Medical Dialogue Review
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Letter from the Editors:

Dear MDR Reader,

We are proud to present the seventh edition of Medical Dialogue Review! We are very excited about this edition and the articles within, having more than succeeded our goal to collect a diverse set of perspectives that displace science from its traditional setting as an isolated discipline, instead analyzing it from a cultural standpoint. All of us on the MDR executive board believe that science is a multifaceted field of study intertwined with numerous other aspects of study and experience, from the sociopolitical implications of scientific developments to the ways that social behaviors impact the trajectory of research and reform. As a result, it is always our intention to include a myriad of topics and opinions within the review that focus on human health without being limited to the details of a certain scientific approach.

Each volume contains its own set of unique and powerful articles written by enthusiastic individuals passionate about a specific cause. Some writers choose to focus on domestic issues, while others look abroad to topics on global health; some will delve into great detail about specific disorders and diseases, while others choose to tackle the state of a constantly changing healthcare system. Whatever the issue may be, each article is characterized by the thought and sincerity involved in its conception.

Thank you so much for continuing to support us and, if you are a first-time reader, welcome. We hope that the contents of this edition will expand your understanding of science and its implications on society as much as past editions, and that you will maintain an inquisitive and earnest attitude towards the field of science as a whole. Read on, see what catches your interest, and start a dialogue with others just as passionate as you about medicine, health, and society.

Sincerely,

The Editors of Medical Dialogue Review

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Cover Image: *Anatomy and Spirit in the Past*

Noella Richman

Multimedia

Ever since I was a little girl, I remember flipping through my parents' anatomy textbooks from their time in med school. One night in my art studio, I stumbled across a diagram and began a sketch. The sketch soon got covered with ink, and shaded with some oil paint. The canvas of acrylic paint, interestingly enough, was left something that got left out in the rain. The rain blurred the paint and moths and leaves clung to the surface. I mounted the sketch on it much later. As I looked at the piece with all its layers, it demonstrated that art and the practice of medicine have a unifying feature: little 'pieces' piled up one-by-one get you to your goals.

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Introduction: A Look at What's in the Fall 2010 Issue

What is pain? It hurts! But it is also an important natural protective mechanism. What would happen if we did not feel pain when there was actually something wrong with our body? It is hypothesized that emotional and psychological suffering accompanies physical pain, for the sensitization process affects regions of our brain involved with thought and emotion. While swallowing pills is one method of quelling pain, numerous other forms of treatment exist as well. Simple physical therapy, exercise, and yoga are known to be helpful, as well as alternative methods such as acupuncture, hypnosis, meditation, and herbal remedies. Read on to find out more about the process of pain sensation in the body and the various approaches to relieve it.

--**Laura Sickles**, *Pain Unveiled: An Exposé on Pain and its Effects*

How will the new healthcare reform plan impact hospitals and the overall quality of medical care? Most experts in healthcare have predicted that healthcare reform means less money for hospitals and doctors. With less money, some hospitals may consider cutting budgets in the research process. If the funding is not protected for hospitals, there will be a decline in the rate of advances in medical science. How does healthcare reform threaten American health, and why should we care?

--**Daniel B. Shulkin**, *The Future of Medical Research in America*

Global climate change is one of the most serious environmental concerns. But have you heard about how the rise in temperature affects our health? Climate change can alter the course of airway diseases by increasing the ground level O_3 (ozone). It is important to note that most of these raw ingredients of O_3 come from gasoline, diesel fuel, and pesticides. Breathing in ozone can induce chest pain or congestion and can also worsen diseases such as emphysema and bronchitis. In addition, ozone can further decrease lung function and cause inflammation of the parietal pleura. Finally, global warming has a huge impact on waterborne diseases. These illnesses are usually caused by a variety of biotoxins and microorganisms, which are directly transmitted as soon as contaminated freshwater is consumed.

--**Parth Patel,** *Climate Change and Human Health*

As college students aim to get higher grades, they are looking for another study aid to enhance their learning ability and retention of material: Adderall. It is a treatment drug for Attention Deficit Hyperactivity Disorder (ADHD), Attention Deficit Disorder (ADD), and narcolepsy that is widely abused by college students. Due to its ability to "increase alertness, concentration, and overall cognitive performance while decreasing fatigue," it is becoming a popular study partner. The widespread use of non-prescribed Adderall is problematic because first, students are becoming addicted to Adderall and second, they are gaining unfair advantages in the academic setting. Moreover, it contains many of the same chemicals as cocaine, which is why its nickname is the "legalized synthetic cousin of crack cocaine." But how do students obtain Adderall, and why are they unwilling to stop?

-- **Stephanie Squicciarini**, *Getting High for High Grades*

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Pain Unveiled: An Exposé on Pain and its Effects

Laura Sickles

What is Pain?

We have all experienced pain at some point in our lives. Whether it be as minor as stubbing our toe or as serious as suffering from a major injury, we all know what pain is. Quite simply, it hurts! However, Merriam Webster's slightly more technical definition describes pain as a "localized physical suffering associated with…disease or injury" and a "bodily sensation…characterized by physical discomfort" (2010).

As negative as this description sounds, pain can actually be incredibly beneficial to us as a natural protective mechanism. Pain acts as a signal to our bodies that something is wrong. For example, when we touch a hot pan we feel a sharp pain and pull our hand away before too much damage is done. The achy, dull pain that lingers reminds us that we need to be more careful with that hand as we recover from the injury. Without the perception of pain, we would not only be more likely to suffer greater damage from injuries, but we would also be less likely to learn to avoid potentially dangerous experiences in the future (Hawthorn & Redmond, 2004).

Luckily, the pain that most of us experience is transient and not too unbearable. A pinch of over the counter medication and a dash of rest usually cure the ailment. Even with an injury where the pain lasts a little longer, it eventually goes away. Unfortunately, there are people for whom pain is ever present. Sources of such chronic pain vary from environmental factors (e.g., sleeping on a poor mattress) to diseases (e.g., arthritis, cancer) even to no apparent cause at all (Rhodes, 2009).

The physiological explanation of pain is complex and not fully understood at this point. However, in simple terms, we do know that it involves a series of connections among your peripheral nerves, your spinal cord, and your brain. It is believed that chronic pain may at least be partly caused by sensitization, a process in which the nervous system amplifies and distorts an initial cause of pain (Max, 2007).

There is more to pain than just a physical feeling. It is hypothesized that emotional and psychological suffering accompanies physical pain when the sensitization process affects the thought and emotion related regions of our brain (Max, 2007). Fear, anger, anxiety, and depression can develop in a chronic pain patient as they realize that their pain may never go away. The psychological aspects of chronic pain become a significant barrier in pain management as the depressed patient may become less engaged with their treatment (Clark & Treisman, 2004).

