EATING DISORDERS
What are they really, and what we can do about them

T-CELLS TARGETING TUMORS
A new type of immunotherapy

ANTIBIOTIC RESISTANCE
Reversing time for modern superbugs

A LIFE WORTH LIVING?
Analysis of the debate on euthanasia

MERGING OF THE MINDS
Reconceptualizing Age-Old Health Issues

SYNAPSE
PENN'S UNDERGRADUATE MEDICAL CONNECTION
FALL 2016
Dear Readers,

Since the dawn of modern medicine, the fusion of ideas and technologies in healthcare has never been greater. There is a pressing need to increase access and quality of care, beyond just the operating table. With the advent of groundbreaking technologies, healthcare policy, and innovative medicine, individuals and entire industries are joining forces to confront healthcare's biggest challenges.

SYNAPSE reaches beyond the realm of conventional medicine and into the coalescence of multifaceted ideas that capture our theme of “Merging of the Minds: Reconceptualizing Age-Old Health Issues”. Our feature articles delve into both the technical and abstract dimensions of medicine. We illuminate the rise of age-old superbugs that threaten the return of microbial dark ages. We explore the innovation of T-cell technology to better target cancerous cells and how they can mitigate toxic effects. In the other sphere of healthcare – we analyze the eating disorder epidemic from the unique lens of students in their most formative years and investigate the debate on euthanasia. Regardless of focus, all of our articles seek to piece together the industry-wide shift in fusing ideas to better target healthcare issues.

In the fourteenth installment of SYNAPSE, we would like to sincerely thank every member of our Editorial, Design & Layout, and Business teams for their contribution this semester and over their collegiate careers. Without the dedication and hard work of our team, this issue would not have been possible.

Ajay Patel and Celena Chen
Editors-in-Chief
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**ON THE COVER**
This issue’s cover art was designed by Victoria Siu, an undergraduate majoring in Biological Basis of Behavior and minoring in Creative Writing. The image expresses duality and integration of the emotional and analytical side of healthcare.
Anorexia does not just result in thinness; it is a slow path to self-destruction. Common symptoms include osteoporosis (which typically occurs after menopause in non-anorexics), brittle hair and nails, yellowish skin, and feelings of around-the-clock coldness.⁷,⁸ If left untreated, the disease will progressively become worse and could even result in an abnormally slow heart rate, muscle loss, multi-organ failure, and infertility. It is not shocking for an anorexic to experience amenorrhea, a condition that causes an individual to miss her period for more than three months. If the disorder has taken a severe toll on an anorexic, he or she may suffer a sudden heart attack and die. A young woman with anorexia is 12 times more likely to die than other women her age without anorexia.⁹

Bulimia Nervosa

At first, only sometimes, I would run the shower so my parents wouldn’t hear, and vomit in the toilet. Now I take a plastic bag up to my room every night and after eating a large meal… I turn up my music and vomit.¹⁰

Bulimia Nervosa is characterized by an excessive ingestion of food, followed by purging. Typically, bulimics can consume between 1,500 and 3,500 calories in a single binge.¹¹ After a period of excessive food...
consumption, an individual will forcibly vomit, use laxatives, fast, or excessively exercise as a way of compensating for his or her binge. An individual will fluctuate between feeling disgusted and ashamed as he or she binges, and then later feeling relieved of tension and negative emotions once or his or her stomach is empty again. Since bulimia is associated with a feeling of being out of control during binge-eating episodes, those who suffer from the illness often binge in secrecy. Evidently, a bulimic’s self-esteem relies on his or her body image and thus, he or she undergoes these unhealthy measures in order to preserve his or her physique. However, unlike anorexics, people with bulimia usually maintain a normal weight.

Though bulimia may provide individuals with a way to maintain normal weight, it is linked to physiological imbalances and damage. The consequences of the illness include: an inflamed and sore throat, swollen salivary glands in the neck and jaw area, dental issues, and acid reflux disorder. At its worst, bulimia can cause an electrolyte imbalance that could result in a stroke or heart attack. The electrolyte imbalance is triggered by dehydration and loss of potassium and sodium from the body, a direct consequence of purging behaviors.

Though victims of bulimia may recognize that their behaviors are unusual, it is often difficult for them to discontinue their bulimic habits. Bulimia is frequently associated with depression and difficulties in adjusting to a new social setting. For bulimics, the risk of death from suicide or medical complications is higher.

AT THE ROOT OF THE PROBLEM

Though there are several studies related to the topic of eating disorders, it is almost impossible to make a definite causal argument. It is virtually impossible to shadow people with eating disorders on a 24/7 basis, and then compare them to those without. Nonetheless, researchers have been able to develop a type of correlation model called the biopsychosocial model.

Think of it as an inverted cone. At the broad top, there are cultural factors; for example, cultures that usually have an abundance of food are more inclined to favor thinness. However, this cannot be the cause of eating disorders; otherwise, there would be a much larger population of people with eating disorders.

The middle level encapsulates familial and social factors. For instance, in college, most students are trying to fit in. Especially at competitive universities, many students feel the pressure to be perfect at everything: academics, sports, social life, attire, and so on. This stress can later transfer to food, and then lead to disordered eating. In questionnaires, college students with eating disorders admitted to comparing their food choices with food on other peers’ plates. Clearly, the competitive nature mixed with the desire to fit in are drivers of eating disorders. However, once again, researchers can only assume that correlation exists.

At the tip of the cone exists individual factors. Personal factors are the best indicators of whether a person is at-risk for an eating disorder. These factors include personality, cognition, and physiology. High levels of perfectionism and self-esteem are associated with both anorexia nervosa and bulimia nervosa. Personality characteristics associated with anorexia nervosa include: rigidity, perfectionism, and inflexible thinking. Feelings of inadequacy, helplessness, ineffectiveness, guilt, and self-doubt are all linked to bulimia.

In general, someone with an eating disorder has experienced a stressful life event that has affected his or her self-esteem. Furthermore, an individual prior to having an eating disorders may feel as if he or she has lost control of his or her life. In desperation, he or she will turn to anorexia or bulimia in hopes of restoring some control and distracting himself or herself from other quotidian problems.

BYSTANDER OR SAVIOR?

What do you do? How do we become normal? I don’t want to obsess over [my eating disorder] or food anymore. I can’t tell [anyone because everyone] knows me only as this great college athlete and soon-to-be doctor.

College students often do not seek treatment because of the stigma surrounding having an eating disorder. However, there should be no shame in seeking treatment. Eating disorders are serious, deadly illnesses that can take over an individual’s life. So, what should you do if you see someone with an eating disorder? Don’t be a bystander—this article cannot stress this enough.

Dr. Giang Nguyen, Executive Director of Student Health Services, recommends that a student contact Student Intervention Services right away. Once contacted, SIS staff will check on the student with the eating disorder; the person who contacted SIS remains anonymous. Timing is important. The longer an eating disorder is left untreated, the more likely an individual will suffer greater permanent damage.

If you are aware that you have an eating disorder, please schedule an appointment with CAPS or SHS as soon as possible. College is stressful and everyone copes in different ways. Sometimes, we all need a little guidance to direct us back to a correct, healthy path. As Dr. Nguyen emphasizes: Penn’s services are there. It’s up to the student to use them.

References
Science has only recently procured the ability to assess and understand the brain; naturally, medicine has followed suit. Knowledge of physical ailments and their treatments has steadily increased since the time of Hippocrates, whereas mental illnesses were often historically attributed to “madness” or even demonic possession. The lagging understanding of neurological processes has left a distasteful mark on the status of mental health in society: conditions like anxiety, depression, and schizophrenia are shrouded in stigma from all sides. This stigmatization, along with the drawbacks of current treatment options, creates an inadequate environment for people suffering from mental illnesses to receive the care they deserve.

Publicly, beliefs about mental health contribute to an unsupportive social climate that can worsen symptoms and further deplete self-confidence. A study by Corrigan and Wassel, two professors from the Illinois Institute of Technology, defines three different types of stigmatization that mental health patients experience—public, self, and label avoidance. Public stigma involves mass perpetuation of stereotypes; for instance, the popular misconception that those with mental illness are unpredictably prone to lash out. Self-stigma occurs when individuals internalize harmful stereotypes, which leads to worrying and further emotional deterioration. Lastly, those who fear a negative social response to their condition display label avoidance when they fail to receive diagnosis or treatment.

Although many people know someone affected by mental health disorders, they often fail to grasp how the condition influences the daily life of their family member, friend, or acquaintance. A study surveying the Dutch population conducted over the course of 21 years illustrates the negative effects of this lack of understanding, finding that the general desire for social distance from people with schizophrenia has increased significantly in the past two decades and has remained strong regarding those with clinical depression. This trend exists partially because the symptoms are not readily observable and are intrinsically linked to the patient’s personal thoughts, emotions and identity. As stated by Dr. Paul Summergrad, Psychiatrist-in-Chief at the Tufts University School of Medicine, mental illnesses are “irrespective of cause—the most intimate and personal of medical disorders, and challenge expectations for self-control and more traditional views of human nature.” How someone copes with their depression is an intimate affair linked to every aspect of their being, including the people around them and even the most trivial daily experiences. Thus, the variability of these mental conditions from case to case leads them to be considered more often as outstanding personal issues than dire medical concerns, a misunderstanding from which treatment suffers massively.

Adding to the hurdle presented by an adverse social climate, drawbacks to the available pharmaceuticals also create a dilemma. Society has begun to recognize the widespread danger of making powerful opiates readily obtainable for use as painkillers, and the class of drugs that treats a variety of mental conditions from anxiety to insomnia—benzodiazepines (BDZs)—is another imminent danger. This class of drugs, often referred to colloquially as “benzos,” includes names such as Xanax, Valium, and Klonopin. Benzodiazepines have been shown to work by changing the conformation of the γ-aminobutyric acid (GABA) type A receptor, which is the site showing affinity for the brain’s most prominent inhibitory neurotransmitter GABA. Their inhibitory activities slow brain func-
However, in spite of their popularity, BDZs often overstep their pharmacological boundaries. In fact, a news report from as early as 2004 explains that benzodiazepines were cut from Medicare benefits because they had extensive side effects, including drowsiness, depression, memory loss, confusion, and physical weakness. Especially when combined with alcohol or other medications, benzodiazepines have the potential to threaten lives, inducing serious cardiac and respiratory conditions. The drugs are also habit-forming, making it difficult or impossible to introduce alternative treatment. Given these undesirable effects, it is clear to see why many mental health patients would choose to deny being prescribed these substances, as they could easily compound existing chemical imbalances. Similarly, a brain weakened by depression or anxiety can be more susceptible to the addictive nature of the drugs, and addiction is a crippling mental illness in its own right.

Fortunately, pharmaceuticals are not the only option for treating mental health issues. The highly personal nature of these disorders makes interdisciplinary psychotherapy (IPT) a particularly serviceable option. A conglomerate of clinical psychology researchers has set out to prove its effectiveness through a meta-analysis of over 90 studies and thousands of individual cases. Taking cases from multiple nations, the researchers calculated the power of different treatment options using Hedges’ g, which is a measure of effectiveness. Results indicated that IPT was the most effective among different treatment options compared to a control group with a value of g = 0.60, surpassing other types of therapy (g = 0.06) and pharmaceuticals (g = -0.13). The effectiveness of IPT is heavily linked to the discussion of relevant personal experiences, so the treatment is directly targeting necessary emotions. Yet, seeing a therapist is costly and comes with an attached stigma, so clinical care remains a less-than-accessible solution for most mental health patients. Part of the issue is that mental health patients do not receive priority in clinical situations. Jane Zhu, a research fellow at Penn’s Perelman School of Medicine studying healthcare systems, recently released a groundbreaking study showing the deficiency of clinical care for patients with mental health disorders. Findings revealed that the number of available inpatient care beds has been steadily declining, down almost 400,000 from 1970, and that hospital patients for mental illness are subject to a stall-and-transfer rate six times higher than that of any other category of patients, postponing necessary treatment. The study also highlights that the disparity between care for mental and physical ailments cannot be explained by the differences in the nature of the conditions and the care they require. Thus, the implication is that significant improvements could be made to the processes for supplying needed treatment in healthcare management, most notably in hospital and emergency department situations.

