treatments (Solanki et al., 2015). Given their current use and increasing demand, it is highly likely that researchers may start tapping into the potential of flavonoids for a COVID-19 antiviral along with future treatments. ❧

...flavonoids are highly accessible in fruits, vegetables, and other plant based products...

AUTHOR BIO

Krithika Shrinivas is a second year in the college majoring in Anthropology and Human Biology with a minor in English. She has also published a poetry collection which is available on Amazon!

Edited by Vyas Muralidharan, Rhea Tumminkatti and Dr. Kim Tran

Placed by Daisy Li

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Mind-altering medications and mental health

Figure 1. Dried magic mushrooms used for psychoactive experiences. Image from Pollan 2019.

SRIDHAR KARNE
Staff Writer

The use of mind-altering medications has been in practice for thousands of years, dating as far back as pre-Victorian times. Psychoactive drugs, or psychedelics, are drugs that can affect mood in ways that also affect various cognitive processes, such as altering a person's perception of reality (Nichols, 2016). Psychedelics are generally considered to be physiologically safe without causing dependence; however, there is still a large controversy surrounding their recreational use and medical prescription (Nichols, 2016). Disapproval of psychedelics has historically stemmed from religious beliefs in the United States (Christianity in particular), due to the association of psychoactive experiences with witchcraft and sorcery. As a result, the use of psychedelics, especially in the field of medicine, was neglected until recent breakthroughs changed the narrative. Today, psychedelics have received attention in medicine as an avenue to treat mental illnesses. Significant progress in the study of psychoactive drugs adopted to combat mental illnesses has led, in particular, to the use of psilocybin to treat depression, and the use of lysergic acid diethylamide (LSD) to treat severe anxiety.

All nineteen patients displayed fewer depressive symptoms one week after treatment.

Psilocybin, a classic psychedelic drug, is better known by its street name: magic mushrooms (Figure 1). The chemical compound of this drug is structurally analogous to that of serotonin, a neurotransmitter that modulates mood (Daniel & Haberman, 2017). In general, increased levels of serotonin release are correlated with brightened moods and happiness. Therefore, it seems fitting to turn towards psilocybin to treat chronic depression. A study done by Carhart-Harris measured cerebral blood flow through functional magnetic resonance imaging (fMRI) in patients with treatment-resistant depression (TRD), a subclass of depression in which the patient does not respond well to antidepressants. The measurements were taken pre- and post- psilocybin treatment. All nineteen patients displayed fewer depressive symptoms one week after treatment. Although the sample size was small and the effects were only short-term, this study documented, for the first time, a decrease in resting-state brain

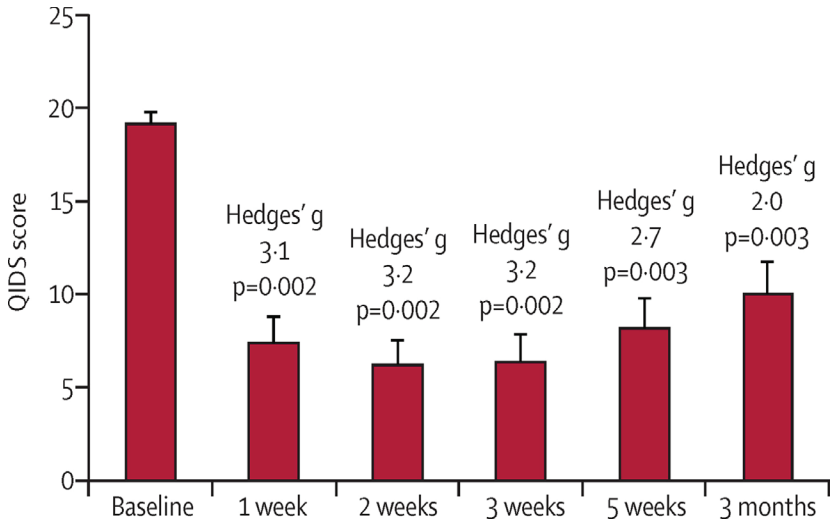

Figure 2. Mean depression scores post high-dose psilocybin treatment session. Image from Carhart-Harris 2016.

blood flow in the amygdala following psilocybin treatment. As seen in Figure 2, reduced activity in the amygdala is associated with patient-reported symptom relief, such as reduced feelings of sadness and helplessness (Carhart-Harris et al., 2016).

A second study of psilocybin, and one that has received considerable attention, was conducted at Johns Hopkins University. Patients were recruited based on the criteria of having a potentially life-threatening cancer diagnosis coupled with severe anxiety and depressive symptoms. Throughout the 9-month program, which employed stringent controls for possible confounding variables, researchers found that the symptoms of depression and anxiety significantly decreased after 6 months following administration of psilocybin, with no adverse effects (Griffiths, 2016). In a book titled, *Medicinal Use of Psilocybin*, the first author of the book Dr. James Rucker writes, "Psilocybin therapy is empowering for patients" (Rucker et al., 2020). Where society and medicine once saw psychoactive drug use as taboo, the narrative has now shifted towards considering these drugs as both a medical aid and tool.

While chronic depression does affect a large proportion of the population, even more common among mental disorders are anxiety disorders. Surveys show that 33.7% of the population will experience an anxiety disorder at some point during their lifetime (Bandelow, 2015). Furthermore, anxiety disorders tend to be comorbid with other mental disorders (Bandelow, 2015). Given its high prevalence as well as the large mental toll chronic anxiety can induce, anxiety disorders can be detrimental to society's health as a whole. In the search for possible treatments, novel research on LSD was done in the 1940s, but the studies were halted due to the stigma surrounding psychoactive drug use in American culture at the time (Sessa, 2016). Nevertheless, because LSD has been widely documented to allow its users to, "see the world as new in all respects," researchers have sought to exploit this change in "vision" as a possible treatment (Fuentes, 2020). The logic goes that if LSD can guide patients to see the world through a new and different lens, then perhaps this new perception can come with alleviated anxiety. LSD is one of the most potent psychoactive drugs listed in Schedule I of the United Nations classification of drugs, meaning that it is among the most highly restricted pharmacological agents, and any current hopes for its legal therapeutic use in medicine is therefore limited (Belouin & Henningfield, 2018). Regardless of this restriction, it is noteworthy that in the studies conducted on LSD, most patients displayed significant short-term benefits following LSD treatment (Fuentes, 2020).

All nineteen patients displayed fewer depressive symptoms one week after treatment.

There have been specific studies conducted to show the safety and efficacy of LSD-assisted psychotherapy. One example is a controlled research study that followed up with patients who experienced heightened anxiety from life-threatening diseases, one year after they had finished LSD psychotherapy. The results from semi-structured interviews are as follows: 77.8% of the participants experienced reduced anxiety and 66.7% experienced an increased quality of life following LSD psychotherapy (Gasser et al., 2015). Overall, this study demonstrated safe and positive treatment

outcomes and reported no serious adverse effects (Gasser et al., 2015). Another preliminary study analyzed resting-state functional connectivity of the amygdala and thalamus, and cerebral blood flow using a LSD microdosing method. Microdosing is the practice of administering repeated, low doses of LSD to improve mood and cognition (Bershad et al., 2019). Experimental subjects were administered a dose of 13 micrograms of LSD, which is below the threshold for hallucinatory effects, and all were required to attend two 5-hour sessions of LSD psychotherapy (Bershad et al., 2019). The fMRI results of the study suggest that there is a strong positive correlation between the LSD-induced changes in amygdala-middle frontal gyrus connectivity and perceived differences in positive mood measured directly after, especially when compared to the control group that received a placebo treatment (Bershad et al., 2019). Ultimately, the study concluded that LSD microdosing treatment is promising and can induce positive mood changes in patients with depression or anxiety by strengthening their brain connectivity.