Treatments – From "Over the Counter" to "Really Not Over the Counter"

We are all familiar with the traditional over the counter medications used to treat various aches in our body. Acetaminophen (Tylenol), aspirin (Bayer), ibuprofen (Advil and Motrin), naproxen sodium (Aleve), and ketoprofen (Orudis KT) have probably made their way into our medicine cabinets at some point in our lives. While these medications are fairly benign, treatment with prescription

medications such as opioid analgesics like vicodin and oxycontin can be hazardous. They can lead to more serious side effects such as drug addiction.

While swallowing pills is one method of quelling pain, numerous other forms of treatment exist as well. Provided the patient is able to, simple physical therapy, exercise, and yoga are known to be helpful. The goal is to improve the mobility of whichever part–of the body is affected. For example, Transcutaneous electrical nerve stimulation (TENS) as well as bioelectric therapy fight against pain by applying electrical currents to nerve endings through the skin. Although there is some discrepancy on the efficacy of these non-invasive processes, they have been reported to bring relief in many patients. A well known alternative treatment for pain is acupuncture, a traditional form of Chinese medicine which involves inserting thin needles into the body to increase energy flow. Other types of alternative medicine include hypnosis, meditation and herbal remedies. Often, psychological treatment is needed to address the depression that accompanies chronic pain (Rhodes, 2009).

A relatively new and controversial treatment involves using the anesthetic ketamine to essentially reboot brain activity. The ketamine treatment is most well known for its use in the pain disorder Complex Regional Pain Syndrome (CRPS) (also known as Reflex Dystrophy Syndrome (RSD)). It is administered through either a low dose intravenous infusion or an extremely high dose infusion while in a medically induced coma (Koffler et al., 2007).

The Plot Thickens: Diagnosis

The diagnosis of many medical problems can be quite simple. For example, X-rays will show a relatively clear result of whether or not a bone is broken, and blood tests can confirm or refute certain diseases. However, when the only symptom is pain, a diagnosis is difficult. This is especially true when there is no clear source of the pain. The doctor is essentially left to rely on the patient's report for his decision making process. This becomes even more of an issue when the doctor believes prescribing pain killers is a viable option for the symptoms being described. It is difficult to determine whether the patient is legitimately in excruciating pain and needs the medication or if they are simply exhibiting a stellar performance of drug seeking behavior.

Fortunately, imaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have recently been used to illustrate activity in the part of the brain that senses pain. This technology has interestingly shown that pain is experienced differently for people with chronic pain than those without it. This is exciting news as it will hopefully lead to better treatments for chronic pain as well as a more standardized "test" for pain (Stojanovic, 2006). However, regardless of whether the patient is honestly in pain or not initially, addiction can become an issue when using pain killers. Therefore, doctors must take the proper precautions when prescribing the appropriate medication

Pain's Effects

Speaking to people who have been affected by severe chronic pain shows how it can hinder them from leading normal lives. These patients are often rendered unable to hold a steady job, due to either the sheer pain, the depression, or the numerous doctor appointments keeping them from going to work. Furthermore, sometimes patients with chronic pain cannot even fulfill routine household tasks such as doing laundry, cooking dinner, cleaning the house, etc. These problems become especially difficult when a parent is suffering from chronic pain with all the responsibilities they have such as maintaining income and a family. Often a situation is created in which the children or spouse of the patient carries the weight which can generate extra stress on the family.

Many people either do not understand or believe the strife of a person in constant pain. While not intentionally being insensitive, they think the person simply needs to "be tough" or "deal with it". This attitude can in fact make coping with the pain an even more difficult task as the patient is made to feel both weak and inadequate.

Despite these negative ways that a pain condition affects the patient and his or her loved ones, sometimes there can be a silver lining in the cloud. Family and friends can be brought even closer as they work together through their struggles. An even stronger bond unites them as they conquer their battle against pain.

Final Words

Pain is an incredibly relevant issue as it is so ubiquitous. Furthermore, issues surrounding pain have achieved notoriety in the media. Ironically, doctors are accused of under treating pain in their suffering patients despite the reputation of pain killers as the most abused drugs in the country (Clark & Treisman, 2004). More investigative work needs to be conducted on this multifaceted topic so that doctors can better understand how to diagnose and treat pain. The general population should be better equipped to support their loved ones who are in a constant battle with physical and emotional anguish.

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The Future of Medical Research in America

Daniel B. Shulkin

With the new healthcare reform plan starting to take shape, there are still many questions about how these changes will impact hospitals and the overall quality of medical care. Most experts in healthcare have predicted that healthcare reform will mean that less money will be available for hospitals and doctors in the near future. While hospital administrators begin to reduce their budgets, one of the most vulnerable areas for hospitals will be their ability to continue to support unfunded research.

It is medical research that helps to find the cure cancer and create new ways to prevent illness such as the annual influenza vaccine. This research is supported in several ways in this country. First, there are grants issued by the National Institutes of Health, or by other governmental agencies. These grants are very competitive and tend to go to a small number of the country's most sophisticated academic medical centers. Second, industry sponsored projects are given to hospitals which in turn test and design new products or inventions accordingly. Finally, some research is done by hospitals and doctors, who are committed to discovering new and better approaches to caring for their patients. It is this last category of research that may be at the greatest risk under the new healthcare reform plan.

Investigations done by hospitals can be quite expensive due to the complexity of conducting research. Funding must be identified for supplies, technology, staff, and for the paperwork that is required to consent and track patient safety. The principal investigator of the research project must take time away from their other activities to focus on data collection and analysis; this time must be supported with funding. Research can be lengthier when it involves the use of live animals or humans since there are many extra steps required to ensure the safety of the participants. Each step of the research process requires extensive staff time to check for the integrity of the project.

After a research topic is chosen, the principal investigator needs to report the information to the institutional review board (IRB), which is required to review all the research protocols that come into the hospital or university and assess them for quality and safety. After the investigators submit a protocol to IRB for review, the IRB will either approve or wait list the protocol and ask the investigator to rewrite it with some changes before the research can be conducted. Once the approval takes place, the investigator may contact participants and get the patient consent form signed by either the patient or a parent if under eighteen. The IRB is under the supervision of Human Subject Protection in the office of Grants and Research at most hospitals across the country.

With less money in the system for hospitals, some hospitals may consider shortcuts in the research process. "Doing research the right way is expensive, and funding for these projects is getting much harder to find", said an executive at Atlantic Health System in New Jersey that does hospital based research.