While technology and medical techniques continue to evolve on a daily basis in today’s society, treatment for mental health continually lags due to a lack of prioritization. A poor social climate fostered by different forms of stigmatization and general lack of knowledge wrongly makes the cases appear less medically compelling. Available clinical treatment options lack accessibility, while pharmaceuticals, specifically benzodiazepines, have been shown to be significantly less effective despite their abundance and prevalence. Greater public education on the nature of mental illnesses is slowly spreading, eventually shifting clinical care efficiency. Paradigms in neuro-pharmaceutical research have shown potential avenues for safer, alternative treatment options that modulate the GABA type A receptor. Thus, there is potential for marked improvement in treatment for mental health, as well as adequate scientific capacity to achieve such a wide-reaching goal.

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French physicist and philosopher Blaise Pascal once said, “All men seek happiness. This is without exception. Whatever different means they employ, they all tend to this end.” Three hundred and 46 years later, his statement has not lost its relevance. Today, the field of positive psychology seeks to understand what it means to be happy, and how one can attain this state of subjective well-being. Through empirical investigation, positive psychology intends to identify, understand, and help individuals implement the mental processes that allow humans to live satisfactory lives. Martin Seligman, a University of Pennsylvania psychologist and the ‘father’ of positive psychology, defines positive psychology as “[a] science of positive subjective experience, positive individual traits, and positive institutions promises to improve quality of life and prevent the pathologies that arise when life is barren and meaningless.” Unlike most branches of psychology, positive psychology does not focus on understanding mental pathologies, but rather tries to shed light on what defines a happy person.

According to Seligman, psychology has three goals: “curing mental illness, making the lives of all people more productive and fulfilling, and identifying and nurturing high talent.” In the decades following World War II, treating and healing of mental diseases took over the academic spotlight due to its profitability. This disease-focused model turned psychology into a discipline devoted to healing which, as a consequence, made research on well-being and personal development less widespread. It was not until the 1960s, when humanistic psychology emerged as a response to psychoanalysis and behaviorism, that experts in the field ceased to consider the individual a “passive vessel responding to stimuli,” but rather “decision makers,” with choices and preferences. This change paved the way for the emergence of positive psychology. While the aims of positive psychology have their origins in classical philosophy and ancient Buddhist sutras, the field remains young with its first international conference held only in 2003.

Two concepts currently dominating positive psychology literature are flow and mindfulness. Flow is the phenomenon colloquially described as being ‘in the zone’. Distinguished Professor in psychology and Management at the Claremont Graduate University Mihaly Csikszentmihalyi was the first to use the term flow, and has dedicated his studies to the nature and effects of a
Mindfulness is a prominent buzz-term in mainstream culture that has its roots in philosophical and religious thought and has found its way into contemporary psychology. The Greater Good Science Center at UC Berkeley defines mindfulness as “maintaining a moment-by-moment awareness of our thoughts, feelings, bodily sensations, and surrounding environment.” Recent mindfulness studies have suggested that an active awareness of the present reduces stress and anxiety. In a study undertaken by Harvard University psychologists Matthew Killingsworth and Daniel Gilbert, volunteers reported mindfulness and happiness levels at regular intervals. Individuals reported mindlessness at least 30% of the time during any given activity other than sexual encounters. The study found consistent correlations between mindfulness and happiness; this suggests that subjective well-being experienced during any given activity correlates with an active concentration on the task.

Several advocates for positive psychology intend to bring their theoretical findings closer to the public. The “Authentic Happiness” initiative at the University of Pennsylvania, for instance, aims to “provide free resources where people can learn about positive psychology through readings, videos, research, opportunities, conferences, questionnaires with feedback and more.” With these tools, anyone can learn how to increase positive emotions and engagement in everyday activities. For example, the initiative suggests individuals to practice yoga, which can be considered a “very thoroughly planned flow activity. It [tries] to achieve a joyous, self-forgetful involvement through concentration, which in turn is made possible by a discipline of the body.” Another such initiative, the ‘World Well-Being Project’, based out of the Positive Psychology Center at Penn, promotes interdisciplinary collaboration to establish “scientific techniques for measuring psychological well-being and physical health based on the analysts of language in social media.” Data made accessible through social media usage can be useful in helping experts identify recurring pointers that can indicate possible physical and psychological malady. The ongoing research into subjective well-being combined with its practical application is known as positive intervention. It consists of approaches that seek to increase happiness and thus prevent or promote the rehabilitation from mental disorders. Anxiety and depression have been repeatedly proven to arise from self-reinforcing, undisputed, pessimistic thinking. Workshops such as ‘learned optimism’ training programs are meant to “teach both children and adults to recognize their own catastrophic thinking and to become skilled disputers.” Individuals that underwent this training were found to be more motivated, self-secure and engaged in daily life.

**CRITICISM**

Positive psychology’s unconventional research focus and methodologies are controversial in mainstream academia. In a 2000 American psychology Association panel entitled “The (overlooked) Virtues of Negativity,” Bowdoin College Research Professor of Psychology and Social Sciences Barbara Held pointed out the “tyranny of the positive attitude.” She warned about the separatism generated within psychology by overwhelmingly optimism-centered approaches as presented by positive psychology. According to Held, universal psychological theories should not neglect the importance of negative feelings for the human experience. She also argues that an entirely positivity-centered approach may impair or even prevent mental rehabilitation. “If people feel bad about life’s many difficulties and they cannot manage to transcend their pain no matter how hard they try [(to learn optimism), they could end up feeling even worse; they could feel guilty or defective for not having the right (positive) attitude, in addition to whatever was ailing them in the first place.”

Positive psychology has sparked the interest of researchers in neighboring fields. In Poland, Nicolaus Copernicus University Professor of Sociology Anna Pluskota is advocating for an approach to education that is inspired by positive psychology research. The increasingly fast-paced, competitive educational systems that exist in our globalized world are seen as one of the possible sources of the “depression epidemic” among young people. The application of positive psychology principles to education could allow schools to “become a place to enable young people to achieve large-scale development, and increase their personal resources and their mental well-being,” says Pluskota.

Positive psychology is far from discovering a happiness recipe. Yet, ongoing research continues to provide insights into how subjective well-being can be increased in everyday life. positive psychology is academia’s contribution towards bringing fulfillment closer to everyone.

**References**

The Neural Processing of Disgust and its Ramifications

BY JONATHAN ZOU

Emotions are often thought to be beyond mental control and characterized by a gut reaction. Interest in the neuroscience of emotions has increased due to the relatively recent introduction of functional magnetic resonance imaging (fMRI), which monitors blood oxygenation levels. While previous research in the field relied on other analysis methods, such as electrophysiological and lesion studies, these more recent fMRI results form the basis for neuroscientific models of emotion that guide research in the rapidly growing field.

Disgust is one of the most prominently featured emotions in research, possibly because it is more easily measured and recognized than other emotions. For example, comparisons of observations of emotional responses between disgusting odorants and other stimulant odorants demonstrated that olfactory and visual responses were stronger when feeling disgust than when feeling other emotions provoked by the stimuli. Likely having evolved from eating habits that protect organisms from ingesting unsafe foods, disgust has served an important role in the basic protection from infectious, inedible, or unsanitary events. Sensory systems have been found to contribute to the feeling of disgust, including those of gustation, olfaction, and interoception, the sense of the body’s physiological condition. The insula, a region of the brain in the cerebral cortex, integrates information from these multiple sensory modes and has been implicated in the neural processing of disgust.

The functional and anatomical relationships between experiencing, expressing, and recognizing disgust remained unclear for some time. In 2003, researchers found a bilateral or left-sided involvement of the insula in stroke patients with a deficit in disgust recognition. However, the specific insula regional correlation to disgust processing remained unclear. Despite the evidence for selective insular activation in disgust processing, other results suggested a less specific role, citing a similar nonspecific neural activation of fear. In a separate study, no specific deficit in disgust recognition was found in 15 consecutive cases of patients with selective resection of the insular cortex.

At this point in time in the field, it was clear that researchers did not agree on the extent and characteristics of regional specificity of disgust processing. In 2016, to thoroughly test for the selective role of the insula in facial disgust recognition, emotion recognition was studied in thirteen patients before, during, and after direct electrical stimulation of the insula. The researchers tested for the recognition of happiness, fear, anger and disgust. After electrical stimulation of the left insula, there was a statistically significant reduction in emotion recognition exclusively for the emotion of disgust. This substantiates the notion that the left insula has a selective role in the processing and recognition of disgust.

FMRI imaging measures the slight differences in magnetic properties of haemoglobin depending on the degree of oxygenation of the blood to determine regions of increased neuronal activity.
Disgust also has important social ramifications. An analysis of the neural basis of disgust perception in racial prejudice found that disgusted faces of races different from that of the viewer resulted in higher engagement of the amygdala and insula when compared to faces of the viewer’s own race. The study measured the implicit racial prejudice of participants by measuring their response time differences of the viewer’s own race or positive emotions with names of the viewer’s own race or unpleasant emotions with names of a foreigner) or “incompatible” (correlating unpleasant emotions with those of the viewer’s own race or positive emotions with names of a foreigner). Disgust sensitivity of the participants was determined through fMRI by measuring the level of neural activation when shown images of various faces either making neutral or disgusting expressions. Individual differences in disgust sensitivity were found to be predictive of implicit racial prejudice.⁹ Taken together, these results suggest a crucial role of insula-centered circuits in racial prejudice.

Furthermore, participants of a study on whether specific emotions would have an effect on the expression of the emotions themselves were exposed to a disgusting odorant and asked to evaluate their feelings towards a variety of social groups. Subjects’ views towards different individuals were then measured through a self-reporting scale ranging from 0 (cold) to 100 (warm). Results indicated that participants exhibited less warmth toward gay men after being exposed to a disgusting odorant than if they were not exposed to that odorant. This effect of inducing disgust was found to be equally strong irrespective of the subjects’ political ideologies.¹⁰ Accordingly, external stimuli that lead to disgust may play a role in the perceptions of social groups. The feeling of disgust, when induced by environmental stimuli, can lead to more negative views towards specific social groups and potentially heighten social tensions regarding sexual orientation.

Disgust thus acts as a medium through which the surroundings can influence social interactions. Since disgust has a role in shaping attitudes relevant to current societal issues, it is essential to better understand the neural processing of disgust and its effects on our behavior and perceptions.

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Thousands of people stare aimlessly at their phones before finally rolling over and falling asleep. However, increasingly more people have begun a very different pre-slumber ritual. Before laying down their devices to charge for the night, many people put in head-phones, log on to their favorite media streaming site, and watch ASMR videos. They become nearly entranced by the seemingly peculiar videos of people whispering to the camera, tapping on ordinary objects, and performing dull, quiet tasks. To an outsider of the ASMR world, this content seems eerily boring-- confusing, even. But for those in this subculture of the Internet, this media triggers a physiological response that remains a mystery largely unexplored by science.

ASMR is an acronym for Autonomous Sensory Meridian Response, and it refers to a phenomenon in which certain auditory and visual stimuli trigger a tingling sensation, precipitating a unique, nonsexual euphoria. The term was originally coined in a Facebook group created to unite people experiencing the colloquially described ‘head orgasms’ or ‘braingasms.’ Those that experience ASMR contend that it provides relief from depression, stress, and chronic pain as an alternative form of medicine. Because of the influx of ASMR media in recent years, a community of thousands has been established on the Internet, in which they discuss and relate to one another through their shared experience. In particular, YouTube has become the media source of choice because of the many ASMR channels that create videos specifically to trigger the response. ASMRtists, the name these media-makers have given themselves, have experienced a surge in popularity since 2014, with many of their channels attracting some millions of views per month.