The potency of psychedelic substances such as psilocybin and LSD for medicinal application in the treatment of mental disorders is very promising (Bandelow, 2015). These breakthroughs are especially important considering that mental disorders are often associated with other, non-psychiatric medical problems. For example, patients with depression have elevated risk of developing type-2 diabetes (Renoir, 2013). Likewise, research investigating the effects of severe anxiety suggests that long-enduring anxiety can impair both short-term and long-term memory (Robinson, 2013). As shown in Figure 3, data gathered from Crisis Text Line, a mental health texting service in the United States, indicates that in six years, the crisis line received over 129 million messages related to anxiety, depression, and suicide. The map lays out mental diagnoses by state to convey the magnitude and extent to which mental health exists in the United States. Furthermore, this is most likely an underestimation because it does not account for all the individuals that did not send a message, but were similarly coping with mental illness. The need for effective treatments for depression and anxiety have directed researchers and therapists to psychedelics – a potent medication – as long as both medical safety and society allow. If proven to be sufficiently beneficial and safe, drugs such as psilocybin and LSD may eventually be valuable in helping mental illness patients move towards purpose, happiness, and fulfillment in their lives. ❧

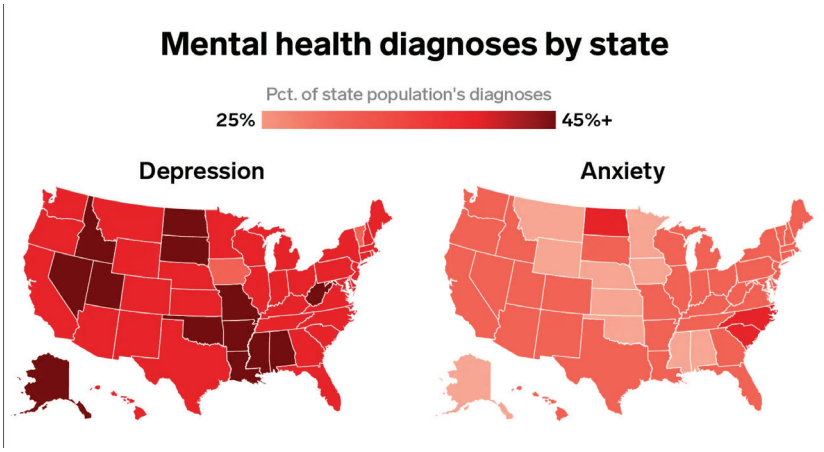

Figure 3. Severity of depression and anxiety diagnosed by state in the USA. Image from Feder 2020.

... LSD can guide patients to see the world through a new and different lens...

AUTHOR BIO

Sridhar Karne is a third year in the college majoring in Neuroscience & Behavioral Biology. In his free time, he enjoys playing soccer.

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Placed by Sri Ponnazhagan

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Cross-cultural treatment for COVID-19: A spotlight on ethnomedicine in America

SABRINA JIN
Staff Writer

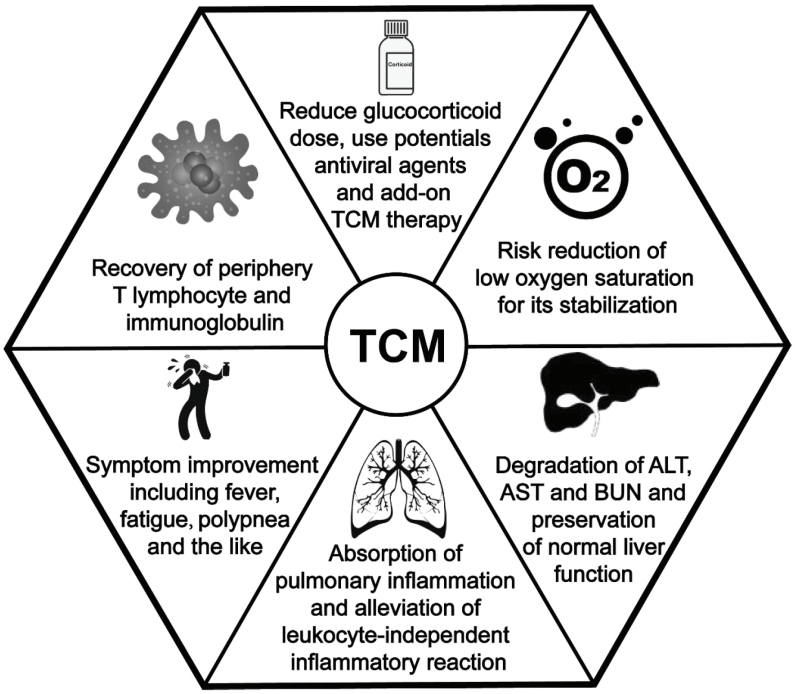

Figure 1. Traditional Chinese Medicine (TCM), a very popular ethnomedical system due to its low risk for toxicity and holistic emphasis on illness treatment, has multiple powerful benefits to recovery from COVID-19 when used in conjunction with biomedical treatments. Note: ALT = Alanine aminotransferase, AST = Aspartate aminotransferase (liver function tests); BUN = Blood urea nitrogen (kidney function test). Image from Zhang et al. 2020.

Ethnomedicine, the practice of disease prevention and treatment as influenced by cultural beliefs, is a prominent topic within medical anthropology that has rightfully been brought to the attention of the world in light of the coronavirus pandemic (Brown & Closser, 2016). The prevalence of ethnomedicine is apparent in my family through the way that my dad promotes the excessive ingestion of raw garlic because of its ability to "sanitize virus particles," a notion popularized on the Chinese communication network, *WeChat*. Upon first instinct I was quick to dispel this belief, but I've come to realize that similar practices are widespread across all cultures. The validity of such methods of treatment should not be immediately disregarded the way that they often are; instead, it is now more important than ever to embrace medical pluralism — defined as the simultaneous practice of multiple ethnomedical systems — in order to respect the diversity of cultures and provide more holistic patient care.

The prevalence of ethnomedicine is apparent in my family through the way that my dad promotes excessive ingestion of raw garlic because of its ability to "sanitize virus particles"...

Examination of my own immediate skepticism towards these different cultural beliefs led me to ponder over the significance of ethnomedicine in how COVID-19 has been managed in the United States. From interactions with peers, any mention of COVID-19 always invoked a common type of imagery: the doctor in the white lab coat, the use of soap, the language of war and infection containment, antiviral therapy, and the hopeful longing for widespread vaccination. Despite the undeniable prevalence of medical pluralism in the United States, there has been little to no recognition of other cultural systems of healing with respect to COVID-19 management beyond the imagery invoked by this Western biomedical model of healthcare (Baer, 1995). Among the myriad challenges that the U.S. healthcare system has to overcome, the lack of recognition given to ethnomedicine is another barrier that must be crossed in order to better provide care for people of different cultural backgrounds.

Due to the heavy focus on the Western biomedical model of healthcare in the United States, other medical systems are often deemed as unreliable and labeled as pseudoscience. However, various countries rely on established

multi-system models of care. To better gain perspective on the U.S. response to COVID-19, comparisons can be made with various other medically pluralistic countries. For instance, Chinese doctors incorporate herbs used in traditional Chinese medicine (TCM) as a health supplement for patients suffering with complications of the coronavirus. The most common herbs being used to treat COVID-19 infection include liquorice root, Baikal skullcap root, pinellia rhizome, forsythia fruit, and apricot seeds. When prescribed in conjunction with Western medicine, patients showed significant signs of improvement compared to those who did not use TCM. Reported benefits from TCM treatment of the coronavirus include symptom alleviation for fevers, coughs, general fatigue, and damage to the respiratory tract (Xiong et al., 2020). Beyond herbal remedies, doctors who prescribe methods of TCM may also suggest regular visits to the acupuncturist, which has also been correlated with reduced duration of illness along with increased relief for shortness of breath (Zhang et al., 2020).