Yet history has taught us that failure to adhere to strict research standards can be dangerous. Studies that have failed to ensure proper patient consent, or review by IRB's have

resulted in significant ethical breeches. For example, in the Tuskegee experiment, prisoners were knowingly exposed to syphilis and were observed for the impact of the disease for years, rather than provide them with the necessary treatment. Research such as this was one of the reasons there are such stringent standards in hospitals that conduct studies on patients.

If we fail to protect the funding stream for hospitals, we will likely see a decline in the rate of advances in medical science, which Americans have come to expect of our healthcare system. One area of important research that needs to be done is reducing infant mortality in the United States. Compared to other wealthy democracies, the United States has higher infant mortalities rates than countries with similar or smaller gross domestic products. This type of research is both complex and expensive since tests performed on infants need extensive consent forms to be obtained from the parents. In most major research hospitals in the country, the neonatal intensive care unit works closely with the Office of Grants and Research not only to raise the funding necessary for the project but also to obtain the consent and permission to undertake research.

Most hospitals utilize some of the money they make through clinical care to subsidize research efforts. If healthcare reform reduces the ability to continue this support by hospitals, some worry that the impact on Americans health will be threatened. Many hospital researchers believe that dedicated funding is needed to support hospital research efforts. The question remains whether this is indeed a priority for Americans to receive the best and whether there will be money to support hospital based research efforts.

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Phytochemicals: Panapae or Fallacy?

Blima Gottlieb

When browsing the supermarket aisles, it appears that the secret for a healthy life has been deciphered. From Kellogg's Brand Cereals claiming to increase attentiveness in children to POM Wonderful claiming to cure heart disease, many products profess to be the "magic elixir" of life. The benefits of eating and drinking foods filled with antioxidants and other phytochemicals that reverse the damage of oxidative stress on the body's cells has become a given truth, fact or fallacy?

Much to the chagrin of thousands of Americans who scamper to find miracle products to prevent medical woes, the pursuit persists. The *Los Angeles Times* recently revealed the Food and Drug Administration's efforts to debunk the myths asserted by various food and drug companies regarding the benefits of their products.

Despite continued research, the antioxidants found in POM Wonderful, despite company claims, have not been proven to cure heart disease, prostate cancer, or even erectile dysfunction. It is true that antioxidants may protect compounds in your body from harmful reactions with oxygen. However, antioxidants have not been proven to cure cancerous tumor growth, the development of heart disease, the risk of diabetes, or even the loss of brain function.

Research associated with antioxidants and other phytochemicals has largely been conducted on rats, not human beings. The claim that antioxidants can lead to a healthy life is based upon research in which rats that were fed antioxidant-infused food were less prone to contracting prostate cancer than rats fed plain food. Researchers question the veracity of such studies because there is no way of knowing whether or not the human body would react in the same way.

Another basis for these claims are population studies, which are done by drawing conclusions from observations based on target segments of the populations. For example, Asians eat more carbohydrates than Americans and as a result they tend to be leaner; therefore, a carbohydrate rich diet results in a leaner population. The consensus in western philosophy is contrary to this hypothesis. The credibility of population studies is affected by a myriad of unknown factors causing the veracity of such studies to be dubious at best.

Despite the variety of studies conducted scientists have been unable to prove the effectiveness of phytochemicals in maintaining health. Research so far continues to be inconclusive; therefore, despite all claims by researchers and product manufacturers, the search continues.

It appears that most foods, from fruits and veggies to soy and dairy-products, contain natural phytochemicals, all of which are beneficial in some way or another. Until proven otherwise, the best one can do is to consume a balanced diet, which will enable him or her to glean the benefits from a variety of foods. Remember, an apple a day keeps the doctor away, but including a smattering of foods from A to Z can't hurt.

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Dr. V.S Ramachandran: A New Way to View Neural Perception

Mohamad Saleh

From the development of a comprehensive understanding of the central and peripheral nervous systems to the breakthroughs made in psychology and psychotherapy, our collective understanding of the brain and how it operates on a fundamental level is more thorough now than it has ever been before, and it is still growing. One of the pre-eminent research physicians working today, whose work has influenced the way psychotherapists and neurologists perceive the behavior of the brain, is Dr. V.S Ramachandran. His work mostly revolves around the behavior of the brain after it has been under some sort of physically traumatic event. If a person's behavior or physiological function changes after experiencing that sort of trauma, Dr. Ramachandran believes that by investigating which part of the brain was affected by it, then it is possible to map, with empirical evidence, what the functions of the different regions of the brain are. Dr. Ramachandran has also published a number of papers on strange behavior associated with neural perception. He is most well-known for his research on the neurological conditions Synesthesia and Capgras syndrome, as well as the effects of visual feedback in restoring brain function ("About V.S Ramachandran"; Hirstein and Ramachandran, 1997; Hubbard et. al, 2006; Ramachandran and Altschuler, 2005).

Synesthesia

Synesthesia is a condition in which the stimulation of one sense causes the stimulation of one or more of the other senses. For example, a synesthetic experience would be one in which listening to notes played on a violin causes the listener to see colors or images that correspond to the notes he or she is listening to. Unfortunately though, Synesthesia has not received the same sort of critical attention in the past as it does now. Dr. Ramachandran explains that the main reason for this has to do with the demographic of people usually characterized as synesthetes. Because synesthesia is eight times more common amongst artists and musicians than it is in the rest of the general populace, it was believed for a long time that Synesthesia may be the by-product of a very distinct lifestyle choice that, at least in the popular imagination, includes the use of hallucinogenic drugs.

However, based on the work of Francis Galton, a 19th century scientist and physician, Dr. Ramachandran believes that Synesthesia is just a hereditary medical condition that is both uncontrollable and involuntary. To prove this he, along with the help of his colleagues, conducted a number of tests on "grapheme-color synesthetes". These are patients whose synesthesia causes them to involuntarily associate colors with graphemes (shapes such as numbers or letters). This form of Synesthesia is far less complex than the one associated with musicians or artists described earlier, so it represents the lowest common denominator of Synesthesia and serves as a portal into understanding the fundamentals of how the condition behaves. Three experiments were utilized to test the effects of grapheme-color synesthesia on patients. The first experiment was used to select the graphemes that elicited the strongest responses from patients. The patients were shown individual graphemes of

different contrasts and asked which graphemes' colors were most apparent to them. The second experiment was a modified version of the first. Instead of showing patients individual graphemes, they were given displays with a huge array of graphemes, including the ones they picked out in the first experiment, and asked which one they noticed the most. Finally, the third experiment reaffirmed the results of the first two by surrounding the graphemes that received the most attention in the first two experiments with a number of control graphemes that did not stimulate any responses from the patients. In all three experiments, the patients chose the same graphemes.