ASMRtists create videos with different stimuli that are meant to trigger the sensation. According to a 2015 survey about those who view ASMR videos, 75% were triggered by whispering, 69% were triggered by personal attention, and more than 50% were triggered by slow movements, repetitive movements, and crisp sounds such as tapping and scratching of various surfaces. These sounds were then compared to sounds not typically associated with ASMR, such as laughing, vacuum cleaner noises, and airplane noises; less than 3% of those surveyed were triggered by these sounds. ASMRtists try several triggers and many experiment with unconventional materials and means of presenting their videos. For example, a genre of ASMR that has gained popularity is roleplay. The ASMRtist pretends to be a doctor, spa specialist, or even just a friend, and speaks directly to the camera as if speaking directly to the viewer, giving them the feeling of personal attention. Then, they perform various actions in front of the camera such as tapping a table, whispering into binaural microphones, which simulate whispering from ear to ear, or blowing into the air while making graceful hand movements.
Very little science backs ASMR, which is why it is so controversial. Many reject ASMR as a distinct phenomenon or speculate that it is a variation of previously studied sensations. Synesthesia, which is one of these phenomena, is a neurological sensation in which the stimulation of one sense leads to an involuntary experience in a second sense. Many have drawn comparisons between ASMR and auditory-tactile synesthesia, in which sounds induce sensations as if being touched.³ This is evident in the many videos that simulate brushing the viewer’s hair or giving them a massage. Another research article suggests that ASMR is a variation of the mind-body experience of frisson.⁶ Frisson is an intensely pleasurable reaction to music, and given the definition of ASMR, it is possible that ASMR is a “softer, quieter version of the same phenomenon.”⁹

A 2016 study by the University of Winnipeg sought to shed some light on ASMR. Researchers explored the resting-state function of the brains of those who have experienced ASMR. The default mode network, which is the brain’s resting-state network, consists of parts of the prefrontal cortex, parietal cortices, and cingulate gyrus, and the research suggests that it may function slightly differently in those that experience ASMR than in those who do not. In the study, the default mode network of eleven self-identified ASMR-experiencers was compared to that of eleven non-ASMR-experiencers through fMRI processing. The results showed that those with ASMR showed significantly less connectivity than that of their controls between the frontal lobes and sensory and attentional regions in the precuneus and parietal cortex. Reduced connectivity between these regions has been linked to reduced emotional inhibition in patients, so it is possible that ASMR reflects a reduced ability to suppress sensory-emotional experiences.¹⁰

Though this study presents interesting evidence and hypotheses, the validity of ASMR as a distinct medical phenomena remains unclear. The study found some evidence in favor of ASMR as a distinct condition, showing that most participants could dampen the intensity of their experience at their own will, which significantly distinguishes it from synesthesia. However, the study also shows that those experiencing ASMR have decreased connectivity of the thalamus, which is a significant feature of synesthesia.¹³ In fact, the aforementioned 2015 survey found that 5.9% of the subjects had experiences with synesthesia, which is a relatively high prevalence.¹² Additionally, the University of Winnipeg study emphasizes that the differences found between the default mode networks of the subjects and controls do not indicate that only certain individuals have the ability to experience ASMR, which backs the claim of many ASMRtists that anyone can experience it. Very few scientific studies have been performed regarding ASMR, so perhaps with a larger testing population and measures of brain activity before, during, and after ASMR media, science can confirm ASMR as a valid and distinct phenomenon.

With the little research on the subject, it is difficult to come to many definitive conclusions about ASMR’s burgeoning popularity and its effect on people. The research that has been done raises more questions than answers: Can anyone experience ASMR? What causes it? Is it even a real phenomenon? Science still cannot affirm its validity as a distinct sensation. However, to the ASMR community, it is a very real and meaningful part of their lives. Whether ASMR media serves to trigger a sensation, to help someone with anxiety, depression or any other condition, or simply to help someone fall asleep, its benefits as an alternative form of medicine are clear. ASMR may not be its own phenomenon but it surely has made its own place on the Internet.

References:
About 720,000 people in the United States suffer heart attacks each year, with cardiac arrest being the third leading cause of death in the U.S.\(^1\) According to the American Heart Association (AHA), over 80% of cardiac arrests occur in home settings.\(^2\) Nationally, less than 6% of people experiencing an out-of-hospital cardiac arrest (OHCA) survive. Many factors, such as local emergency provider protocol, determine local survival rates, but differences in rates of bystander CPR intervention cause wide disparities in patient survival rates across the nation. In many large cities, such as New York City and Chicago, OHCA survival rates are in the single digits, while in Seattle and overarching King County, over a fifth of OHCA victims survive (King County’s cardiac arrest survival rate is 62%, four times the national average). If the entire country adopted the policies of King County, where bystander CPR response rates are significantly higher, over 30,000 lives could be saved annually, according to one estimate.\(^3\) According to Dr. Benjamin Abella, director of the Center for Resuscitation Science and Vice Chair of Research of the Department of Emergency Medicine at the University of Pennsylvania’s Perelman School of Medicine, "Bystander CPR is probably the most important thing people can do to save lives. As physicians we often concentrate on medications and other sophisticated ways of saving lives, but in truth, all of that pales in comparison to bystander CPR."

As OHCA survival rates have remained stable for nearly 30 years, initiatives to increase bystander CPR intervention should be implemented in earnest.

**CPR AND BYSTANDER RESPONSE**

A wealth of research has shown that the time between the onset of cardiac arrest and the first chest compression during CPR is a key determinant of the probability of survival. The goal of CPR is to restore breathing and circulation, but if nothing is done, permanent brain damage is possible after just four minutes and very likely after 6 minutes.\(^1\) Similarly, the amount of time elapsed prior to defibrillation (delivery of electrical shocks to the heart to allow it to re-establish a normal rhythm) greatly affects patient outcomes 4-6. Since the time elapsed before care is very important, OHCA victims require a timely response from bystanders. One landmark meta-analysis found that survival rate doubles when OHCA is witnessed by a bystander and quadruples when the bystander performs CPR.\(^7\) Furthermore, numerous studies have shown that layperson CPR (usually compression-only CPR without assisted breathing) and defibrillation are greatly associated with increased patient survival compared to no bystander intervention.\(^2\)\(^8\)\(^-\)\(^10\) Although 53% of OHCAs are witnessed by bystanders, only 32% of these victims receive bystander CPR. Thus, increasing the amount of bystander intervention and public access to automatic external defibrillators (AEDs) is a top priority to increase OHCA survival rates. This includes encouraging CPR-certified laypersons to provide care and increasing public access to CPR training. According to the AHA, 70% of Americans feel helpless to act during a cardiac emergency because they either never learned CPR or their training had significantly lapsed.\(^1\) Another study found that annual rates of U.S. CPR training are low and vary widely across communities, with most areas in the single digits.\(^1\) Based on a survey of over 9,000 adults in one of his studies, Dr. Abella estimates the national rate of CPR training as 18%, a number he finds “really low.”

**FIXING THE PROBLEM**

There are many ways to increase layperson CPR training rates. Education departments can integrate CPR and AED training into graduation requirements, and cities can organize free community...
Telecommunicator CPR, in which 911 dispatchers provide CPR instructions by phone in real time (this is currently not available in most areas), can help increase bystander participation and CPR quality. Also, increased public availability to AEDs and smartphone apps showing where AEDs are located can help laypeople quickly locate a defibrillator. In telecommunicator CPR, if AED locations are registered with the appropriate emergency medical officials, 911 dispatchers can guide bystanders to the nearest AED. In some places, health departments are encouraging people to download smartphone apps that alert bystanders who can perform CPR whenever there is a cardiac arrest; these bystanders often arrive before emergency personnel can. Departments of health and education should partner with community groups, service providers, and professional organizations to promote public education and scalable training. For example, the Mobile CPR Project (another Dr. Abella project) travels to public places in Philadelphia to train people for free. It is supported by the city government, police department, fire department, and several hospitals – an inspirational community collaboration.

However, in order to replicate such initiatives, the disconnect between policy and research must be overcome. It is unclear which governmental body should take the lead – currently, no federal agency has cardiac arrest as a priority. The system is fragmented and it is up to local communities to implement their own solutions, hence the large disparities across counties. A national governmental organization must spearhead the fight against OHCA's with the same passion with which the government introduced the War on Cancer. Perhaps one day, an OHCA will no longer be a death sentence, but rather a medical emergency that entire communities can work together to help fight. But for now, we have a lot of work to do.

References:
The Guardian described the completion of the Human Genome Project (1990-2003) as “Biology’s Holy Grail.” The public and scientific community believed they had uncovered the blueprint—the biological programming—that generates genetic disorders and all the traits that make us who we are.

Naturally, the excitement shifted from characterizing the human genome to designing preventative and specialized care. As Paul Horn suggested 17 years ago, wouldn’t it be possible to predict your genetic disposition for certain disorders, and take steps to prevent them?

Fourteen years after the human genetic code was declared sequenced with 99.99% accuracy, we would expect to be able to control our environment and behavior, or even modify our own genetic makeup to change our hereditary destiny. These ambitions have applications in both disease prevention and genetic healthcare.

While burgeoning technologies exist, the Human Genome Project still hasn’t achieved the goals it was projected to complete, such as clinical genome sequencing and genetically-tailored doctor visits. Huge gaps in our expectations have yet to be filled. Understanding the challenges that genetics has faced explains not only why these expectations came to be but also helps us predict the future of the field.

Has the study of genetics hit a brick wall, or will the field break through into extraordinary achievements?

HIGH EXPECTATIONS

Perhaps some of the perceived “holes” that we currently see in genetics were due to excess enthusiasm that was not congruent with actual advancements in the field. Whether advancements in mapping, sequencing, and DNA replication before 1990 were enough to merit the scope of the Genome Project, the success of its mission to map the entire human genome, and its $3 billion public investment, is up to individual discretion.

As James Watson was the main source of enthusiasm for the Genome Project and genetics in general, we strive to understand his intentions for the field through the lens of his contributions and status in science.

In 1953, Watson worked alongside Francis Crick to create a model of DNA that both matched Rosalind Franklin’s x-ray crystallography data and explained all of its properties. Watson was offered a position at Harvard University in 1956 and a Nobel Prize in 1962. Modern Library named his autobiography the Double Helix one of the 100 Best Nonfiction Books of the 20th Century.

Watson was the world’s most popular geneticist, the head of the NIH, and the director of the Human Genome Project. It is no wonder why he might angle the NIH and the operations of many of the best laboratories in the world toward genetics, whether supported by hard evidence or not. Due to Watson, our inflated expectations for genetics may be partially responsible for the field’s shortcomings.

DISASTER STRIKES

The Human Genome Project did complete many individual scientific feats over its course. However, to understand the apparent shortcomings of the field, we must understand the medical challenges that genetics has faced.

In 1984, at the age of 3, Jesse Gelsinger was diagnosed with ornithine transcarbamylase (OTC) deficiency, a disorder where one’s genes do not have the complete sequence that codes for OTC, a necessary enzyme produced by the liver. The year 1994 marked a surge of articles that supposed that viral vectors could be used for gene therapy.