With the simultaneous biomedical and TCM approach, China has an impressive emphasis on medical pluralism within their healthcare system. The fight against COVID-19 has resulted in further integration of TCM doctors into the biomedical hospital setting after the evident success from dual treatment plans (Zhao et al., 2020). Not only does this diversify the supply of healthcare professionals working in modern hospitals, but it also benefits patients by lowering their risk for potential side effects compared to the consumption of biomedical drugs (Ang et al., 2020).

In other regards, COVID-19 has provided a unique opportunity to establish camaraderie among many countries across southeast Asia. Due to prior cultural stigmatization, many indigenous healing practices have faced decades of adversity because they were viewed as illegitimate compared to the dominant Western biomedical model. With the lack of a specified cure or a widespread vaccine for the current pandemic, traditional forms of healing have seen a resurgence as cultural groups tout homeopathic remedies as they celebrate their unique cultures in medicine (Nguyen, 2020). This revival in traditional medicinal culture is also strongly backed by governmental support for medical pluralism, as the majority of Southeast Asian countries have national offices for traditional and complementary medicine.

From interactions with peers, any mention of COVID-19 always invoked a common type of imagery: the doctor in the white lab coat...

In many of these countries, popular media largely impacts cultural practices. For instance, Cambodian and Indonesian influencers have brought attention to the use of various vegetables—namely garlic, turmeric, and ginger—as effective measures in reducing susceptibility to the coronavirus. Garlic has long been known to have potent antimicrobial properties due to its compound, allicin, which helps the body's own immune system in fighting against pathogens (Dwivedi et al., 2020). Laboratory studies have also recently identified several bioactive chemical constituents from other vegetables, including piperdardiine and piperanine from peppers, and 8-Gingerol and 10-Gingerol from ginger. The effectiveness of these compounds as coronavirus inhibitory agents is comparable

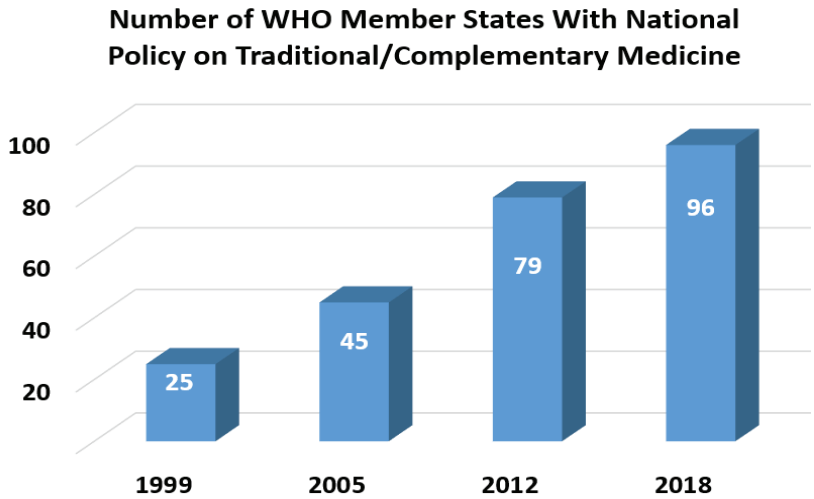

Figure 2. The prevalence of integrative medicine has steadily increased since national policy evolved to embrace the practice of medical pluralism. Image from WHO 2019.

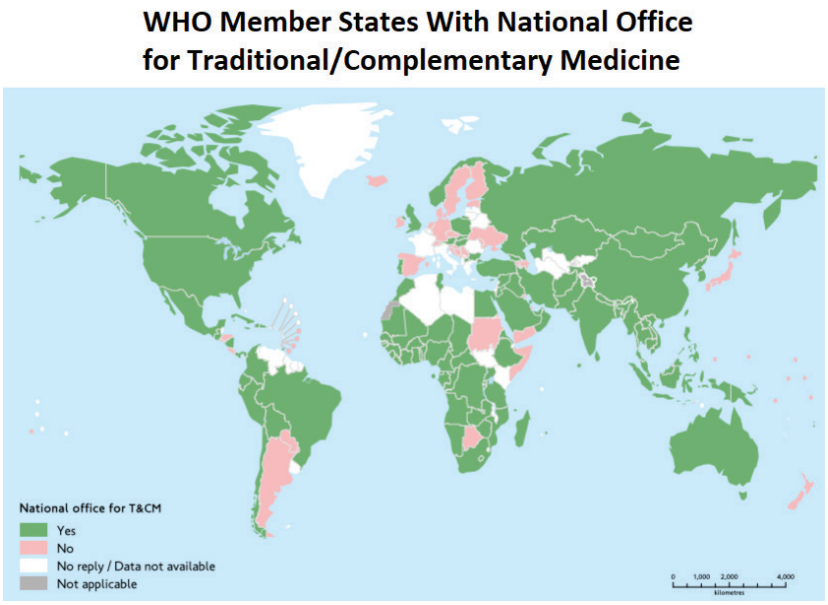

Figure 3. Many countries have established national offices for Traditional, Complementary and Integrative Medicine; however, acceptance of medical pluralism continues to vary in hospital settings depending on the level of structural support provided for other ethnomedical practices. Image from WHO 2019.

to the effectiveness of other biomedical treatments, including the controversial drug hydroxychloroquine (Rajagopal et al., 2020).

Latin American countries boast a diverse range of ethnomedical practices ranging from naturopathic remedies to spiritual healing. While the Western biomedical approach to healthcare places sole emphasis on the doctor, Latin American systems of healing also involve spiritual leaders as experts of interconnected bodily and spiritual matters. With the waves of Latin American immigration into the United States, the highly malleable practices of *Curanderismo*, or folk healing, have since adapted to new cultural landscapes as communities of Latin American descents settle in America.

Especially notable in the southern U.S., many practices of curanderismo have incorporated Judeo-Christian beliefs into the system of healing while simultaneously integrating folk remedies from African American history (Trotter, 2001). Instead of visiting a hospital when ill, many people opt to visit *curanderos*, or folk healers. This ethnomedical practice is often viewed as more trustworthy and holistic because of the emphasis on building interpersonal relations and rapport between the healer and the patient. The efficacy of its natural remedies as well as the emphasis on primary care makes it a prominent form of treatment not just among immigration populations, but also among many native-born Americans today (Cavender et al., 2011).

...perhaps it is also time to reevaluate the efficacy upon which our evidence is evaluated in order to provide more room for acceptance of other forms of healing.

The U.S. is an incredibly diverse nation, built from a melting pot of integrated cultures from immigrant populations; however, this diversity in ethnomedical practices is woefully unrepresented by a lack of structural support for medical pluralism within the healthcare sector. The Western biomedical model remains the predominant approach to healthcare, and while different cultural groups continue to embrace their own healing traditions, the U.S. hospital setting is often unaccepting of other practices.

This lack of awareness or regard for other ethnomedical practices remains one of the greatest barriers to effective patient care not just in the U.S., but all around the world. Language barriers and cultural incompetence continue to alienate already vulnerable populations from seeking treatment and often produce iatrogenic effects on patient health, defined as illness induced by improper medical treatment (Konczal & Varga, 2012). In order to better reflect the diversity of our nation and provide healthcare comparable to other industrialized countries, there has to be greater emphasis on educational programs to increase cultural literacy among healthcare workers. The U.S. National Center for Complementary and Integrative Health, the office that supports ethnomedical practices, should welcome a greater integration of traditional healers into hospital settings to provide options for

patients who desire dual treatment plans. Acknowledgement of healthcare professionals should not remain limited only to those who pave their way through the rigorous process of medical school; curanderos and other spiritual healers often play an equally important contribution to patient care. While the strictly evidence-based principle of Western medicine has brought the scientific community far in providing cutting-edge treatment of many diseases that were once untreatable, perhaps it is also time to reevaluate the efficacy upon which our evidence is evaluated in order to provide more room for acceptance of other forms of healing.