The results from the experiments prove that Synesthesia is a very specific condition. It is not random and it will cause the senses of those who possess it to intermingle within very strict limitations. Those who do possess an involuntary ability to stimulate several senses through the stimulation of one are, first, not in control of the stimulation, and second, incapable of controlling what causes the stimulation ("A Conversation With Neurologist V.S Ramachandran"; Hubbard et. al, 2006; Hubbard & Ramachandran, 2005).

Capgras Syndrome

While Synesthesia is a hereditary condition, Capgras syndrome is not. Capgras syndrome is a condition that usually occurs after a patient suffers very serious trauma to the skull. Patients with Capgras syndrome regard people whom they know well, even their parents and siblings, as "impostors". For example, they will look at a parent's face and deduce that, although that person looks like his or her parent, he or she is not. Further complicating the situation is the fact that, when these patients speak with their parents over the telephone, they interact with them normally.

Previous physicians concluded that this might just be a result of damage to the "fusiform gyrus", the area of the brain responsible for facial recognition. However, this explanation does not explain why patients with Capgras recognize their parents' faces at all. That phenomenon is actually another much more well-known delusion known as prosopagnosia, which is characterized by an inability to recognize anyone's face. Dr. Ramachandran believes that this is the result of a very unique kind of damage to the fusiform gyrus. He hypothesizes that the cause of Capgras is damage to the neurons that connect the fusiform gyrus to the limbic system of the brain, the area responsible for emotional responses to internal and external stimuli.

His reasoning for this is the result of the way in which patients with Capgras treat their parents. They recognize their parents, meaning that the damage cannot be contained exclusively to the fusiform gyrus. However, they refuse to accept that their parents are, in fact, their parents. Dr. Ramachandran explains that this may be because the patients do not have any sort of emotional response to their family anymore. For if the patients believed that their parents were truly their parents, then they would feel emotion related to their memories together. This explains why the damage to the fusiform gyrus in Dr. Ramachandran's hypothesis is exclusive to the areas connecting it to the emotional region of the brain.

To test this hypothesis, Dr. Ramachandran and his colleagues tested the electrodermal response of patients to images of familiar and unfamiliar faces. An electrodermal response is related to skin activity. When testing for an electrodermal response, electrodes are used to measure the activity of the sweat glands non-invasively. If a patient has some sort of emotional response, the electrodes pick up changes in the skins electric potential. According to Dr. Ramachandran's hypothesis, therefore, a patient with Capgras should have the same electrodermal response to images of both familiar and unfamiliar faces.

The results of the test confirmed Dr. Ramachandran's hypothesis and proved that Capgras syndrome relates the fusiform gyrus to

the limbic region of the brain (Hirstein and Ramachandran, 1997; Hubbard & Ramachandran, 2005; Malmivuo, J. Plonsey, R. 1995).

The Effects of Visual Feedback in Restoring Brain Function

Finally, Dr. Ramachandran has also done a considerable amount of research on visual feedback and how it relates to restoring very specific functions of the brain. His most famous experiment revolves around a patient suffering from a phenomenon known as "phantom limb".

Phantom limb is a term used to describe a limb whose presence, after being amputated, still continues to be experienced by the patient. Dr. Ramachandran and his colleagues worked with a number of patients who suffered from very painful paralyses to their arms for months before said arms were amputated. Unfortunately, the patients' phantom limbs caused them the same sort of pain. Dr. Ramachandran hypothesized that during the time period in which the arm was still intact, the patient developed a sort of "learned paralysis". He describes this type of paralysis as due to visual feedback, for when a patient would give a motor command to the paralyzed arm, he or she can *see* that the arm does not respond. This would go on for months until the patient's brain is conditioned, through visual perception, to believe that the arm will always be paralyzed. As a result, even after the arm is amputated, the patient suffers from a phantom limb that behaves in the same way that the paralyzed limb did.

To prove whether or not this "learned paralysis" is the reason why patients suffered from severe pain due to their phantom limb, Dr. Ramachandran believed that it was necessary to create the impression that a patient's amputated arm was restored. Theoretically, the patient's brain should be more or less fooled into thinking that the paralyzed arm was restored, and is once again moving and the pain would disappear. To restore a patient's limb, Dr. Ramachandran created a contraption he named "The Mirror Box", which was a cardboard box with a hole in one of its sides, and a mirror pasted to one of the sides perpendicular to the hole. The patient would place his or her amputated arm in the hole. Then, he or she would raise his or her intact arm so that he or she can see its reflection in the mirror on the side of the box. This would create the illusion that the patient's amputated arm was restored. When this experiment was utilized by Dr. Ramachandran, the patient who it was being tested on said that he miraculously felt his phantom limb moving! After a number of sessions using the mirror box, the patient said that his phantom limb had disappeared all together. This was explained by Dr. Ramachandran as the brain getting rid of an anomaly; a limb that it was conditioned to believe is paralyzed, but keeps regenerating with no observable reason.

The results of the experiment once again confirmed Dr. Ramachandran's hypothesis. His ideas on visual perception and its role in paralysis have today spread to a number of other fields, including stroke rehabilitation, and are being utilized in hopes of discovering a cure to a number of other paralyzing conditions ("A Conversation With Neurologist V.S Ramachandran"; "Ramachandran and Altschuler, 2005).

Conclusion

The way in which the brain and its behavior is perceived has changed over the past century in a number of fascinating and divergent ways. Where once psychological answers seemed to be the only ones that made sense of the chaos of neural activity, today scientists and physicians are discovering empirical ways to describe the way the brain works. Dr. V.S Ramachandran and his work have blazed a new trail in the way the mind is studied. His methods and point of view on the brain are refreshing, and they add an extra dimension of creativity to a field of study once characterized simply by its

difficulty. Future generations of neurologists will look back at Dr. Ramachandran as the beginning of a completely new and different movement to understand the brain on a genuine and factual level.

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The Increased Spread of HIV through Sex Trafficking in Asia

Monica Kohli

Since the late 19th century, the rapid growth of two epidemics has dramatically impacted global populations—Sex trafficking and HIV. The social epidemic known as sex trafficking, the selling of sex through forced prostitution is a consequent practice of grave social, economic, and health conditions. Of such health issues includes Human Immunodeficiency Virus [HIV] which has been undergoing a rapid rate of expansion in correlation with sex trafficking. Developing nations in Asia are areas of significant concern. Advancements in the study of HIV are vital to these nations facing the spread of HIV through the sex trafficking; a better understanding of the virus, after all, allows for better public policy towards treatment and preventative education.