The idea was that if a person lacked a certain gene, a virus could infect the target cells and, like viruses do, implant its own DNA. If the virus carried the gene that the person lacked, the individual’s genetic code would effectively gain that gene. By 1999, viral vector therapy would come into fruition, and Gelsinger would be the first human trial. A long awaited 15 years after his first diagnosis, under the oversight of the University of Pennsylvania, his liver was injected with a crippled adenovirus that carried the gene necessary...
to produce the OTC enzyme, and the virus began to enter his cells.⁸

Two days later, Gelsinger was dead. According to a death report, the virus spread beyond Jesse’s liver to other organs, and his body reacted with an inflammatory response that brought his fever to 104.5 and put him in a coma. The ventilator could not oxygenate his blood via his fluid-filled lungs.⁹

The subsequent lawsuits (whose settlements totalled $517,496 from UPenn and $514,622 from Children’s National Medical Center in Washington, D.C) caused hesitation among the scientific community regarding gene therapy.⁹ Whereas the government had reviewed 331 gene-therapy trials by August of 1999,¹⁰ by the coming January, the FDA had cancelled all trials at the University of Pennsylvania and had begun investigations on 69 others.¹¹ There was great skepticism among scientists about the viability of gene manipulation as a medical technique, and some hesitation among medical doctors to put gene therapy into practice. It seemed as though the Gelsinger case was a death sentence for genetics. Would genetic medical therapies ever see the light of day?

**ADVANCEMENTS IN GENETIC TECHNOLOGY**

While the study of genetics has had a certainly tumultuous past, the pursuit of genetic technologies has been all but fruitless. There have certainly been major advancements resulting from research succeeding the Human Genome Project.

**FUTURE**

Despite the setbacks that genetics has faced, studying genetics has undoubtedly generated life-saving technologies, and expanded the frontier of human knowledge.

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**References**

You have just purchased health insurance for the first time from your state’s online health insurance exchange. Your timing was impeccable since you happened to come down with a nasty cold two days later. You call up your family doctor’s office, expecting to schedule an appointment within 48 hours or so, but you are shocked to find out that there are no openings for the next two months. This situation sounds unimaginable, given that primary care doctors typically don’t need more than a few minutes to diagnose and prescribe medication for a simple illness. Unfortunately, the reality of this situation is not too far off.

BY RYAN LEONE

OVERALL, IT IS CLEAR THAT MENTAL HEALTH IS AN ISSUE THAT MUST BE ADDRESSED TO PREVENT PHYSICIAN BURNOUT FROM TAKING PLACE AND TO REDUCE THE NUMBER OF MEDICAL STUDENTS OR PHYSICIANS WHO SUFFER FROM MENTAL ILLNESSES

On the opposite end of the age spectrum, the millennial generation is altering healthcare in a variety of ways. With 15% of physicians being under the age of 35, the issues facing millennial doctors are increasingly relevant to the healthcare field. These include the findings that over 50% of physicians reported at least one symptom of burnout. This also corresponded with an 8% decrease in satisfaction with work-life balance amongst physicians across the country. Additionally, the rate of physician suicide is noticeably higher than the rate in the general population. In fact, the yearly rate averages to one physician suicide per day. The measured increase in stress levels and mental health issues in medical students is seen as a product of medical school training since the students typically enter school with stress levels similar to their peers in other fields.

OVERALL, IT IS CLEAR THAT MENTAL HEALTH IS AN ISSUE THAT MUST BE ADDRESSED TO PREVENT PHYSICIAN BURNOUT FROM TAKING PLACE AND TO REDUCE THE NUMBER OF MEDICAL STUDENTS OR PHYSICIANS WHO SUFFER FROM MENTAL ILLNESSES

The factors contributing to this shortage are varied and somewhat disparate. For example, one pressure faced by the physician workforce is the aging population of patients. As the elderly demographic gets larger and larger, the many chronic conditions and patient cases they bring with them increase, but it is clear that they are not always receiving proper care for their maladies. One study showed that many elderly patients who were formally diagnosed with having a “lack of community support” were actually suffering from true, tangible illnesses. In addition to the fact that elderly patients require greater amounts of medical attention, the increasing life expectancy of Americans means that they will live longer than members of previous generations and require care for a longer period of time.

Similarly, the inexorable aging of patients is paralleled by the aging of physicians who care for them. The growing number of physicians who are nearing or surpassing retirement age in recent decades means that there will be a significant decrease in the population of physicians over a short span of time when they retire in the near future. There are further concerns that those physicians who choose to stay in practice during their “golden years” might not be in the right mindset to practice. It may be necessary to evaluate the competency of these elderly physicians to ensure that they are able to provide proper medical attention to patients, with whom they may be facing the same health issues. If some physicians do not pass an established set of competency standards, the workforce size will continue to decrease even further.

On the opposite end of the age spectrum, the millennial generation is altering healthcare in a variety of ways. With 15% of physicians being under the age of 35, the issues facing millennial doctors are increasingly relevant to the healthcare field. These include the findings that over 50% of physicians reported at least one symptom of burnout. This also corresponded with an 8% decrease in satisfaction with work-life balance amongst physicians across the country. Additionally, the rate of physician suicide is noticeably higher than the rate in the general population. In fact, the yearly rate averages to one physician suicide per day. The measured increase in stress levels and mental health issues in medical students is seen as a product of medical school training since the students typically enter school with stress levels similar to their peers in other fields. Overall, it is clear that poor mental health is an issue that must be addressed to prevent physician burnout and to reduce the number of medical students or physicians who suffer from debilitating and life-threatening mental illnesses.

UPSTREAM, WITHOUT A DOCTOR

Picture this:
You have just purchased health insurance for the first time from your state’s online health insurance exchange. Your timing was impeccable since you happened to come down with a nasty cold two days later. You call up your family doctor’s office, expecting to schedule an appointment within 48 hours or so, but you are shocked to find out that there are no openings for the next two months. This situation sounds unimaginable, given that primary care doctors typically don’t need more than a few minutes to diagnose and prescribe medication for a simple illness. Unfortunately, the reality of this situation is not too far off.

PHYSICIAN SHORTAGE OF UP TO...

31,100 PRIMARY CARE DOCTORS

63,700 NON-PRIMARY CARE DOCTORS

...IS PREDICTED IN THE NEXT DECADE

Medical care is often taken for granted by insured individuals, but what happens when the patient population becomes too dense for the limited amount of doctors to support them? The answer to that question is unfortunately unfolding before our eyes; a physician shortage of up to 31,100 primary care and 63,700 non-primary care doctors is predicted in the coming decade. This shortage has the potential to increase wait times dramatically and reduce the number of individuals who have access to care at any given time.

The factors contributing to this shortage are varied and somewhat disparate. For example, one pressure faced by the physician workforce is the aging population of patients. As the elderly demographic gets larger and larger, the many chronic conditions and patient cases they bring with them increase, but it is clear that they are not always receiving proper care for their maladies. One study showed that many elderly patients who were formally diagnosed with having a “lack of community support” were actually suffering from true, tangible illnesses. In addition to the fact that elderly patients require greater amounts of medical attention, the increasing life expectancy of Americans means that they will live longer than members of previous generations and require care for a longer period of time.

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On the opposite end of the age spectrum, the millennial generation is altering healthcare in a variety of ways. With 15% of physicians being under the age of 35, the issues facing millennial doctors are increasingly relevant to the healthcare field. These include the findings that over 50% of physicians reported at least one symptom of burnout. This also corresponded with an 8% decrease in satisfaction with work-life balance amongst physicians across the country. Additionally, the rate of physician suicide is noticeably higher than the rate in the general population. In fact, the yearly rate averages to one physician suicide per day. The measured increase in stress levels and mental health issues in medical students is seen as a product of medical school training since the students typically enter school with stress levels similar to their peers in other fields. Overall, it is clear that poor mental health is an issue that must be addressed to prevent physician burnout and to reduce the number of medical students or physicians who suffer from debilitating and life-threatening mental illnesses.
On the patient side, it is clear that the Affordable Care Act’s focus on increasing access to healthcare has resulted in more previously uninsured individuals obtaining insurance. The growing insured population will consequently be able to see doctors more often and the principle of moral hazard - a term describing the tendency of insured individuals to be more careless about using medical resources - dictates that they are likely to use even more healthcare resources than before. Given that they will not have to pay in full or at all for their healthcare, insured patients are likely to worry less about their behavior since they view insurance as a safety net.

This wide variety of causes leads to a complex dilemma with a potentially simple solution - medical schools should stop rejecting so many applicants and increase the class sizes to produce more doctors in the long run. Only 21,643 of the 52,536 applicants to medical school in the 2015-2016 application cycle were accepted; this means that 58.81% of medical school applicants were rejected this past year, so a lack of aspiring doctors is certainly not the problem. Accepting more students to medical school and waiting for them to become doctors sounds like a reasonable solution, right?

In reality, this situation merely increases the number of indebted graduates who cannot make it through the bottleneck process that limits the amount of spots in residency, a training period that is necessary for medical school graduates to become certified practitioners.

A Congressional bill called The Resident Physician Shortage Reduction Act of 2015 is focused on increasing residency slots, but our current political gridlock does not bode well for the timely passage of this bill. If it were passed, the bill would create another 15,000 residency spots across a 5-year period of time, so it is imperative that the bill be put at the forefront of Congressional voting decisions. Coupling these political complications with the increasing concerns about physician and medical student mental health, we see an occupation that faces many obstacles in the coming decade.

The lack of primary care physicians is being addressed systematically by components of the Affordable Care Act. The Obama administration has approved measures to alleviate the shortage. For instance, it has taken steps toward increasing investment in primary care training programs in hospital and community clinics, expanding mental and behavioral health training, strengthening the National Service Health Corps, and providing monetary incentives for individuals who enter primary care fields.

Another alternative could be increasing the responsibilities of nurse practitioners and physician’s assistants. If laws were passed in each state that give nurse practitioners the freedom to write prescriptions and practice independently, the need for extensively trained physicians to spend their time dealing with less intensive patient cases could be reduced. Physician’s assistants could also help alleviate the burden on doctors by working with patients who do not need prescriptions or complex procedures.

Furthermore, employing medical scribes could help doctors increase the amount of time they spend seeing patients by reducing the amount of time doctors spend completing documentation. Scribes record the information that is released during patient-physician conversations, saving it for use by the physician at another time and opening the physician up to see more patients every day. These changes might not make significant impacts on their own, but collectively, they could prevent this shortage from worsening over the next several decades.

While the physician shortage is an inevitable shortcoming of the American healthcare system, support for the aforementioned initiatives and cooperation between providers, insurers, and patients can optimize our limited resources to reduce the burden of illness faced by Americans.

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On March 14, 2016, the American Board of Medical Specialties approved certification for yet another new subspecialty: addiction medicine. The novel specialty aims to prevent, screen, intervene, and treat substance use and the corresponding physical and psychological complications coming from addiction. However, following its creation, several have questioned its use. Only 10% of the American population requires attention for drug abuse, and there is already certification for addiction psychiatry from the American Board of Psychiatry and Neurology.1 Additionally, critics feel that general practitioners have the knowledge and tools to treat such cases and feel that a separate physician focused on these cases is not required.2

The above example highlights the general trend within medicine of increased specialization and subspecialization that many are worried will fragment our already fractured system of patient care. By adding so many different types of specialties and subspecialties to our healthcare system without a reliable system of organization and communication between physicians, patient care will become uncoordinated, with an excess number of physicians dedicated to each clinical case and a surfeit of procedures performed by these different specialists. From the physician’s perspective, this trend will force doctors to have a much more narrow and limited focus within their fields, and it will also influence how the next generation of doctors will be evaluated and labeled. And the hospitals and healthcare networks housing the physicians will be forced to dedicate more funds towards hiring these various specialists, which can be financially challenging with the large salaries some specialists command. Hospitals which cannot afford large numbers of specialists will lose their ability to provide comprehensive care.