Lastly, it is imperative that our modality of treatment shifts from solely focusing on the illness to also understanding the context of each patient; after all, we are treating humans, not disease (Centor, 2007). COVID-19 can be understood as a viral infection from the scientific perspective of pathogenesis, yet the symptoms and responsiveness to treatment vary greatly from individual to individual (Mason, 2020). Preference for different modalities of treatments, likewise, vary greatly among different cultural groups. As such, there is no better time than now to follow suit with other countries, and adapt under this state of pandemic to better establish the structural groundwork necessary for medical pluralism in our nation. ❧

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AUTHOR BIO

Sabrina Jin is a third year in the college double majoring in Biology and Cultural Anthropology. An interesting fact about her is that she raised about nine insect species last semester and was fortunate enough to witness the hatching process of around 120 wheel bugs.

Edited by Sarah Kim, Aditya Jhaveri and Dr. Kim Tran

Placed by Jocelyn Chow

Fatality declines with fetal surgery for Spina Bifida

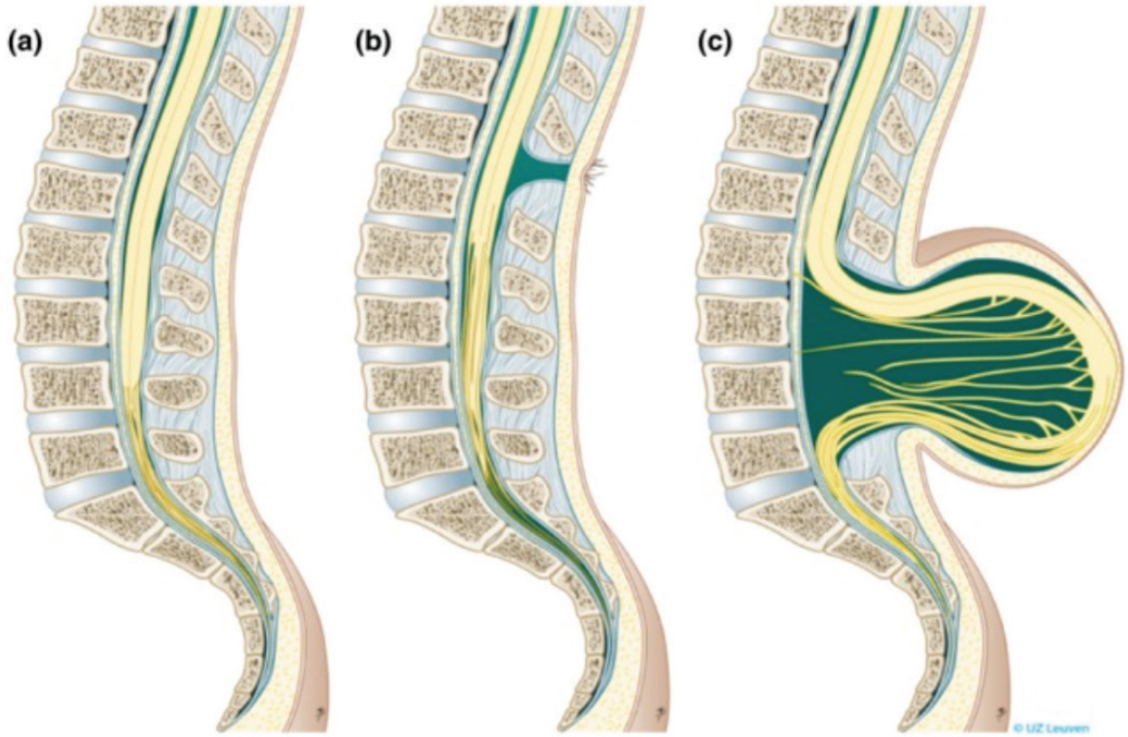

Figure 1. Spina bifida can manifest in different levels of severity. Shown above is (a) a normal or unafflicted spine, (b) spina bifida oculta, and (c) myelomeningocele. Image from Sacco et al. 2011.

NIKI PATEL
Staff Writer

Life is composed of probabilities. The sum of these stochastic processes leads to great variation in life outcomes, beginning at the fusion of egg and sperm. Countless mitotic events ensue, influencing the course of this tiny zygote's new life; however, not all developments result in a healthy newborn. One such developmental setback is myelomeningocele, the most severe and pervasive form of spina bifida. Myelomeningocele is a form of spina bifida in which the spinal cord and nerves protrude from the backbone, usually due to a build-up of a sac of cerebrospinal fluid (Adzick et al., 2011). The less severe form of spina bifida is spina bifida oculta, which has near negligible symptoms that do not impair one's quality of life to a comparable extent ("Spina Bifida", n.d.). Worldwide, the average mortality rate within the first week of life for an infant diagnosed with spina bifida was 6.9% between 2001 and 2012, with the majority of deaths occurring on the child's first day of life (Bakker et al., 2019). Those afflicted with myelomeningocele suffer from debilitating lifelong conditions such as paralysis, hydrocephalus (fluid accumulation in the brain), mobility and walking difficulties, and joint and bone deformities ("Spina Bifida", n.d.). Advancements made in fetal surgery to correct the more severe form of spina bifida, myelomeningocele, have been shown to improve infants' survival rates compared to postnatal surgery, implicating a greater probability of successful life outcomes for those individuals.

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Fetal surgery is a complex *in-utero* procedure reserved for qualified candidates who undergo a comprehensive screening process before being recommended to undergo the operation. Most hospitals outline a standardized list of criteria that must be met for myelomeningocele fetal surgery. Most importantly, the

fetus must present with hindbrain herniation, meaning the lower part of the brain abnormally moves down onto the top of the spinal cord, with the myelomeningocele occurring between levels T1-S1 of the spinal cord. In addition, it must be a single fetus pregnancy, with the gestation time not exceeding 25 weeks at the time of surgery, and the mother must be in good health with at least 18 years of age ("Fetal Surgery Guidelines for Prenatal Myelomeningocele", n.d). Once these criteria are met, a team of specialized surgeons perform a laparotomy (an incision of the abdomen) followed by an incision of the uterus and removal of the myelomeningocele sac. The spinal cord is then returned to the spinal canal and the tissues surrounding this region are repaired before closing the uterus and abdomen ("About Fetal Surgery for Spina Bifida", n.d.).

Advancements made in fetal surgery have proven to be more effective at reducing the symptoms of myelomeningocele than postnatal surgery

Advancements made in fetal surgery have proven to be more effective at reducing the symptoms of myelomeningocele than postnatal surgery (Adzick et al., 2011). Researchers closely monitored infants born to mothers who were randomly assigned to prenatal or postnatal surgery for the first 30 months of their lives and found that by 12 months, only 40% of infants in the prenatal group needed shunt placement compared to 82% of babies in the postnatal group (Adzick et al., 2011). Shunt placement is a process in which a surgeon places an alternative path in the infant's head to drain excess fluid that is putting too much pressure on the baby's brain ("Health Issues & Treatment for Spina Bifida, 2020"). Hindbrain herniation was also significantly less pronounced in the prenatal group versus the postnatal group (Adzick et al., 2011). By 30 months, children in the prenatal group were two times more likely to be able to walk on their own without the need for orthopedic devices (Adzick et al., 2011). Lastly, motor function was consistently more advanced in the prenatal group (Adzick et al., 2011). Although this study was groundbreaking as it produced clear evidence suggesting the reduction of myelomeningocele symptoms associated with prenatal surgery, it must be noted that individuals were only followed up to their first 30 months of life. Overall, these findings demonstrate that neurological development during gestation is a dynamic process that can be significantly assisted by performing this surgery.