Study of the HIV in the past century has strongly indicated that particular factors have allowed for the pathogen's successful proliferation. Generally, medical primatology and genetic study have revealed that the modern strain of HIV in humans emerged from a related strain of the virus in primates, known as SIVS. Thus, it is possible that a primitive form of the virus has been present for thousands of years. (Marx 2004: 221-22).

HIV is transmitted by the crossing of an infected mucous membrane with another. This makes the heavy use of drugs and sex in the field of sex trafficking breeding grounds for the virus. A general lack of condom use allows for the consequential infection in sex workers. For example, it has been reported that sixty percent of sex work encounters in China are unprotected. Additionally, the increased popularity of "sex tourism" in Asian countries has become a source of national profit them (Narang 2007: 36)..

The HIV directly colonizes cells of the immune system, utilizing the enzyme reverse transcriptase to embed its DNA within the genetic material of the host cell. The viral abundance and immune response fluctuate over the course of the infection; the immune system is often successful in initial maintenance of the viral population. But, it is through the pathogen's continual mutation and creation of "escape mutants" that it ultimately avoids destruction by the immune response. Helper T cells that are colonized by the virus no longer can initiate their normal defensive response and are destroyed by the body in an auto-immune attack. Generally, when the count of helper T cells is beneath 200, the immune response is deemed wholly ineffective. The consequential susceptibility to various pathogens that are typically harmless to a healthy immune system is what characterizes the development of full-blown AIDS (Nowak 1995: 58-60). However, the onset of AIDS from the viral infection is often prolonged and largely asymptomatic. This characteristic of HIV makes it especially threatening for infected individuals; thus, those involved in the sex trade [i.e. workers and customers] essentially continue to engage unknowingly in unprotected sexual intercourse and further its transmission.

According to the United Nation's 2009 Epidemic Update Report, the total number of individuals infected with HIV in 2008 was at 33.4 million (2009: 3). Although the number of victims with fully developed AIDS has drastically decreased, the number of infections

of HIV globally is at a high. Particularly, geographic variations display patterns of infection that correlate with specific lifestyles of subsections of populations. It is also in these populations [notably Africa and Asia] where preventative efforts tend to be especially low (Narang 2007: 34).

Of the population of sex workers present in Asia, a growing percentage of it is composed of victims of sex trafficking, adding a difficult and important aspect to the already challenging issue of the spread of HIV through sex work. The term itself refers to the forced engagement in prostitution and selling of people--usually women and children through illegal migration. In a publication presented by the UNDP Regional HIV and Regional Development Programme for Asia Pacific, sex trafficking and HIV were stated to stem from the same causal factors of "gender inequalities, poverty, lack of economic opportunities for women, stigma and discrimination, rights violations, and a life without dignity." The difficulty in filtering traffickers from neutral migrates has paved a route for the spread of HIV infections across international borders.

Within Asian nations, the disparities in opportunity, education, power, and legal rights compose weak national infrastructures that traffickers have successfully exploited. A striking case study of trafficked Nepalese girls and women provides such evidence for the gender-based discrimination and subsequent spread of HIV infection in Nepal. The case study involved a subject group of 287 women trafficked to Mumbai, India to engage in coerced prostitution. Of the 287 women examined, 109 tested positively for HIV infection—an astounding 38%. Annually, seven thousand women and girls are reported as being trafficked from Nepal to India.

The study further examined the specific factors within trafficking that affected the observed HIV infections. It was deduced that the highest rate of infection was found among girls under the age of 15 due to the strong preference of male clients in younger females. Again bolstered by predominant constructions of gender, male clients fervently sought sex with virgins and young girls in concurrence with mythical belief that it would be safer and could cure maladies (Silverman 2007: 539, 541).

Governments of Asian nations inflicted with sex trafficking and HIV are often inadequate in their efforts to combat either issue. In Nepal, for example, programs promoting education for young girls that have been seen to effectively reduce initial capture into trafficking are often rare and poorly funded(Silverman 2007: 542). The general need for reduction of gender disparity is another factor that is difficult to alter, as it calls for the complete dismantling of a social infrastructure that has been dominant for centuries. The lack of safe sex education and understanding of the nature of the virus and its transmission are dominant shortcomings of governments and therefore targets of reform in public health policies.

The nature of the HIV to mutate at different stages of the infection has allowed for innovative treatment targeting specific times of viral growth. It has been seen that infection instigates competitive response amongst the body's own immune cells, causing the "confusion" of the system and its inability to solicit a strong, targeted defense. Treatment has been determined as being most effective when administered prior to the stages of mass mutation of the virus (Nowak 1995: 65).

The potential of the virus for infinite mutation characterizes the inherent challenge posed in developing a single-strain vaccination (Narang 2007: 13). The progression of the infection must be closely monitored in order to correctly administer the commonly utilized antiretroviral drugs. In addition, the correct usage of combination therapies can allow for the successful, temporary management of the infection and prolonging of the stagnant stages of the virus (Nowak 1995: 65). Although governments generally have made antiretroviral

drugs that combat the core mechanism of the HIV virus proliferation more available, poor instruction of their correct usage and lack of monitoring in inflicted individuals have resulted in overall ineffective public health initiative (Marx 2004: 221).

Legislation against prostitution has been suggested as a plausible solution to the present institution of sex trafficking. However, public health officials and sex workers themselves have protested this initiative. In India, for example, the passage of such a law resulted in official and civilian uproar. The critical argument against the legislation proclaimed that banning the trade would only cause it to move underground. Public health officials fear this as it would impede efficient monitoring of HIV/AIDS and prevent administration of preventative education and post-infection treatment. Such legislation would also limit the ability to differentiate between sex workers that voluntary entered the trade and those who were coerced through trafficking. This is argued as ultimately compromising the rights of sex workers as a whole and their potential for safer sex practices (Chatterjee 2008: 975-976).

It can be seen that extensive research of HIV and an increased understanding of it has allowed for efficient strategies to combat the epidemic's spread.

Initiatives of public health policy can only be successful with appropriate funding and government regulation of the sensitivities of the existing sex trades. General motive towards bettering economic and educational opportunity for lower socio-economically positioned Asians has been continually indicated as the underlying source of empowerment [specifically for females] and prevention of future sex trafficking. Providing education for girls and women would deter the acceptance of enticing offers falsely made by traffickers for a better life. Additionally, greater funding needs to be allocated to knowledgeable public health organizations that can distribute information and drugs for HIV/AIDS more effectively. Through actions such as these, the trafficking and viral exploitation of existent weaknesses in national infrastructures can be addressed and resolved.