The increased specialization of our healthcare providers has led to an increased level of disorder and incoordination within the healthcare system. Currently, there are over 120 medical specialties and subspecialties reported by the American Board of Medical Specialties (ABMS), and it continues to receive requests for several new subspecialties, including medical informatics, clinical pharmacology, vascular medicine, and obesity medicine.4 With so many different specialists available, physicians increasingly rely on referrals, with referral rates in the past decade doubling from 5% to 9%, and the care of each patient has become increasingly distributed over too many physicians.1 Communication among these several doctors for a single clinical case is difficult to maintain and thus has not always been executed adequately. This slew of specialists with little coordination has led to an excess of medical procedures, diagnostic tests, and medical expenses. In fact, from 1940, when there was little specialization, to 1975, when various medical boards for Oph-
thalmology, Psychiatry, and others began to be founded, medical expenses increased from $3 billion to $75 billion. Unfortunately, this excess has not always benefitted patients.

Already, there have been a number of observations by several noted physicians on the negative consequences of such a trend. In "One Patient, Too Many Doctors: The Terrible Expense of Overspecialization," Dr. Sandeep Jauhar describes how his 50-year-old patient had a month long stay at the hospital for shortness of breath. During this time, he was treated by a hematologist, an endocrinologist, a kidney specialist, two cardiologists, a cardiac electrophysiologist, an infectious-disease specialist, a pulmonologist, an otolaryngologist, a urologist, a gastroenterologist, a neurologist, a general surgeon, a thoracic surgeon, and a pain specialist. He left the hospital having undergone 12 procedures. The net result was only minimal improvement in his condition, a bill to his insurance company for upwards of $100,000, and scheduled follow-up visits from seven specialists. Needless to say, the system failed the patient in this case.

The trend has also had a significant impact on the medical profession itself. Physicians within broad specialties such as gastroenterology and radiology are being forced to limit their focus even further to one specific organ or clinical technology, becoming what are called “subspecialists.” For instance, radiologists are increasingly pressured to become further specialized into interventional radiology, endovascular surgical neuroradiology, musculoskeletal radiology, etc.

The rise of subspecialists have caused many to question how we should evaluate and label the upcoming generation of physicians. If a radiologist chooses only to focus on musculoskeletal cases and does not maintain his knowledge and skill in other areas of radiology, can he still be considered a radiologist? If required, such as in an emergency situation, will he still be able to perform echocardiograms or embolizations?

Increased specialization is also making it increasingly difficult for hospitals and healthcare facilities to maintain their ability to provide comprehensive care. Hospitals will be stressed to allocate more funds towards hiring a variety of different physicians, which can prove to be an expensive endeavor. A endovascular neuroradiologist alone can make up to around $336,000. Even with funding for their salaries, many specialists or subspecialists may not be readily available for hire considering limited fellowship or training positions available, significant investments in time and money to train the physicians, and the fact that most subspecialists currently decide to stay near an academic center or large referral center in big cities to maintain a sufficient number of patients for their niche skills. The hospitals unable to hire specific specialists or subspecialists will lose their expertise in those fields and will not be able to provide complete care to their patients. Rural healthcare facilities, which already have a shortage of primary care physicians (typically only 68 internists per 100,000 residents) will have a significant challenge in acquiring the services of various specialists and subspecialists, and this unequal distribution of advanced, modern medical expertise favoring big cities will only worsen rural healthcare inequalities.

The environment of modern healthcare is changing and doctors are becoming more trained and specialized than any other time in history. Unfortunately, this is leading to a lack of coordination within our healthcare system, doctors too limited in their expertise, and hospitals unable to provide inclusive service to patients. How can we rectify the situation? One possible measure, proposed by the Affordable Care Act, includes developing “accountable care organizations,” where teams of physicians would be paid according to their patients’ clinical outcomes. This would force teams of specialists and subspecialists with specific expertise to coordinate and formulate a general health care plan to improve the overall outcome of the patient. As for the inability of hospitals to provide comprehensive care, there have been plans proposed to have several local hospitals organized under a local healthcare network. This network would then include a central hospital nearby housing all the various specialists and subspecialists. The local hospitals would refer all complex clinical cases requiring further expertise to this select, nearby hospital for further care. Both solutions offer a potential solution to exploit the fact modern day doctors are more highly trained and focused while solving the associated waste, disinorganization, and overload associated with overspecialization.

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It seems like no matter what we try, obesity rates continue to rise. Why does this happen if we are constantly being told what is healthy and what is not? Fad diets targeting fat and carbohydrates promise to make us skinny, healthy, and happy. But there is one product that has unfairly avoided the stigma of being an unhealthy food: sugar. This is largely due to a research study sponsored by the Sugar Research Foundation.

FROM RARE BOOST TO RISK FACTOR

Today, sugar is in almost everything on grocery store shelves, but sugar was not always so abundant. For a long time, sugar was not accessible to our ancestors.¹ Besides honey, hunter gatherers often did not consume anything sweeter than a carrot.² Even fruit, containing natural sugars, was smaller than the fruit grown today. Long ago, a human’s “sweet tooth” was extremely advantageous. When food was scarce, our ancestors could quickly convert the sugar into fat. As time went on and food sources were more reliable, the human craving for sweet food became less beneficial. 10,000 years ago in New Guinea people chewed the stems of sugarcane. In 500 A.D., processed sugar was used in India to treat ailments. By 1700, the average Englishman consumed four pounds of sugar annually and by 1800 consumed eighteen pounds annually. In 2013, the average American consumed 77 pounds annually.³ As of 2016, the American Heart Association recommends that men should have no more than 36 grams of sugar and women and children should have no more than 24 grams of sugar daily.⁴ The excess sugar eaten today is likely to lead to bigger problems later.

Sugar’s effects on and links to health have been realized for quite some time. In 1675, Thomas Wills, an English physician, discovered that the urine of people with diabetes mellitus tasted sweet. At Columbia University, Haven Emerson recognized a link between the rise in sugar consumption and the rise in deaths caused by diabetes from 1900-1920.³ Overconsumption of sugar can cause many health problems such as high blood pressure, high cholesterol and increased abdominal fat.⁵ Additionally, high sugar consumption increases risk for coronary heart disease and non-alcoholic fatty liver diseases.⁶ If sugar can be so detrimental to health, why are people generally more concerned with their consumption of fats and carbohydrates?

INDUSTRY INFLUENCE

By the 1950s, high mortality rates from coronary heart disease in American men prompted investigations to discover the cause. In the 1960s, two prominent physiologists came to conflicting conclusions: John Yudkin blamed sugar while Ancel Keys blamed only fat and cholesterol. It would be advantageous to the Sugar Industry if fat was the sole culprit. On July 11, 1965, the New York Herald Tribune released an article stating that new research reaffirmed the case that having a diet high in sugar increases one’s risk of a heart attack. On July 13, 1965, the Sugar Research Foundation approved project 266, a review on carbohydrates and cholesterol metabolism, hoping to deemphasize sugar’s negative health effects. The Sugar Industry paid an equivalent of $48,000 2016 dollars to Hegsted, a professor of nutrition, and Robert McGandy, a nutritionist, to conduct this review. On July 30, 1965, Hegsted received information from the Vice President of the Sugar Research Foundation regarding the goal of the review stating:

“Our particular interest had to do with that part of nutrition in which there are claims that carbohydrates in the form of sucrose make an inordinate contribution to the metabolic condition, hitherto ascribed to aberrations called fat metabolism. I will be disappointed if this aspect is drowned out in a cascade of review and general interpretation.”

In 1967 the review was published, concluding that “the only dietary intervention required to prevent CHD [Coronary Heart Disease] was to reduce dietary cholesterol and substitute polyunsaturated
fat for the fat in the American Diet.” Conveniently, there was no mention of the sugar industry’s influence and role on the project. The study had a lasting effect on how Americans were advised to eat. In 1980, government guidelines prompted Americans to “avoid too much fat, saturated fat, and cholesterol.” However, the guidelines failed to warn Americans about the possible implications of sugar consumption. For example, the guidelines stated that “the major health hazard of eating too much sugar is tooth decay,” and the illusion of a lower total content. In reality, agave nectar, brown sugar, cane crystals, dextrose, fructose, fruit juice concentrates, and maltose are all sugars and should be considered when calculating total sugar content. With so much to think about when looking at the nutrition facts of processed food, consumers should be aware that the whole is more than the sum of its parts. Just because a product has an appealing label does not mean it is a good choice.

Human consumption of sugar over time is a sticky situation. Long ago, eating sweets was a quick fix for a lack of energy. But in current times our bodies neither need the quick fix nor are well equipped for it. This is evident through the many disastrous health effects excess sugar can have on our bodies. Since sugar’s impact on health was brushed away in the 1960s and clever marketing strategies to push high sugar products still exist today, consumers need to be aware of what lies behind the label.

References
IS THE PHARMACEUTICAL INDUSTRY ON YOUR SIDE?

BY EVANIE ANGLADE

The pharmaceutical industry has played an increasingly pivotal role in the lives of many. Last year, 4,065,175,064 retail prescription drugs were filled at pharmacies in the US, and from 1999 to 2012, the overall use of prescription drugs among US adults has increased 51% to 59%.1,2 Both a blessing and an affliction, this industry provides the public with the medication necessary to get and stay healthy, but it has a tendency to financially swindle its consumers. Many who are unaware of the less ethical aspects of the industry are quick to praise how far it’s come. While these companies provide remedies to treat or cure an illness or relieve suffering in some capacity, the indiscretions of the pharmaceutical industry make us wonder if it is truly on our side.

THE GOOD

Pharmaceutical companies can be viewed positively for the treatment and relief they provide to the public. By virtue of the rising pharmaceutical industry, the average life expectancy has risen from 45 to 77 years over the course of a century.3 The World Health Organization (WHO) has compiled a list of 325 essential drugs, most of which are available in bulk generic forms provided by low-cost suppliers.4 Essentially, people have access to the necessary drugs to treat or cure their illnesses. For example, as of now, about 1.6 million Americans live with Crohn’s disease, a chronic inflammatory bowel disease that affects the gastrointestinal tract.5 However, Humira, a tumor necrosis factor (TNF) inhibitor that targets and blocks sources of inflammation, is a popular AbbVie drug that has treated many suffering from Crohn’s.6

THE BAD

In another respect, pharmaceutical companies can be viewed through a more condemning lens because some of them take financial advantage of their consumers. The transgressions of the industry partially derive from socioeconomic disparities evident in society. If everyone were able to afford the medications provided by the pharmaceutical industry, these wrongdoings would not be considered as egregious. The misdeeds of the pharmaceutical industry most negatively affect those who struggle to pay for medical care—members of the lower and middle class. Although the high cost of drugs seems appropriate because R&D for some drugs can be incredibly expensive, some do not believe the pharmaceutical industry is justified in price hikes on patients. Price hikes on those who can afford it, such as health insurance providers enriched by Obamacare, are more appropriate.10 Take Turing Pharmaceuticals for example; this company has hiked prices on commercial insurance providers to fund R&D for drugs correcting Toxoplasmosis.11

THE MISDEEDS OF THE PHARMACEUTICAL INDUSTRY MOST NEGATIVELY AFFECT THOSE WHO STRUGGLE TO PAY FOR MEDICAL CARE—MEMBERS OF THE LOWER AND MIDDLE CLASS.