In a recent study published in 2020, researchers followed infants diagnosed with myelomeningocele into their childhood

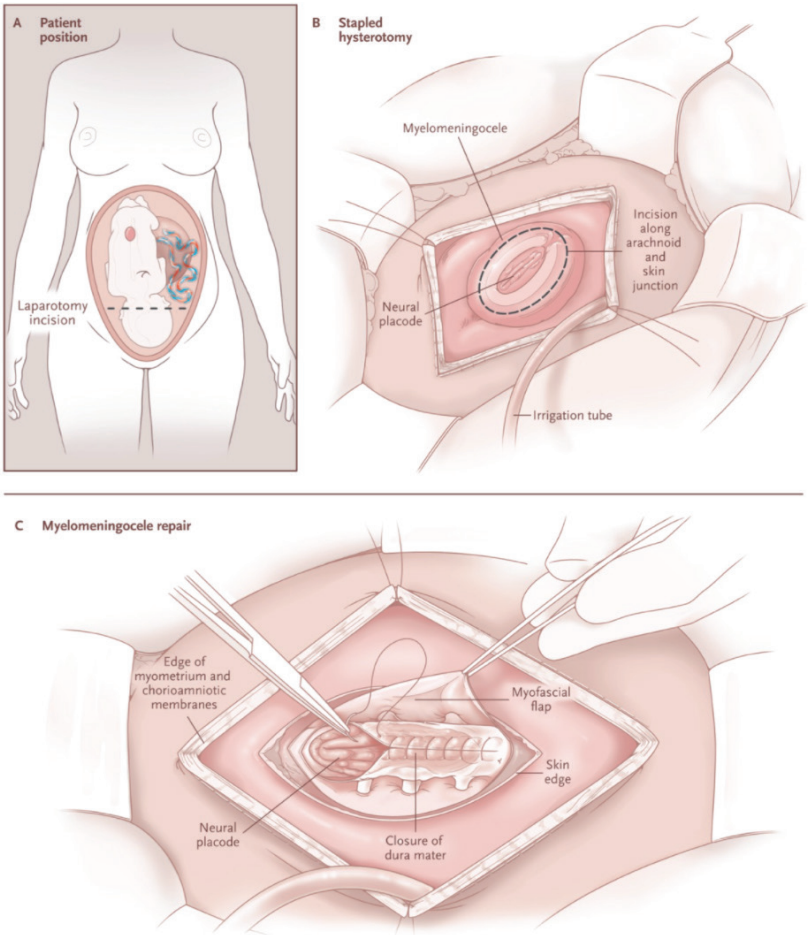

Figure 2. The prenatal operation for spina bifida repair involves the incision of the abdomen and uterus before the myelomeningocele sac can be removed. Image from Adzick et al. 2011.

Figure 3. Hindbrain herniation is a condition in which the lower, backside part of the brain descends upon the top of the spinal cord. Image from the NIH n.d.

and found that children born after prenatal surgery continued to benefit from reduced symptoms and a lesser need for shunt placement compared to those who underwent postnatal operations (Houtrow et al., 2020). This study compared these outcomes amongst children in the two groups between the ages of 5.9 and 10.3 years of age (Houtrow et al., 2020). Some notable findings include that children in the prenatal group walked without assistive devices more often, had significantly lower incidence of hindbrain herniation, and had a decreased need for shunt placement for hydrocephalus (Houtrow et al., 2020). This study also found that the parents of the subjects in the prenatal operation group reported, on average, a higher quality of life for their children, compared to parents whose children underwent postnatal surgery (Houtrow et al., 2020). However, no significant findings could be generated regarding the differences in cognitive ability between the groups. Based on the literature, it appears that children diagnosed with myelomeningocele will be at risk for learning challenges regardless of which surgery is performed (Houtrow et al., 2020). That said, fetal surgery is a relatively recent advancement in medicine, with the first procedure having only been completed in 1997, and more longitudinal studies regarding the benefits of this procedure are needed to bolster our understandings of its specific effects on myelomeningocele (Houtrow et al., 2020).

The ethical considerations surrounding fetal surgery have been debated in both the legal and medical fields. There are numerous discussions surrounding the status of the fetus as a life form independent from the mother, as well as the mother's mortality risk when undergoing prenatal surgery (Sacco et al., 2019). By electing to go through with prenatal surgery, the parents have the power to interrupt the natural progression of this devastating disease; however, fetal surgery has a slightly higher (but not statistically significant) risk of fetal death than postnatal surgery (Sacco et al., 2019). Furthermore, fetal surgery poses risks to the mother who cannot directly benefit from the operation. These risks include uterine rupture in subsequent pregnancies as well as pulmonary edemas during the actual surgery. Nevertheless, the

Regardless, the possible complications of fetal surgery should be discussed with parents beforehand to ensure they are well informed to make their decision.

incidence rate of these events is low and will only decrease as surgical techniques are refined (Al-Refai et al., 2017). Regardless, the possible complications of fetal surgery should be discussed with parents beforehand to ensure they are well informed to make their decision.

It is important to remember that, ultimately, the people who are making the decisions about fetal surgery are humans. Parents want to give their children the best life outcomes possible, and learning that their baby will be born with a congenital birth defect takes an emotional toll on parents for the remainder of the pregnancy. Some parents may elect not to proceed with the operation due to financial strain or wariness about the procedure itself. While the literature points to fetal surgery as the current best option to correct this birth defect, not all women are ideal candidates, even for some who desperately want it. For those lucky enough to be selected, such as Colette Hagler of Dallas, Texas, the benefits outweigh the risks. Colette said, "[w]e wanted to give our baby the best chance possible…[and] we named her Faith because at many points in our journey, it was faith that kept us going." Faith, fortunately, was born at the Texas Fetal Center at Children's Memorial Hermann Hospital with no complications ("Faith", n.d.). The decision-making process is stressful, as with any surgery, and the benefits and risks toward both fetus and mother must be considered in turn. ❧

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AUTHOR BIO

Niki Patel is a second year in the college majoring in Neuroscience and Behavioral Biology with a minor in Spanish. She has experimented with different forms of dance since she was five.