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Climate Change and Human Health

Parth Patel

Of the myriad of problems facing human beings in the 21st century, global climate change is ranked as one of the most evident and awe-inspiring environmental concerns. Newspapers and magazines often present articles focusing on this issue, whether mentioning the melting polar ice caps in the Artic or the dried and fragmented land in Africa caused by severe drought. High school and college courses also teach students about how global warming is deteriorating our planet, causing widespread impact on the land, valuable resources, biodiversity, and oceans. It is quite rare, however, to read or hear about how this rise in temperature is affecting the human population in terms of health and disease. Unsurprisingly, most of the research done so far has only been concentrated on environmental, and not human, effects. This is because the consequences of climate change on our health usually tend to be long-term and complex, which means that isolating and understanding them is a challenging research endeavor. Developed countries are likely to focus more on the ecological and environmental aspects of climate change as opposed to the health aspects as a result of landscape and wildlife problems that have generated increasing concern. Developing countries, on the other hand, must responsibly focus on human effects because diseases and illnesses due to the changing state of the environment take the greatest toll on the public in these areas.

When we think of environmental diseases, respiratory illnesses such as asthma usually come to mind first. Indeed, allergic diseases alone impact around fifty million individuals in the United States and consequently, are related to the increasing health care cost in the country. The rest of the world has also seen a rapid increase in the occurrence and austerity of these respiratory diseases, which have been indirectly related by experts to climate change. Management of asthma and other related respiratory diseases like atopic dermatitis relies on many factors, one of them being strict control of factors that seem to aggravate the disease. Many of these triggers are environmental, for instance air pollutants and allergens. As a consequence of all this, even the slightest change in environmental variables could negatively affect the brutality of these "climate-dependent" diseases.

Likewise, climate change can alter the course of airway diseases by increasing the ground level O_3 (formed by a chemical reaction between oxides of nitrogen, such as NO and NO_2, and volatile organic pollutants, such as acetone, benzene, formaldehyde, and 1, 3-butadiene). It is important to note that most of these raw ingredients of O_3 come from gasoline, diesel fuel, and pesticides. When the particles given off by these detrimental human activities come in contact with heat and sunlight, they combine to form ozone smog. Breathing in this ozone can induce chest pain or congestion and can also worsen diseases such as emphysema and bronchitis. In addition, the ozone can further decrease lung function and cause inflammation of the parietal pleura.

Moreover, temperature rise and elevated CO_2 levels in the atmosphere result in premature flower blooming, which affects the circulation of aeroallergens like pollen. It is not much of a surprise that people with pollen allergies can go

on to develop asthma. Although this asthma might recur during each pollen season, it can eventually become chronic. Pollen counts tend to be high during warm, dry, and breezy days and extremely low during chilly and wet periods. Pollen concentration in a specific area can also be largely impacted by other environmental conditions such as land use, population growth, deforestation, and pollution.

In addition to affecting respiratory diseases, global warming also has a huge impact on waterborne diseases. These illnesses are usually caused by a variety of biotoxins and microorganisms, which are directly transmitted as soon as contaminated freshwater is consumed. Some examples of these microorganisms are bacteria, protozoa, viruses, amoeba, and algae. In the modern industrial era, chemical contamination of water that is used to drink, wash, and serve a multitude of other purposes is an issue of great concern because of the widespread discharge of toxic materials into rivers, lakes, ponds, streams, and oceans. Fecal matter of human or animals and organic matter of dead organisms can be a serious source of pollution and contamination. Globally, the occurrence of waterborne diarrheal disease is quite high and is expected to peak higher with global warming.

An article in *The Washington Post* by Kari Lydersen written in 2008 examines the correlation between rising water temperature and the occurrence of diseases:

"Rainfalls will be heavier [due to evaporation], triggering sewage overflows, contaminating drinking water and endangering beachgoers. Higher lake and ocean temperatures will cause bacteria, parasites and algal blooms to flourish. Warmer weather and heavier rains also will mean more mosquitoes, which can carry the West Nile virus, malaria and dengue fever. Fresh produce and shellfish are more likely to become contaminated."

Furthermore, during drought (caused by increased temperatures), reuse of water and use of sources of water that are of poor quality will most likely increase. As a result, waterborne diseases will inevitably cause problems for people living around drought regions, especially in developing nations near the equator.

It is obvious that there are numerous efforts being made in today's society to change human habits so that we do less damage to the environment. Countries are trying their best to collaborate through climate conferences like the one held in Copenhagen, Denmark in 2009. The environmental phase "reduce, reuse, and recycle" is now more popular than ever and we have even officially added "green collar job" (a job connected to eco-friendly products and services) to the dictionary. But are we making a just effort to understand human health effects of environmental problems? Are we conducting enough research projects to examine and analyze these effects? Are we rigorously training medical school students in the field of environmental health? The answer to these questions is a resounding no but the answer to whether we can or should is a definite yes.

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Getting High for High Grades

Stephanie Squicciarini

When exam time rolls around each semester, one concern usually dominates the mind of every college student – how to do well on exams and papers. While most students often follow the traditional methods of rigorously studying material, attending study sessions, or reviewing notes with peers, many students are now looking towards another study aid to enhance their learning ability and retention of material : Adderall.

In a clinical setting, Adderall is a prescription drug that is most commonly recommended by doctors for patients diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), Attention Deficit Disorder (ADD), or narcolepsy, a sleep disorder. However, because of this drugs ability to "increase alertness, concentration, and overall cognitive performance while decreasing fatigue," it is becoming a popular study partner to many college students across America (U.S. Newswire). Many students consume this drug despite the fact that it has not been prescribed to them for specific conditions such as ADD or ADHD. In fact, the National Survey on Drug Use and Health conducted a survey in 2009 and found that full-time college students, aged 18 to 22, were twice as likely as their not full times student counterparts, to have used Adderall non- medically in the past year (U.S. Newswire). Nonmedical use of a prescription drug is defined as use without a prescription belonging to the respondent or use that occurs simply for the experience or feeling the drug caused (OAS).