Furthermore, the pharmaceutical industry has been known to decrease healthcare expenditures. Breakthrough therapies have reduced medical costs in the long run, thus less money is spent on overall healthcare. For example, in the 1990s, pharmaceutical spending rose 5.5% to 8.5%, while hospital expenditures decreased 37% to 33%. This trend is still observed today.7,8

Additionally, some believe the pharmaceutical industry is deserving of sympathy and thus seemingly absolved of its transgressions. Pharmaceutical companies are under great fiscal duress because of political pressure; governments increasingly scrutinize drug costs in hopes of containing them and the general cost of healthcare. Government intervention and regulation of drug prices negatively affects the pharmaceutical industry in that it has “lower revenue growth, poor stock performance, the lowest number of new chemical entities (NCE) approvals and the poor late-stage R&D pipelines prevalent throughout the industry”.3

Currently, the average price to earnings ratio of large pharmaceutical stocks is trading at a discounted rate relative to the entire market.3 Back in July of 2015, the health sector began declining and is now down 4%. Since July of 2015, Standard & Poor’s (S&P) Pharmaceuticals Select index has fallen 38%.9

The high cost of drugs is often justified because an entire industry's worth depends on the price of its products. In July 2015, Turing Pharmaceuticals hiked the price of the essential drug Mylan to $75,000, a drug that previously sold for $475.12

One way in which consumers are taken advantage of is through generic-drug monopolies. Pharmaceutical companies make a majority of their money from recently made drugs that fall under a patent. Twenty years after a patent is originally filed, other drug companies can begin making their own generic versions of the drug. However, sometimes if there is not a high demand for the drug, generic-drug companies will not invest in making a cheaper, generic version of the drug.
drug. Therefore, the brand-name drug companies will have a simple price monopoly. Between 2013 and 2015, prices of Daraprim, Doxycycline, Isuprel and Nitropress have increased exponentially (Daraprim from $13.50 to $750, Doxycycline from $20 to $1,849, Isuprel from $215.46 to $1,346.62 and Nitropress from $257.80 to $805.61). And to protect their exclusivity and monopoly, these brand-name drug companies will “evergreen” their product by constantly adding new patents for minor, ineffectual variations made to the drug, such as changing the coating, crystalline form, manufacturing process or delivery system.

Furthermore, pharmaceutical companies can be looked upon negatively due to chronic deception present within the industry. Some drug companies have been known to be disease-mongers who promote their product to healthy people who may believe they are sick. Disease mongering occurs when ordinary ailments are transformed into medical problems (e.g. baldness), mild symptoms are seen as forewarnings for serious diseases (e.g. irritable bowel syndrome), personal problems are treated as medical ones (e.g. social phobia), risks are denoted as disease (e.g. osteoporosis) and disease prevalence estimates are framed to maximize fear of medical problems (e.g. erectile dysfunction). Often times, pharmaceutical companies, doctors and patient groups ally themselves and use media to disease monger. The boundaries of what qualifies as a treatable illness have been extended to widen the market for new products, making healthy people amenable to fraudulent claims.

The deceptive nature of pharmaceutical companies is also demonstrated through the bias present in clinical research. Studies have shown that research funded by companies is more likely to yield positive outcomes in clinical trials than research funded by other, less biased types of sponsorship, such as governmental organizations. The bias in clinical research is introduced through comparisons (i.e. similar drugs used to make the marketed drug seem more effective), disproportion between publication of positive trials and non-publication of negative trials, reinterpreting data submitted to regulatory agencies, dissonance between results and conclusions, conflict-of-interests, ghostwriting (i.e. recruited writers writing with a favorable “spin”) and “seeding” trials (i.e. studies done after the drug is already on the market). Such findings bolster the distrust the public may have in the pharmaceutical industry.

**INTERVENTION**

Changes have been made and must continue to be made in the pharmaceutical industry to combat its ability to financially con and deceive its consumers. The federal government has intervened in pricing to achieve consistency of retail prices of the same drug across the country in order to guarantee affordability and equitable access. However, this process is not perfect for a variety of reasons, one being high pharmaceutical expenditures. Measures to control drug expenditures include promotion of rational drug use, use of generic names, and simple capping of expenditures. Additionally, financially reasonable access to pharmaceuticals can be improved through various financing methods like expansion of insurance coverage.

Despite its medical aid to society, the pharmaceutical industry is corrupt in ways that recant its positive, valuable assets. Transparency is what will help affirm or reaffirm the public’s trust in this industry.

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Do students from low-income backgrounds still lack access to a secure food source during college?

BY KAMALJOT GILL

College is a place to gain new friends, knowledge, and passions. What most students do not hope to gain is the “freshman 15,” a phrase notoriously used to describe the amount of weight most students put on after their first year of college. While studies have shown that the weight gain is closer to 7-10 pounds, this is still a significant amount when placed in context with the age of students. Weight gain during the late teens and early twenties have been correlated with higher rates of obesity in later ages, and so while college provides an environment for learning, it should also instill healthy eating habits in students.

WHY FRESHMAN 15

A great deal of research has been conducted on understanding the causes and consequences of the freshman 15. A professor at Cornell University, Dr. David Levitsky, has researched the root causes of the freshman 15, and connected them to ‘all-you-can-eat’ college dining halls. Student questionnaires reveal that students ate more in these types of dining halls and left with a greater sense of fullness. It is important to note that both adults and students consume food that is proportional to the amount that they are served; thus, part of the reason for overconsumption and increased calorie intake is due to the concept of college dining halls. While decreased physical activity and altered sleep patterns affect eating habits, the consumption of junk food, meal frequency, and proportion of meal size are considerably more significant indicators of weight gain in the first year of college. Research from Dr. Christakis and Fowler of Harvard Medical School point out that obesity and weight gain in all age groups are influenced by the appearance and behaviors of those surrounding them. Their study also found that an individual’s risk of becoming obese increases by an alarming 57 percent if he or she has a friend who is gaining weight within that time period.

TIES TO INCOME LEVEL

To frame this discussion before we begin, it must be stated that households closer to or below the poverty line are more likely to house overweight and obese individuals. The trend is the same — if not stronger — for families with lower levels of education. Families that are less educated are more likely to score lower on the Healthy Eating Index (HEI), a 100-point scale developed by the USDA to measure the quality of the total diet. This correlation of low socioeconomic status relating to poorer health has been established by researchers in both the late 20th century and the early 21st century in several nations such as Canada, France, and the UK.

A WORK-STUDY STUDENT WHO WORKS MINIMUM WAGE TEN HOURS A WEEK WILL LOSE AT LEAST A HALF OF THEIR WORK STUDY MONEY ON FOOD.

For many students, transitioning to college is a major step. It entails the student getting used to a new set of academic standards, moving away from parents, and having to learn how to live on their own. Low-income college students go through the same experience, but without the added benefit of having financial consistency to rely on.

CLOSER TO HOME

Taking a deeper look into the experience of college students in the United States, specifically at the University of Pennsylvania, one notices differences within the student body. Students who are First-Generation and/or Low-Income (FGLI) often have different stories to tell of their eating habits than those from more privileged backgrounds.
Freshmen meal plans at the University of Pennsylvania are meant to provide easy access to dining halls for the entire academic year. One recommended dining plan is Best Food Fit meal plan (BFF), which offers around eight meal swipes a week and $500 to last approximately 110 days. This equates to $4.50 that can be spent on food per day in addition to the included meal swipes. Buying food outside the dining plan may not be an issue for higher-income students; however, for low-income students, it is quite costly. Spending just $10 a day on food can quickly add up to over $1000 a semester. For a student whose family income is under the poverty line, this is a huge expense. To put this into context, a work-study student working 10 hours a week at minimum wage will lose at least half of their earned money on food. Comparatively, the average moderate cost of food for an individual between the ages of 19-50 is only $305.60 a month, which is lower than the $500-a-month at Penn if the meal plan is considered. Besides the cost of food, access to dining halls throughout the week also raises concern in low-income students. During weekdays, dining halls are closed between 2pm and 5pm and after midnight. On the weekends, the dining halls are open only from 11am to 3pm and 5pm to 8pm. Students on work-study may find it difficult to fit in meals if they eat late lunches or dinners.

To assess the impact of cost and accessibility on campus, a dozen Questbridge Scholars – students from low-income backgrounds who received admission to Penn under a full-ride contract – were interviewed and asked about their experiences on the meal plan. Often times work-study students and Questbridge scholars reported that the meal plans generally did not cover all their meals during the week. They found themselves eating bigger portions at each meal if they anticipated not being able to eat again later in the day. Even more concerning is the practice of these unhealthy habits of skipping meals and binge-eating at an early age. Katherine Tallmadge, dietician and author of Skipping Meals but Bingeing Later: Workaholics Need to Plan for Regular Meals EATING RIGHT, reports that skipping meals or eating in an unplanned fashion throughout the day is a frequent occurrence that significantly contributes to weight problems. This reason is often overlooked when it comes to understanding the freshman 15 in FGLI students. Students from more prosperous backgrounds are able to afford outside meals. At an institution like Penn, where 52 percent of the students pay full-tuition of $51,464, being a low-income student is not common. While Penn’s financial aid covers the cost of meals, the meal plans may be inadequate for lower-income students who rely on it the most.

The student interviews at the University of Pennsylvania reveal that meal plans show unique eating patterns in first-generation and/or low-income students. The irregular eating habits and guilt of spending money on food while on a meal plan that costs upwards of $5000 contributes to the unhealthy consumption of food in college. It comes as no surprise that these eating patterns have been correlated with the freshman 15 in college and obesity later in life. While it is easy to give freshmen advice about avoiding weight gain in their transition to college lifestyle, the problem may be deeply rooted in the availability, cost, and access to food through the meal plans.

Gaining weight in college is not inevitable. First-generation and low-income students have additional pressures of having work schedules and lack of resources to purchase meals outside of their meal plans, which can cause them to exhibit unhealthy eating behavior. Even in college, foundational aspects of the system in place can make it harder for low-income students to receive nutritious meals. Thus the freshman 15 belies deeper insight into why some freshmen may be struggling more than others in their transition to college.

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Euthanasia, which literally means ‘good death’, was first used by the historian Suetonius to describe the Roman Emperor Augustus’ demise. He succumbed to his illness in the arms of his wife, as he had desired. However, as medicine progressed, euthanasia began to morph into something completely different. It transformed into what euthanasia is now – intentionally ending a life with the purpose of relieving pain and suffering. In practice, medical documents signed by patients give the doctor authority to perform euthanasia while in other cases the patients may make the decision themselves. This concept of euthanasia has given rise to a debate between those who are “pro-life”, and those who are “pro-choice”. Each side has its own views on the right to end a life, similar to the debate on abortion. Both of these issues are grounded on a mixture of people’s socio-cultural, ethical, economic and political views. However, euthanasia specifically focuses on the complex reality of deciding when life is no longer worth living.

A number of social factors come into play when considering the choice of euthanasia. In many cases, terminally ill patients become physically and financially dependent on their families. The patients may want to undergo euthanasia to overcome the lack of dependence they feel, and to relieve the family of the burden of taking care of a dependent, which could affect the family dynamic. In addition, some supporters of euthanasia believe that its legalization frees humans from the belief that there is dignity in suffering. It lets people exercise their autonomy, even at their deathbeds. This is because ultimately, the decision of whether it is worth suffering through the pain of an illness rather than undergoing euthanasia is highly subjective, as one can see through the stories of Brittany Maynard and J. J. Hanson.

Brittany Maynard, who had terminal brain cancer, made headlines when she moved from California to Oregon so she could legally take life-ending drugs. The pro-choice movement progressed as she helped remove part of the social stigma that surrounds euthanasia. Maynard’s husband continues to fight for euthanasia legalization after her death and her mother wrote a memoir, Wild and Precious Life, to document her experience throughout her daughter’s illness. However, there are some movements that work to discourage individuals from choosing euthanasia, including one lead by former marine, J. J Hanson. In 2014, J. J. Hanson, was diagnosed with glioblastoma- the same aggressive brain cancer that Maynard had. Euthanasia was not legal in the state where he lived, so Hanson fought a desperate battle against his disease. He enrolled in a clinical trial, which eventually turned out to be successful. Hanson claims that if he had lethal drugs within reach when he was at his weakest and most vulnerable, perhaps he would have given up and lost his life prematurely. Ultimately, he founded the Patient’s Right Action Fund to help end physician-assisted suicide and to have a platform to share his story.

From an ethical point of view, supporters of euthanasia argue that every individual has the right to self-determination. This means that if individuals can choose the terms in which they die, they should also be able to choose the terms by which they die. No one other than the patients themselves are aware of the suffering and misery, so what gives others the right to interfere in their decision? Additionally, this decision would reduce the misery of the patients’
loved ones, who struggle as they watch their family member suffering.