Edited by Rhea Tumminkatti, Sarah Kim and Dr. Gregg Orloff

Placed by Alicia Yin

The possibilities and ethical risks of neural implant technology

AASTHA BANSAL
Staff Writer

MURIEL STATMAN
Staff Writer

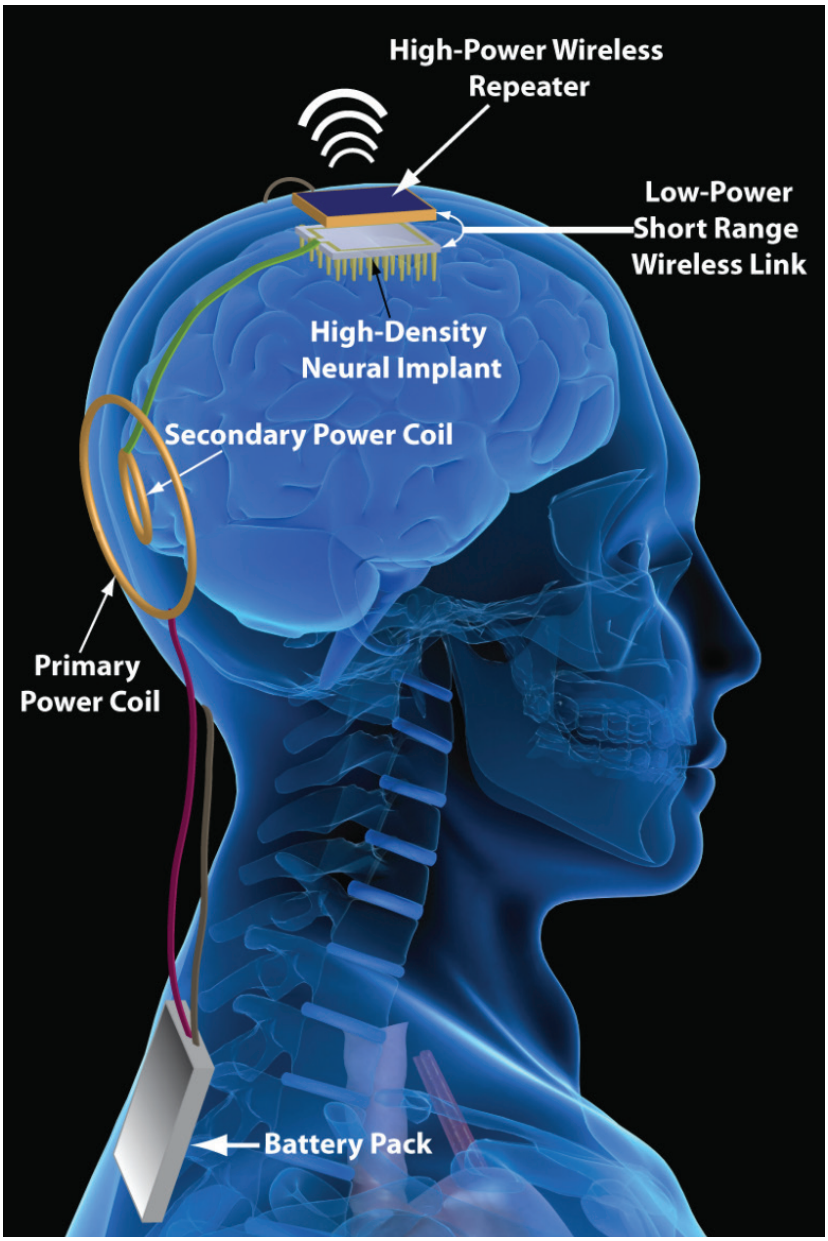

Figure 1. The device (typically an electrode of some kind) is inserted into the brain as a neural implant and communicates with neurons. Image from USciences n.d.

Imagine living your whole life paralyzed from the waist down, hence unable to live life to its highest potential. With neural implant technology, however, the possibility of regaining movement has the potential to completely transform your life. Although neural implant technology may be years away from human implementation, Elon Musk's company, Neuralink, recently made great strides in advancing the technology. Musk revealed the latest version of the implant technology in late August, and the scientific community is hopeful that his model could transform lives for the paralyzed and blind. Neuralink has vast potential and has been coined as a "breakthrough device" by the FDA; however, there are several ethical risks concerning issues of privacy, accessibility inequality, and identity issues that should be considered before this technology is deemed fit for the public.

Neural implants are human-made devices placed in the body via surgery or injection and have the ability to communicate with neurons in the nervous system. Neurons are cells responsible for receiving sensory input, sending signals to the muscles, and relaying electrical signals throughout the body (Woodruff, 2019). Neurons also play an important role in the integration of incoming signals and the relay of these signals to target cells via action potentials, which allow for the rapid transmission of information across long distances. Neural implantation involves placing one or more electrodes to interact with neurons and record "native neural activity," allowing researchers to better understand how neural circuits communicate (Waltz, 2020). These implants can send electrical impulses to neurons, overriding normal firing patterns and forcing neurons to communicate in different ways. Usually, neural implants are used

in deep brain stimulation (DBS) to help regulate abnormal electrical impulses arising in certain areas of the brain. Electrodes are placed deep in the brain to stimulate certain structures and reduce symptoms induced by various brain disorders ("Deep brain stimulation," 2020).

One of the most established and well-known types of neural implants are cochlear implants, which are designed for patients with sensorineural deafness. The implant is a small electronic device made up of an external portion outside the ear and a second portion surgically placed under the skin. It consists of a microphone, speech processor, transmitter and receiver/stimulator, and an electrode array. A cochlear implant functions by bypassing damaged portions of the ear and generating signals sent through the auditory nerve to the brain for recognition ("Cochlear implants," 2017). Although cochlear implants have greatly improved over the years and allow deaf patients to gain a useful representation of external sounds and understand speech, they are still far from producing 'normal' hearing.

Other approaches to neural implant technology include phrenic-nerve stimulators, which involve the electrical stimulation of the phrenic nerve through a surgically implanted device. An external transmitter and antennas send radio waves to implanted receivers under the skin and cause the diaphragm to contract repeatedly, creating a normal breathing pattern in patients suffering from respiratory insufficiency ("Phrenic Nerve Stimulation," 2020). Another technology is optogenetics, which modifies neurons so that they can be turned on or off when illuminated by light of appropriate wavelengths. There have also been approaches to restore sight through artificial retinas/chips and visual-cortex stimulators and methods to reduce pain through transcutaneous electrical neural stimulation.

In 2020, Neuralink announced the entirely wireless design of their device, which relays data through a Bluetooth radio.

Musk's startup, Neuralink, is expanding the horizon of neural implant technology. In 2019, they announced their three main goals for this technology: to create flexible material, integrated circuit technology, and wireless interactions (Lewis & Stix, 2019). In 2020, Neuralink announced the entirely wireless design of their device, which relays data through a Bluetooth radio and is more practical for human use. As shown in Figure 2, this device is the size of a coin attached to thinner and more flexible electrodes that allow for easier robotic insertion into the brain (Lewis, 2020). With a more streamlined and effective design, Neuralink hopes to prevail in their efforts and thereby revolutionize neural implant technology.

Two main purposes of Musk's invention are to restore voluntary motor function in patients with paralysis and to restore vision in those suffering from blindness. Paralysis occurs when damage occurs to nerve cells in the brain or spinal cord that prevents the cells from delivering neural signals to muscles, thereby resulting in loss or lack

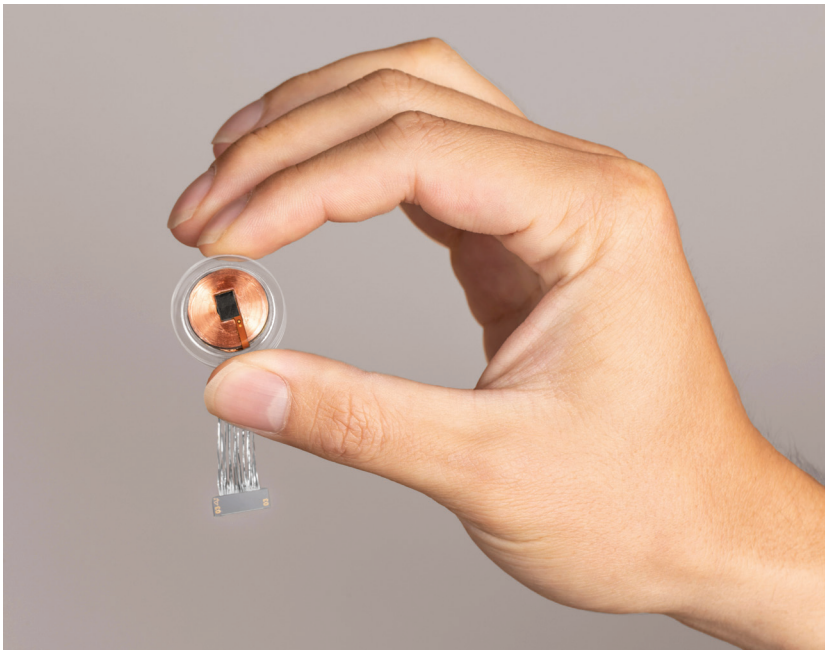

Figure 2. Musk's neural implant device is the size of a large coin and attached to 1,024 thread-like electrodes that extend into the cerebral cortex in the skull. The device contains a customized computer chip that amplifies signals from the cortex and relays them to a computer. Image from Neuralink 2020.