The problem that arises from the growing, widespread use of non-prescribed Adderall is two fold: not only are students becoming addicted to Adderall, but they are also gaining unfair advantages in the academic setting. Adderall's chemical components make it a potent central nervous system stimulant that increases neurotransmitters such as dopamine and norepinephrine. These augmentations, in turn, increase the amount of brain signals that are transmitted (Daley). Additionally, Adderall contains many of the same chemicals as cocaine, which is why its nickname is the "legalized synthetic cousin of crack cocaine" (Dubose). Therefore, the "addictive" nature of Adderall does not necessarily cause cravings and withdrawals; the addictiveness stems from the student's dependence on the academically favorable outcomes that often result from usage of this drug. This dependence is the justification for Adderall's is classification as a Schedule II drug.

It is unfair to state that all students who use Adderall are at fault because some students truly do need this drug to manage diagnosed ADD and ADHD. For those who are not diagnosed with a condition that warrants the use of Adderall, taking Adderall essentially yields them an unfair advantage. Non-prescribed Adderall usage is comparable to athletes who utilize steroids to enhance their prowess and ability in certain sports.

One of the most shocking facts about college students recreationally using Adderall is that many students obtain the drug from friends or relatives to whom it has been legitimately prescribed. In an article by Britton Drown, an avid Adderall user describes the availability of Adderall as being "one phone call away," which

speaks to a separate issue of Adderall being overly available to the public. Many people may feign symptoms and "seek out psychiatrists who will give them Adderall prescriptions with little to no therapy, diagnostic detail or consideration of non- medication alternatives" (U.S. Newswire).

A long-term problem of recreational use of Adderall among college students is not only the dependence that can arise but also an increase in the probability that the students who use Adderall will abusively use other substances as well. Statistics show that approximately 90% of the full-time college students who had non-medically used Adderall in the past year had also been binge alcohol drinkers in the previous month. More than half of them were heavy alcohol users during that period. These students who non-medically used Adderall were more likely to have been polydrug users in the past year than their non-Adderall using counterparts, and in the past year, they are more likely to have used illicit drugs than their non-Adderall using counterparts. They are almost three times more likely to use marijuana, eight times more likely to use cocaine, eight times more likely to non-medically use tranquilizers and five times more likely to non-medically use pain relievers (OAS).

In conclusion, the non-medical use of Adderall is most likely due to the increasing competition in the job market and also the increasing number of college entrants. Ergo, students are more likely to go to greater lengths to stand out amongst their peers. With this preoccupation of achieving high test scores and boosting one's GPA can come a dependence on Adderall, especially during times of stress such as the weeks of midterm and final exams. However, students often do not realize that while they take Adderall to shine brighter in a sea of their star peers, they also leave themselves vulnerable to the influence of other substances such as alcohol, marijuana, and cocaine.

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Killing the Messenger: Vector Eradication Strategies in Trinidad

Noah Lumsden

The Caribbean island of Trinidad contained a high concentration of *Plasmodium vivax* well into the 20th century. The malaria caused by the *Plasmodium* parasite greatly hindered the sugarcane and cacao farming on which Trinidad's economy depended. The poor East Indian farmers and plantation workers were especially hard hit, as they were located in the areas where the disease was most common (Fonaroff 543). The capital, Port-of-Spain, was also continually threatened by malaria outbreaks originating in the large mangrove swamps that bordered the town. Even along the coast, large swaths of land were essentially uninhabitable because of the malaria that emanated from the brackish coastal thickets (British Medical Journal 477).

The island environment was well suited to keep a state of constant malaria transmission going indefinitely. Despite this, malaria was successfully eliminated from Trinidad and has only returned in a few isolated cases (Ellis 1048). An effective assault on the mosquito vector that transmits malaria was the key to this accomplishment. The *Plasmodium* parasite itself is constantly changing and is consequently very difficult to target, but its vector is much easier to eliminate. In Trinidad, malaria eradicators sprayed pesticides and destroyed mosquito breeding sites, preventing insects infected with *Plasmodium* from flourishing and spreading the disease.

Despite the Trinidadian success, these tactics are not perfect. In addition to the concern of environmental damage, malaria eradicators must be wary of overusing pesticides. This can lead to new generations of mosquito that are resistant to the pesticides and therefore much more difficult to wipe out. This is a significant obstacle to eradication efforts in places that are larger and less easily organized to fight malaria than Trinidad was. As a result, the measures that eliminated malaria in Trinidad must be applied in conjunction with an evolutionary understanding of mosquito resistance if they are to be effective elsewhere today.

The mosquito eradicators fighting malaria in Trinidad had to overcome the host of geographic and ecological features that had made malaria so endemic. Among the fifteen species of mosquito native to the island, two acted as significant disease vectors (Fonaroff 533). One, *Anopheles bellator* lays its eggs in the water reservoirs of bromeliad flowers that grow on trees in the rainforests of the islands interior. At dusk, the females fly to nearby villages in search of blood meals (Fonaroff 548). The other, *Anopheles aquasalis* breeds in fresh or brackish water, often coastal mangrove swamps and rice paddies. It flies, sometimes miles from its breeding grounds, seeking blood meals in coastal areas, including Port-of-Spain (Fonaroff 533). The females invade houses at night and bite animals and people for sustenance (Fonaroff 555). Between the highland *A. bellator* and the coastal *A. aquasalis*, potential mosquito vectors inhabit nearly the entire island. Worse, the densest human populations inland and on the coast are close to some of the biggest mosquito breeding grounds on the island. These conditions were the primary reason for the historically high malaria rate in Trinidad.

The agricultural practices used on the island were another factor abetting the spread of malaria via mosquito. The artificially constructed tree layout on cacao farms is ideal for the reproduction of *A. bellator*. The trees on the cacao plantations are separated from each other to maximize the productivity of each tree. This allows much more sunlight to reach close to the ground then is natural in rainforests with their typical dense canopies. As a result, the bromeliad flowers that live in the trees but need lots of sunlight have many more places to grow then their usual restricted range in the canopy (Fonaroff 546). The bromeliad flowers contain pools of water and detritus. These tucked-away basins are the ideal breeding site for *A. bellator* (Fonaroff 547). The proliferation of bromeliads allows the mosquitoes to greatly increase their numbers. These localized mosquito population booms are necessarily centered on large cacao farms, which are near the homes of the workers farming the trees. In addition, the growth of the flowers lower on the trees encourages the mosquitoes to live closer to the ground, putting them in contact with the farm workers more often (Fonaroff 546). The increased human contact with *A. bellator* causes the incidence of malaria to skyrocket. Large outbreaks of the disease in inland areas typically centered around large cacao farms (Fonaroff 552).