There is also a more sinister side to the argument. Euthanasia, which was also known as "racial killing" in Nazi Germany, gained acceptance in the medical community post World War II as a way to develop a healthy master race. Hitler first endorsed euthanasia at the request of a severely disabled child's father. Following that, he gave permission for widespread euthanasia programs, so that individuals who were deemed inferior because of their disability, race, ethnicity or character traits could be eliminated. These people were believed to be a burden on the economy, and it was sometimes even argued that the exterminations were mercy killings.⁵

Germany recently passed an Assisted-Suicide Law, steering clear of putting euthanasia in its title because of its ties to Nazi Germany. Other countries have been fighting for euthanasia legalization for years; one of the earliest movements for euthanasia took place in England during the year 1835, showing that this dilemma has been unresolved for over 180 years.⁶ In 2014, Belgium legalized euthanasia for patients of all ages and in September 2016, the first child in Belgium chose to undergo euthanasia. On the other hand, some countries still struggle with this ethical dilemma; in the United States, euthanasia is legal only in the states of Washington, Oregon, California and Vermont. The acceptance of euthanasia is increasing in the country overall, but legalization of the procedure remains a controversial topic due to its historical and ethical implications.

Although euthanasia and abortion share a common theme, in the United States they are not given the same spotlight in politics. For example, despite polling that suggests support for various forms of euthanasia conforms closely to political party allegiance, U.S. candidates for political office are almost never asked their positions on euthanasia, as they often are on abortion. Euthanasia only sporadically becomes a political issue because it is believed by most Americans to be a highly private and family-oriented matter, in which the government should not have a say.⁶

A few questions arise as we consider what euthanasia is and what it stands for- does it actually offer us increased control over our lives? In the face of pain, are we trying to grasp onto control, or just the illusion of control? A historical medical practice that contributes to this debate is that of Twilight Sleep--a state of semi-consciousness produced by injection that helps a woman undergo relatively painless childbirth.⁴ Women undergoing the procedure would lose partial control over their movements and get partial amnesia, and so were often strapped to the bed.

So why was this seemingly unjust practice so popular amongst women? The answer is that it gave women the illusion of control. The decision of whether or not to undergo Twilight Sleep was their own, and in an era of male-dominated medicine, women clung to this opportunity to make decisions for themselves. In reality, the women clearly ended up with less control than they would have had with normal childbirth. The psychological basis of euthanasia works in the same way. Humans associate helplessness with fear and so as long as they feel as if they have control over their death, death does not seem as mysterious and terrifying. We try to grasp onto dignity and control, even as it inevitably slips through our fingers.

In the midst of all these questions and beliefs, the decision to undergo euthanasia becomes very subjective. The vehement debate on euthanasia ultimately boils down to a race between cutting-edge research and possible treatments. If a disease is incurable in 2016, it may not be that way a few years down the road. It is no longer a matter of life versus death, but rather a disagreement about the timing and manner of an inevitable death.

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Deploying T-Cells to Target Tumors

BY MAHIP GREWAL

Following heart disease, cancer is the second leading cause of death worldwide. Currently, the most common cancer treatments include surgery, chemotherapy and radiation therapy, all of which have numerous drawbacks. Chemotherapy and radiation therapy can result in extensive hair loss, nausea, blood disorders, and even organ damage, while surgery is often not an option for patients because their tumors are too complicated to safely excise. Therefore, recent reports of successful trials with a new type of immunotherapy, adoptive cell transfer (ACT), which involves engineering a patient’s own T-cells to target the cancerous cells, have raised significant excitement and hope among doctors and patients alike. The results of such trials have led researchers to believe that immunotherapy may become a major pillar of cancer treatment.

WHAT ARE T-CELLS?

T-cells are lymphocytes, or white blood cells, that play a vital role in detecting and targeting foreign or abnormal antigens. In cancer patients, the T-cell response is either not aggressive enough to prevent tumor growth, or the T-cell response becomes “exhausted.” The term “exhaustion” describes a state of dysfunction, in which T-cells cannot effectively target the abnormal antigen. However, over the past few years, scientists have experimented with immunotherapy, which utilizes treatments that attempt to harness and strengthen the immune system to more effectively recognize and attack cancer cells. T-cell responses are an ideal platform for immunotherapy because they are antigen-specific, robust, can traffic to distant antigen sites, and have memory against resolved infections.

ADOPTIVE CELL TRANSFER (ACT)

The goal of ACT therapies is to enhance the T-cell response by extracting T-cells from the tumor-bearing patient, engineering the T-cells with specific tumor receptors, culturing the T-cells by the billions, and then infusing the T-cells back into the patient. There are two major approaches for ACT. The first involves gene-modified T-cell receptors (TCRs), which recognize tumor antigens associated with human leukocyte antigens. The second approach employs chimeric antigen receptor T-cells (CAR T-cells). CAR T-cells connect a single-chain variable domain, or an engineered peptide linkage of the heavy and light variable regions of an antibody, to one or more signaling elements of a TCR complex.
ACT is a powerful example of the growing trend towards person-
alized medicine in that each patient's treatment is directly derived
from his or her own immune system. However, since there is no
single, general treatment that can be administered, the therapy is
costly, with prices ranging from $36,000 to $204,000, as a unique
“drug” has to be developed for each patient. Thus, immunothe-
rapies could be inaccessible to those who cannot afford the high cost.

ACT TRIALS
In 1988, the first major T-cell immunotherapy trial, which
utilized unmodified tumor-infiltrating lymphocytes (TILs) against melanoma,
was led by Steven A. Rosenberg at the National Institute
of Cancer. In the trial, regression, or a decrease in tumor size, was
observed in nine out of fifteen patients, and their cancer regres-
sions lasted between two and thirteen months. Between 1987 and
1992, eighty-six metastatic melanoma patients were treated with
TILs. The overall objective response rate, which is generally de-
efined as the sum of complete responses, or total disappearances
of the tumor, and partial responses, or reductions in tumor size
of at least 50%, was 34%. This is particularly noteworthy because
melanoma patients receiving chemotherapy only have a one-in-
eight chance of having their tumors shrink. Later studies with
mouse models suggested that ACT therapy could be improved by
conducting lymphodepletion, or irradiation of the patient’s lym-
phocytes via chemotherapy, prior to infusing the T-cells. Thus, a
series of clinical trials conducted in the early 2000s, with a total
of ninety-three patients, investigated the efficacy of administering
ACT in conjunction with increasing levels of lymphodepletion. In
these trials, the efficacy of ACT was gauged by the Response Eval-
uation Criteria in Solid Tumors, a set of guidelines created by the
national cancer institutions of the United States, Canada, and Eu-
rope that indicate when a patient improves, stays stable, or worsens
with treatment. Collectively, objective response rates ranged from
42% to 79%.

Other exciting advances in ACT have recently been achieved in trials with leukemia and lymphoma patients. For example, a 2014 trial was conducted at the Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania that involved thirty acute lymphoblastic leukemia patients, whose cancers had returned after intensive chemotherapy. However, after receiving infusions of CAR T-cells, twenty-seven of the thirty patients sub-
sequently experienced complete remission. Similarly, another
study, published in 2014, investigated the efficacy of administering
anti-CD19 CAR T-cells to patients with B-cell malignancies, such
as B-Cell lymphoma and chronic lymphocytic leukemia. T-cells
engineered with anti-CD19 CARs recognize and kill CD19+ target
B-cells. Of the fifteen patients treated, eight achieved complete re-
sponses and four experienced partial responses.

THE FUTURE OF ACT THERAPY
While these clinical trials are encouraging, it is important to recog-
nize that ACT therapy has been successful predominantly in blood
cancers. Therefore, perhaps the most pressing objective in immu-
notherapy research is to widen the reach of the therapy and opti-
mize ACT so that solid tumors can be effectively targeted. Current
major areas of immunotherapy research include identifying ideal
cancer antigens, finding cancer biomarkers for ACT, and working
to improve in vivo persistence and survival of infused T-cells. A
major challenge to improving immunotherapy outcomes is identi-
fying cancer antigens that can be targeted without triggering severe
toxicity responses. Establishing acceptable levels of toxicity will be
a key step in developing larger scale trials in a wider range
of cancers. Furthermore, the transition from clinical trial
drugs to FDA-approved treat-
ments will likely require part-
nerships between academia and
industry. Continuing progress in the expanding field
of immunotherapy presents a promising avenue for administering
more effective cancer treatments.

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Epidemics have historically ravaged the human population since its early existence, but are they a problem of the past? Will we ever have another Scarlet Fever, Spanish Flu, or Black Plague? In 1928, Alexander Fleming discovered the antibiotic, penicillin, the first highly marketed, mass-produced antibiotic. By the early 1940s, when it was commercially produced, Penicillin was bringing more order to the disarrayed world of illnesses. At the time, demand for more drugs increased, and with 12 new antibiotics being churned out a year, widespread disease was deemed to be under control from the public viewpoint. However, even after years of scientific development, the chance for an epidemic still exists.

**THE COUNTING TOLL**

Despite our advances, 2 million Americans are infected by drug resistant “superbugs,” and more than 23,000 of them die per year. Fleming warned of drug-resistant bacteria after observing that many microbes were withstanding penicillin. Sustained applications of new drugs have resulted in multidrug resistant bacteria, such as Methicillin-resistant Staphylococcus aureus (MRSA). Methicillin used to be the primary method of treating Staphylococcus aureus but is now ineffective against MRSA. This resilience has had far reaching consequences. The Centers for Disease Control (CDC) found that between 2000 and 2008, cases of sepsis, a life-threatening condition caused by infection, rose from 621,000 to 1,141,000, and deaths rose from 154,000 to 207,000. Additionally, officials discovered a sample human E. coli with the mcr-1 gene for resistance to colistin, a last resort pharmaceutical used in the event that no other drug is effective. Economist Jim O’Neill projects that by 2050, an estimated ten million people will die annually due to resistant disease. The estimated GDP lost to resistant disease will be $100 trillion. The impacts of antibiotic inefficacy could mean a possible throwback to the microbial dark ages, where a thorn prick can kill you and a hip transplant is no longer worth the risk.

**UNDERSTANDING THE PROBLEM**

Before taking the proper steps to remediate the situation, we must understand the cause. The continued exposure of bacteria to intense and diverse antibiotics has wiped any susceptible microbes, naturally selecting those with the favorable mutations to survive and thrive without competition. These new strains force scientists to move to a new drug, continuing the cycle. In addition to developing resistance through natural selection, bacteria have the ability to transmit resistance through the use of plasmids, loops of self-replicating DNA in bacterial cytosol that carry potentially useful genes. Once resistance develops, the plasmid, can swap between bacteria of the same and of other species through conjugation, in which the bacterial cell membranes are connected through a pilus and the plasmid is replicated and horizontally transferred. However, the ability to resist an antibiotic requires resources; in order for a bacterium to produce a molecule or an enzyme for defense, it must allocate resources away from another important cell function. With no exposure to antibiotics, these bacteria are ecologically less fit and naturally are surpassed by others of their kind. Resistant bacteria would be scarce in nature, however, the introduction of large doses of antibiotics exerts an ecological stress that now favors resistant strains. Antibiotics create a naturally selective system that necessitates these survival systems that did not exist under typical conditions.