Figure 3. The prototype of the original 2019 Neuralink device. Image from Neuralink 2019.

of ability to move, deteriorating strength, or defective muscular control (Cleveland Clinic, n.d.). In addition, Neuralink hopes to treat blindness, when it stems from optic nerve or visual cortex damage. Creating a visual prosthesis would enable patients to receive "a meaningful perception of the image" from their external surroundings by delivering image information to the visual system (Maghami et al, 2014).

Neuralink has greatly advanced its neural implant device in the past year. Since the device records electrical signals produced by neurons, it would eventually allow scientists to track muscle movement. The electrodes are robotically inserted into the brain so they can record and generate the electrical signals produced by each neuron. Neuralink is currently working to analyze and use these signals to restore movement. In Musk's 2020 presentation, he demonstrated how Neuralink impacts movement in pigs, by converting their brain signals into audible bleeps. One pig, Gertrude, had been implanted with Neuralink for two months in a region of her cortex that was connected to neurons in the snout. As she sniffed across the pen while searching for tasty treats, the bleeps became more frequent, representing her movement (Lewis, 2020). Musk's demonstration showed the advancements of Neuralink's neural implant and how the device could eventually help millions of lives.

Although neural implant technology can possibly transform the lives of those with paralysis and blindness, ethical concerns must be considered in order to protect the privacy and identity of vulnerable populations, and improve the accessibility of the technology in general. Neural implant technology might evolve to not only restore normal function in paralyzed and blind patients but also enhance normal human abilities. While this possibility may seem more like science fiction than reality, in 2019, Elon Musk himself stated that this was one intended consequence of the technology. Musk said that he sought to give humans "superhuman intelligence" by allowing them to "merge" with artificial intelligence (Lewis, 2019). A prominent implication of this "superhuman intelligence" could be improved memory, which may present serious psychological effects, especially for patients with past trauma. Considering that selective memory loss may actually benefit certain subsets of patients, an improved or even perfect memory may have serious side effects (Hansson, 2005). Additionally, these enhanced qualities could fundamentally change society's notion of normality. Using neural implant technology to achieve superhuman qualities may become the new normal, and individuals with

natural human abilities may be categorized as subnormal (Hansson, 2005). Such categorizations can become extremely problematic and cause heightened societal inequalities.

Wealth inequalities raise additional ethical issues since lower-income communities will most likely have limited access to new and expensive technologies. Neural implant technology is no exception. This disparity may further marginalize vulnerable groups and heighten pre-existing inequalities. Total artificial heart research in the 1980s, for example, sparked a debate concerning how the cost of these devices would impact socio-economic disparities, and some argued that the research should be halted because the distribution of its benefits across society would be unequal (Hansson, 2005). When curative treatments are developed to treat illnesses, social inequalities regarding health intensify, and the wealthy benefit from the new technologies the most (Weiss, 2018). Cost and accessibility are two key factors in ensuring that neural implant technology does not disproportionately exclude lower-income communities.

The personality and identity of patients are also at stake with neural implant technology, so it is vital that regulations dictate what types of neural implants can be used. Neural implants introduce a foreign object into the patient's brain, and "curing" a condition may cause significant changes to the patient's personality and their feeling of autonomy. In a 2016 study, a man with a brain stimulator used to treat his depression recounted that it altered his sense of self and that he no longer felt in touch with his identity: "it blurs to the point where I'm not sure … frankly, who I am" (Yuste, 2017). These findings encapsulate how neural implants can potentially influence and even transform the ways in which individuals behave. Issues of identity may also arise due to conflicting perceptions of curing and disability. Within the deaf community, for example, there is widespread debate about cochlear implants. Many members of the deaf community argue that just because they use cochlear implants, does not mean they are disabled or sick. They are merely using a different language to communicate and have adapted to a different culture (Hansson, 2005). It is possible that similar controversies may arise for neural implants in the future.

Using neural implant technology to achieve superhuman qualities may become the new normal, and individuals with natural human abilities may be categorized as subnormal

These issues were addressed in 2017, when the Morningside Group, a team of neuroscientists, neuro-technologists, clinicians, and ethicists came together to propose ethical guidelines for neural implant technology. One of their proposals recommended including provisions in international treaties, such as the 1948 Universal Declaration of Human Rights, to protect individual identity and agency in regards to neurotechnologies (Yuste, 2017). Such a proposal emphasizes the grave importance of explicitly defining the functions of neurotechnologies so that they do not threaten an individual's autonomy and identity.

The neural implant technology that Neuralink developed is truly a medical breakthrough — its wireless and less invasive design has revolutionized neural implants. As demonstrated in their experiment with pigs, the technology is advancing at a rate that may eventually land it in clinical trials. Yet, while it is easy to fixate on the incredible possibilities when a high-profile celebrity like Elon Musk releases such a technology, it is equally important to consider the risks. The exciting aspects of neural implants, namely the potential it possesses to treat the paralyzed and blind, must not overshadow the ethical dilemmas the public might face if it is approved for human use. Skewed versions of normality, amplified inequalities, and identity crises are all serious consequences of neural implant technology, and each must be carefully addressed to ensure that the technology's incredible scientific breakthroughs can positively impact society to its fullest potential. ❧

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Placed by Rachel Xue

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AUTHOR BIO

Aastha Bansal is a first year in the college intending to major in Neuroscience and Behavioral Biology. An interesting fact about her is that she has been a vegetarian her entire life.

AUTHOR BIO

Muriel Statman is a first year in the college intending to major in Human Health. An interesting fact about her is that she spent kindergarten in Harare, Zimbabwe.

ADVISORY BOARD

MICHAEL CRUTCHER Ph.D.

Senior Lecturer and Director of Undergraduate Studies at Emory University

EUMR's main advisor is Dr. Michael Crutcher, one of the many distinguished faculty members in Emory's Neuroscience and Behavioral Biology Department. Having received his PhD in Physiology from Johns Hopkins University, he joined the Department of Neurology and of the Neuroscience Ph.D. program at Emory in 1991. His research is primarily focused on the neural mechanisms of visually guided reaching movements in monkeys.

Dr. Crutcher has taught many NBB courses over the years such as: freshman seminar courses (NBB 190) on Brain Enhancement, Curiosities of Neurology and Neuroscience, and Neuroethics as well as Perspectives in Neuroscience and Behavioral Biology (NBB 401 SWR), Biology of Movement Control (NBB 370), Neuroscience Research Methods (NBB 221), Functional Neuroanatomy (NBB 470), and Topics in Neuroscience and Behavioral Biology (NBB 270).

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MUHAMMAD AZEEM

Medical doctorate in Child Psychiatry at Yale University

Dr. Azeem's primary clinical and research interests include Autism Spectrum Disorders, ADHD, child and adolescent psychiatry training, global mental health, and looking into innovative ways in reducing seclusions and restraints in inpatient child and adolescent settings.

TYLER CYMET

Medical doctorate from Nova Southeastern University College of Osteopathic Medicine

Dr. Cymet is an internist with research interests in joints and the musculoskeletal system. He discovered a new syndrome in 2006 which was named for him called the Erondu-Cymet syndrome. He now serves as the chief of clinical education for the American Association of Colleges of Osteopathic Medicine.

ARRI EISEN

Doctorate in Biochemistry from the University of Washington

Dr. Eisen is a professor of pedagogy at the Center for Ethics at Emory University. He aims to engage undergraduate students in the exploration of science and its applications in broad contexts. He has led the Emory-Tibet Science Initiative since 2005 and continues to be involved in many projects at Emory.

LAWRENCE MARKS

Doctorate from Harvard University

Dr. Marks is professor emeritus of epidemiology and public health at Yale. His research interests center around sensory disorders and perceptual experiences such as synesthesia. Though retired, he is active in writing and collaborates with other researchers in his areas of interest.

ADVISORY BOARD

LYNN O'NEILL

Medical doctorate from Vanderbilt University School of Medicine

Dr. O'Neill is a palliative medicine physician who is active in both clinical and educational pursuits. When she isn't providing medical counseling, Dr. O'Neill oversees all the educational activities of the Emory Palliative Care Center of which she is associate director.

GREGG ORLOFF

Doctorate from Emory University

Dr. Orloff is a senior lecturer at Emory University teaching biology to undergraduates and the director of the CancerQuest program which he founded back in 1998. He created the program to provide accurate information about cancer to inquiring patients and it is now been operating for more than two decades.

MOHAMMED SHAHAIT

Medical doctorate from the Jordanian University of Science and Technology

Dr. Shahait is an attending urologist who also teaches at the Perelman School of Medicine at the University of Pennsylvania. His research focuses on the use of robot-assisted radical prostatectomy as a method of treating prostate cancer.

KIM TRAN

Medical doctorate from the University of Medicine and Pharmacy at Ho-ChiMinh City, Vietnam and doctorate in Medical Sciences from Hamamatsu University School of Medicine

Dr. Tran is a professor of physiology and pharmacology at Des Moines University. His research interests include cardiovascular pathobiology and therapeutics, especially the role of GPCRs in disorders such as menopause, heart failure and hypertension.

LAURA OTIS

Doctorate in comparative literature from Cornell University

Dr. Otis had her beginnings in science, earning a bachelors in molecular biophysics and biochemistry from Yale and then a masters in neuroscience from the University of California at San Francisco. Now at Emory, she teaches the intersection of science and literature with special interest in nineteenth century novels.

SARAH BLANTON

Clinical doctorate in physical therapy from Emory University

Dr. Blanton is an associate professor of rehabilitation medicine at Emory with a research interest in improving the delivery of family-centered care in rehabilitation. She also serves as editor-in-chief of the Journal of Humanities in Rehabilitation whose mission is to integrate the humanities into rehabilitation science.

JESSE SOODALTER

Medical doctorate from the Warren Alpert Medical School of Brown University

Dr. Soodalter is a hospice and palliative care specialist in the Emory Healthcare network. She also collaborates with physicians from places as far as Pittsburgh where she most recently completed a fellowship in 2019.

Executive Board

NATHAN JACOB

Editor in Chief - Copy

Nathan is a third year majoring in Biology with a minor in Philosophy. He began as first-year liaison, went on to serve as the club secretary, and now as editor in chief - copy, he hopes to expand EUMR's impact on bringing about awareness of the interdisciplinary nature of medicine. Outside of EUMR, he is also involved in organizations such as club tennis and is a pre-health peer mentor. Nathan was an extra in Spider-Man Homecoming and you can actually see a blurry image of him during the first ten minutes of the movie!

DAISY LI

Editor in Chief - Layout

Daisy is a third year majoring in Anthropology & Human Biology and co-majoring in Integrated Visual Arts. She originally joined EUMR as a first-year liaison and organized the first Suture Lab with the Emory School of Medicine. Since becoming editor-in-chief, her main goal is to continue expanding EUMR's presence and reach across campus. That aside, there is nothing she loves more than a day with no agenda spent on all sorts of creative endeavors.

ANJANAY NANGIA

Secretary

Anjanay is a second year majoring in Chemistry and co-majoring in Quantitative Sciences. He originally joined EUMR as a first-year liaison and organized the first Data Science Symposium with the School of Nursing. As secretary, he is involved in events planning, facilitating the editorial process, and social media initiatives to advance EUMR alumni engagement. He has survived quarantining by learning how to cook and catching up on his favorite movies and shows.

GANESH CHILUKURI

Treasurer

Ganesh is a second year majoring in Neuroscience and Behavioral Biology with a minor in South Asian Studies. He began as a contributing writer for EUMR's Open Access and now as treasurer, he works on budgeting for all of EUMR's operations and the club's dealings with SGS. Outside of EUMR, he is also involved in Emory Synapse and works as a student ambassador for prospective/incoming students. In his free time, Ganesh loves listening to music of all genres and later composing them into pop sonnets.

THALIA LE

Events Chair

Thalia is a third year majoring in Biology and minoring in Chemistry. She began as a staff editor on the Editorial Board and now as the Events Chair, organizes the many on-campus events that EUMR puts on every year. Outside of the club, she does research in medicinal chemistry, volunteers through Emory Hope and CHOA, and enjoys mentoring/tutoring underclassmen. In her free time, she enjoys cooking and baking. Thalia also has alektorophobia, a condition characterized by an intense fear of chickens!

Editorial Board

copy editors

Aditya Jhaveri

Aditya is a fourth year double majoring in Neuroscience & Behavioral Biology and Quantitative Sciences.

Alex Sandberg

Alex is a fourth year majoring in Chemistry. He hates cheese!

Andy Chen

Andy is a fourth year double majoring in Anthropology & Human Biology and Neuroscience & Behavioral Biology.

Bushra Rahman

Bushra is a third year double majoring in Anthropology and Spanish & Portugese. She has written a play before.

Edward Xue

Edward is a second year double majoring in Psychology and Chemistry. Drinking coffee makes him sleepy.

Helen Griffith

Helen is a second year double majoring in Neuroscience & Behavioral Biology and Spanish. She has a yellow lab puppy.

Lauren Flamenbaum

Lauren is a fourth year majoring in Neuroscience & Behavioral Biology and minoring in Anthropology. She grew up in France.

Lizzy Wagman

Lizzy is a second year majoring in Anthropology & Human Biology with a minor in Ethics. She plays golf!

Luisa Taverna

Luisa is a second year majoring in Biology and minoring in Philosophy. She is fluent in Italian!

Nivetha Aravind

Nivetha is a third year majoring in Human Health. She has been learning a classical Indian dance form since she was 6!

Rhea Tumminkatti

Rhea is a third year majoring in Anthropology & Human Biology. She enjoys singing.

Sarah Kim

Sarah is a third year studying Chemistry and Psychology. She loves taking walks and exploring music videos.

Vyas Muralidharan

Vyas is a fourth year majoring in Quantitative Sciences and minoring in English. He once managed to sleep 25 hours straight!

Editorial Board

layout editors

ALBERT LIU

Albert is a third year pursuing a bachelors of arts in Economics.

ALICIA YIN

Alicia is a second year majoring in Biology. Her favorite place that she's traveled to is Jordan.

ANSHRUTA DHANASHEKAR

Anu is a third year majoring in Neuroscience & Behavioral Biology and Creative Writing. She has a black belt in karate.

CARISSA WU

Carissa Wu is a second year majoring in Biology. She has visited countries on five different continents.

HENRY MANGALAPALLI

Henry is a third year double majoring in Biology and Sociology.

JOCELYN CHOW

Jocelyn is a third year majoring in Neuroscience & Behavioral Biology with a minor in Music. She has a pet betta fish.

RACHEL XUE

Rachel is fourth year majoring in Human Health. She enjoys making friendship bracelets in her free time.

SHREYA RANA

Shreya is a third year majoring in Neuroscience & Behavioral Biology and minoring in Computer Informatics.

SRI PONNAZHAGAN

Sri is a fourth year majoring in Psychology with a minor in Astronomy.

VIVIAN HUANG

Vivian is a fourth year double majoring in Biology and French Studies. She has been playing piano for 17 years.