If the presence of an antibiotic is what causes resistance, one solution is to reduce the use of antibiotics. Society favors the extensive use of antibiotics. For instance, forty million people receive antibiotics every year while only thirteen million have bacterial infections that can actually benefit from these pharmaceuticals. Accurate and economical diagnosis of patients can drastically reduce the overuse of antibiotics. In addition, agriculture employs the widespread use of antibiotics to supplement the growth of animals. In America, 70% of the medically useful antibiotics are used in the growth and treatment of livestock, these drugs are used as dietary or growth supplements to make up for poor farming practices. Similarly, colistin is widely used in Chinese livestock. The continued usage of these drugs provide more avenues for microbes to gain resistance and transfer the gene and the resistance through food or contaminated soil. As bacterial resistance continues to spread, treatment options become more limited. Simple operations and small infections can become life-threatening. Doctors find themselves relying on colistin despite its undesirable nature. It is a half-century-old drug that poses health concerns to the kidney, but with fewer viable options, physicians have no choice. Perhaps soon, even colistin will lose its efficacy.
Having recognized several sources of the problem, why hasn’t any thing been done? With so few tools at hand, why not make more antibiotics? After Penicillin, there was a flood of pharmaceuticals hitting the market. Scientists were developing antibiotics from the dirt in their backyard. The thought of running out of more new drugs was inconceivable. However, having harvested all the low hanging fruits from the 50’s to 70’s, antibiotic production has sputtered to a crawl. For example, the newest antibiotic discovery, as of 2016, is teixobactin. If approved (a process of 5 years), it will be the first antibiotic produced since 1987. Antibiotic production suffers from decreased availability of natural sources, as well as decreased funding. Drug investment has stagnated since the 70’s as large pharmaceutical companies dropped their antibiotic programs. Why? The average expenditure per pharmaceutical is $2.5 billion and because only 1-2% of pharmaceuticals ever reach the market, companies must make many billions of dollars in profit for every successful drug they can pass. Pfizer, a pharmaceutical giant, was historically a leader in antibiotic development, manufacturing penicillin for troops during World War II. With the advent of resistant bacteria, it ended up closing antibiotic research in 2011. This decision was made for financial reasons. The profits earned by creating expensive drugs for chronic diseases that last a patient’s lifetime disproportionately overshadowed the profits earned by acute diseases because “the customers stick around longer.” For instance, the cholesterol-lowering drug Lipitor earned $13 billion per year for Pfizer, a profit that cheaper, temporary pills cannot compete with. This brings us to a point, posed by Matt Cooper, a medicinal chemist at the University of Queensland: “We also need to think long and hard about antibiotic drug pricing and whether it’s ethically acceptable to pay so much for life-extending drugs but still expect to pay peanuts for life-saving antibiotics.” Obviously, the threat of bacterial resistance isn’t solely attributed to the production of new antibiotics. However, the practices of large pharmaceutical corporations exhibit an apparent, “mismatch between value to society and value to capitalist economics”.

How about antibiotics in agriculture? Despite the FDA’s acknowledgment of the growing resistant trend and the role agricultural antibiotics play, the FDA has only implemented a policy of voluntary restrictions. Current efforts in Congress include Pass the Preservation of Antibiotics for Medical Treatment Act (PAMTA), voluntary restrictions. Current efforts in Congress include Pass the Preservation of Antibiotics for Medical Treatment Act (PAMTA), which would regulate the amount and types of antibiotics that can be used in agriculture to prevent routine use of antibiotics where they are unnecessary. However, there have been several gauntlets that have created a 1% change for bill approval. For one, there are few means of documenting the use of antibiotics in the U.S. for researchers to verify results that would support the bill. Second, if a bill involves agriculture, it is very difficult to pass the legislation. When bills pertaining agriculture arise, “agriculture and pharmaceutical industries have extended their well-funded lobbying arms to push back” in order to protect their interests. To give one example, “Pfizer has filed more than 20 lobbying briefs against antibiotics legislation and has spent nearly $900,000 lobbying against PAMTA alone.” It is obvious that once again, pharmaceutical giants are prioritizing monetary gains over public health.

**MOVING FORWARD**

The looming problem of superbugs is one that can be avoided. The discovery of new antibiotics must once again be prioritized. For one, Congress has passed the Generating Antibiotic Incentives Now (GAIN) act, signed by Obama, which creates a drug development task force, extends patent exclusivity for 5 additional years, extends FDA fast track and increases FDA trial guidance. Additionally, the economist O’Neill comes back with a few proposed solutions. He suggests a market-entry reward, payments for corporations who develop a new antibiotic, and global innovation fund for early stage research, which could provide the economic stimulus to tip research back to the antibiotic arena. More important, however, is a decreased usage of antibiotics. By exposing microbes to less ecological stress, their development of resistance is immensely diminished. We need expansion in the diagnostic sector to enable doctors to accurately determine what type of disease they are dealing with so they can make an effective treatment procedure. Antibiotics do not need to be used in cases of non-bacterial diseases. There are obvious avenues where antibiotics are unnecessary. While antibiotic regulation is being stifled in Congress, ultimately regulation falls to the hands of the consumers. Choosing antibiotic-free meat in the store, and using antibacterial soaps sparingly are some ways of not only preventing antibiotic resistance, but also promoting personal health. Through active education of the risks of resistance, sponsoring of antibiotic research, and reduced usage of our current antibiotics - we can restrict the spread of microbe resistance before it begins to restrict the ways in which we live.

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**WHEN BILLS PERTAINING AGRICULTURE ARISE, “AGRICULTURE AND PHARMACEUTICAL INDUSTRIES HAVE EXTENDED THEIR WELL-FUNDED LOBBYING ARMS TO PUSH BACK” IN ORDER TO PROTECT THEIR INTERESTS**

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**Why Aren’t We Making More Antibiotics?**

For every 100 drugs developed At $2.5 billion spent developing each drug, antibiotics are not profitable enough to recoup losses

Only 1 or 2 make it onto the market

GRAPHIC/CLAIRE SONG

**COMPANIES MUST MAKE MANY BILLIONS OF DOLLARS IN PROFIT FOR EVERY SUCCESSFUL DRUG THEY CAN PASS**

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**References**

**THE CURRENT SITUATION**

Most people understand that heroin is a very addictive drug with great potential for abuse. What most individuals don’t realize is that prescription opioid abuse is far more common than heroin use. According to the U.S. Department of Health and Human Services, the United States is currently experiencing a prescription opioid epidemic.¹ The National Survey on Drug Abuse and Health revealed in 2012 that 2.1 million Americans had a substance abuse disorder related to prescription opioids, while fewer than half a million were addicted to heroin.² By 2013, overdoses due to prescription opioids reached over 16,000, a figure that had more than tripled since the year 2000.³ Drastic increases in opioid prescriptions, intense advertising by pharmaceutical companies, and an increased social acceptability for consuming drugs for nonmedical use have been responsible for exacerbating America’s opioid crisis.⁴ The crisis is likely to grow worse, and combatting this epidemic will require innovative solutions. Emerging research suggests that medical marijuana may be helpful in tackling this crisis due to its ability to alleviate opioid withdrawal symptoms and its potential to serve as a suitable substitute for treating chronic pain.

**THE PROBLEM WITH OPIOIDS**

Opioids are addictive due to the unique way they affect the central nervous system. The body has its own endogenous opioid system that is important in regulating pain. There are three types of opioid receptors found in the body: mu, delta, and kappa opioid receptors. The body produces its own opioids, known as endorphins and enkephalins, which bind to these receptors to block pain signals. Prescription opioids work much like the body’s own opioids, alleviating pain by binding to opioid receptors. Although, administration of synthetic opioids causes the body to greatly lower production of its own opioids. This lowered production, in turn, contributes to the severe withdrawal symptoms opioid addicts experience when they stop taking their medication. Chronic activation of opioid receptors by medication also leads to the adaptation and desensitization of these receptors, leading to tolerance. This phenomenon means that higher doses of opioids are needed to produce the same analgesic effect.² However, using higher doses of opioids puts patients at a greater risk of an overdose, since higher doses can lead to respiratory depression.⁴ Prescription opioids are also addictive because they activate the brain’s reward system, producing pleasure and a sense of well-being.² Overall, the ability of prescription opioids to cause withdrawal, promote tolerance, and activate the brain’s reward system explain why they are so addictive.

Increased opioid use has resulted in more overdoses among all races; however, Caucasians and Native Americans have experienced the greatest increases in overdoses. According to the New York Times, lower rates of opioid overdoses seen in Latino and African Americans may largely be due to racial stereotypes. Studies have reported that doctors are less likely to prescribe opioids to these two groups out of fear that they will become addicted to the drugs or sell them.⁵ Rates of overdose are still higher among men; however, rates of overdose among women have risen more sharply in recent years. A major reason why rates have risen faster for women is that they’re more likely to suffer from chronic pain than men. As a result, physicians are more likely to prescribe them opioids, are more likely to give them higher doses of opioids, and are more likely to keep women on opioids for longer periods of time.⁶

**THE POTENTIAL OF POT**

Recent research suggests that cannabis-based therapies are effective at alleviating pain and reducing dependence on prescription opioids. Many human studies have shown that cannabis-based therapies provide significant pain relief for those who suffer from cancer, rheumatoid arthritis, and chronic neuropathic pain (pain due to nerve damage or dysfunction).⁴ There is also evidence that cannabis is effective at managing postoperative pain, pain due to multiple sclerosis, and migraine headaches. The anti-inflammatory properties...
of cannabis may even prove effective at treating fibromyalgia, a disease that causes generalized pain throughout the body.7

Studies even show that cannabis use prevents opiate withdrawal and tolerance, offering a safe way to wean patients off of prescription opiates.4 Cannabis is much less addictive than opioids and is practically impossible to overdose on due to the lack of cannabinoid receptors in the cardiorespiratory areas of the brainstem. As a result, unlike in the case of opioids, high doses of cannabis do not produce respiratory depression. In fact, no deaths have ever been linked to cannabis use in the United States.7

Despite all of the potential medical marijuana in treating opioid abuse, the federal government has not focused its efforts on utilizing non-opioid treatments.8 There are no cannabis treatments approved in the U.S. to treat chronic pain. Instead,

FINAL CONSIDERATIONS

the federal government has focused on enhancing prescription monitoring programs, opioid education initiatives, and increasing access to naloxone, which is a drug used to treat opioid overdoses.2,8 While these initiatives have shown some efficacy, they do not adequately explore alternatives to opioid medication.

At the state level, however, using medical marijuana as a treatment is being explored, and there is already evidence that cannabis is reducing opioid abuse in states with medical marijuana laws. According to a study by the University of Michigan, patients who used medical marijuana to control pain reported a 64% reduction in the use of prescription opioids.9 Additionally, states with medical marijuana laws have lowered rates of opioid overdoses compared to those without cannabis laws.5

REFERENCES


THE PHARMACOLOGY OF WEED

Cannabis’s psychoactive ingredient, delta-9-tetrahydrocannabinol (THC), is a natural cannabinoid that exerts its effects on the body via activation of cannabinoid receptors. The cannabinoid system is very important in modulating neurotransmission and is key in regulating pain perception, mood, appetite, and memory. The body produces its own cannabinoids—anandamide and 2-AG—and expresses two main types of receptors: CB1 and CB2. Studies have shown that anandamide is very important in regulating pain. For example, a study from Nature demonstrated that rats treated with an anandamide blocker experienced more severe and extended pain responses.4 Other studies have also concluded that CB1 and CB2 receptor activation results in anti-inflammatory effects and other analgesic effects that result in pain reduction. Additionally, CB2 activation indirectly leads to activation of opioid receptors and the promotion of endogenous opioid synthesis.7 The ability of cannabis to increase the synthesis of endogenous opioids may account for why cannabis is able to alleviate opiate withdrawal, especially since prescription opioids lower endogenous opioid synthesis.

FINAL CONSIDERATIONS

Cannabis may prove to be a useful drug in alleviating opioid dependence and could serve as a substitute to prescription opioids. Cannabis is much safer than prescription opioids, is much less addictive, and does not produce the severe withdrawal effects seen with opioids. As more states legalize marijuana for both medical and recreational use, more people will have the chance to benefit from its medicinal properties. Perhaps, with the help of cannabis, prescription opioid use will no longer be an epidemic.