This disproportionately affected East Indians because they made up much of the labor force responsible for tending the cacao trees. East Indians spent the most time among the trees, and so were exposed to malarial mosquitoes more than any other segment of the population (Fonaroff 543). This disparity in malaria rates increased as the cacao business declined in the early 20th century. When the farms began to shrink, the pay shrunk with them. This forced the East Indian laborers to find some work elsewhere to stay afloat. Working away from the farms meant that the only time they could tend the cacao trees was in the evening. This is the time of day when *A. bellator* is most active and, consequently, the risk of malaria infection is greatest (Fonaroff 555). This was reflected in the especially high toll that the illness took on the poorest East Indian workers (Ibid.).

The East Indians also got malaria at a higher rate along the coast. As with the cacao example, the differential was largely due to agricultural practices. The exposure to *A. aquasalis* in association with rice farming was an important malarial risk factor among coast-dwelling East Indians (Fonaroff 535). A large part of the East Indian population participated in rice farming because of the cultural value that they placed on the crop. They considered it a symbol of plenty and used it in some religious rituals in addition to its use for food (Fonaroff 541). Unfortunately for the East Indian community, rice paddies are one of the preferred breeding sites of *A. aquasalis*. The location of villages around rice farms greatly increased exposure to malaria. The fact that the rice-growing season corresponded to the worst season for malaria compounded the problem (Fonaroff 541).

The endemic malaria raging in the rice paddies, in the highland forests and all over the island was a major concern of the Colonial British authorities. They tried to rein in the disease in several ways during the 19th and first half of the 20th century, but met with only limited success. One strategy was to force rice farmers to drain their paddies occasionally. This decreased the number and scope of coastal outbreaks somewhat, but it did not affect the clouds of malarial mosquitoes coming from the mangrove swamps (British Medical Journal 477). In the hillside cacao farms, the British tried to kill off the *A. bellator*-harboring bromeliads with partial success and also used various pesticides to try to kill the mosquitoes directly. These efforts at controlling the disease generally had relatively small and temporary effects until the introduction of DDT in the middle of the 20th century (Fonaroff 552).

The use of DDT completely reshaped the battlefield of the fight against malaria. The

pesticide was so effective that tiny doses could be feasibly spread over large areas and keep the mosquitoes down for months. With the coordination of a massive worldwide initiative, led by the World Health Organization, malaria began to be forced back in Trinidad. Workers sprayed an application of DDT on the interior walls and ceiling of nearly every house (Gladwell). This killed the mosquitoes that had taken a blood meal from a person before they had a chance to bite anyone else and possibly infect a new victim. This worked because after biting a person at night, mosquitoes fly to a nearby wall and rest there while they digest (Gladwell). Every female mosquito does this, so the pesticide residue in every treated house killed nearly all of the mosquitoes that fed in there. This stopped the vast majority of malaria transmissions and ground the disease to a halt on the island. Malaria was officially eradicated from Trinidad in December of 1965 (UN Malaria Report 55). The rest of the Caribbean (except for the Dominican Republic and Haiti) was officially cleared of malaria by 1982. Over a couple of decades, the old scourge of malaria had been beaten in many places, mostly thanks to DDT. It was a significant triumph of humans over disease.

Despite the impressiveness of the eradication of malaria on the island, it was not a guarantee of future success. The disease was eliminated with pesticides alone largely because Trinidad is relatively small and, as an island, isolated. Also, the DDT spraying was comprehensive and done quickly. The pesticide managed to kill off enough malarial mosquitoes to wipe out the disease before the vectors began to develop resistance to it. These conditions and the corresponding successful results are not typical for most of the world. In most places it is not possible to wipe out the disease before too many DDT-resistant mosquito mutations are selected for and the sprayings become useless. This resistance was a major reason that the WHO abandoned its attempt to eradicate all malaria with pesticides (Hemingway 96).

The obstacle of pesticide resistance is not insurmountable though. With an understanding of the evolutionary factors that produce resistance it is possible to find ways to counter it. One useful way of utilizing this knowledge is to catalogue the genomes of vectors. This allows researchers to discover the specific forms of the mutations that confer insecticide resistance in malaria-carrying mosquitoes. This knowledge will help us predict the effects that different pesticides will have on the mosquitoes. If we can see what chemicals may still kill a mosquito with a particular set of resistance mutations, then we can deploy pesticides only in mixtures that will be effective (Hemingway 97). This will protect us from using ineffective pesticides and unnecessarily building up resistance in the *Anopheles*. This exploration could also reveal characteristics of the vectors' proteins that could be targeted by new chemical mixtures (Hemingway 97).

This approach could be combined with the strategy of zooprophylaxis, which relies on the fact that cattle are dead-end hosts for human *Plasmodium* but are also potential food sources for the vector. If the mosquitoes can be induced to feed on cattle rather than humans, then the cattle will become infected but the *Plasmodium* will be unable to continue their life cycle (Kawaguchi 301). The closed path of transmission from person to mosquito to person will be stopped and the malaria will die out. Since the necessary increase in cattle density to induce zooprophylaxis also increases malarial mosquito density, this is not a workable strategy when used alone (Kawaguchi 301). However, if it is appropriately balanced with effective pesticide use, zooprophylaxis could be a part of a successful malaria control effort (Kawaguchi 309).

This multi-pronged attack on malaria vectors is a promising strategy in the fight against the disease. By accounting for and confronting the evolutionary factors that make targeting malaria vectors so difficult, it is theoretically possible that malaria could be

eradicated worldwide. However, this is only true if, as it was in Trinidad, the assault on malaria is coordinated and carried to completion and this is only likely to happen in wealthy or isolated countries. It is practically impossible on a global scale. Wars, political instability and conflicting national and personal interests would prevent any attempt to impose the necessary discipline to eradicate all malaria. Unfortunately for the millions of people who suffer and die from malaria every year, the Trinidad success story will not be repeated on the world stage in the foreseeable future.

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The Mysteries of Arthritis

Kevin Chu

Arthritis is a crippling illness that has been omnipresent since the pre-historic times of dinosaurs and early land-walking species. The disease currently afflicts millions of victims worldwide. According to the Centers for Disease Control and Prevention (CDC), in the United States alone, 46 million Americans have some form of arthritis, and millions more are diagnosed every year. The debilitating ailment can cause severe pain for its victims, and many are hospitalized annually. Contrary to what many people think, a small percentage of sufferers actually die from arthritis related complications. Over 50% of those over the age of 65 report being diagnosed with the disease.[1] With such staggering numbers, it's hard to believe that arthritis is not a contagious illness spread by a bacteria, virus, or other microbe as postulated by the germ theory of disease. In fact, almost every human being is at risk of developing arthritis regardless of the precautions they practice.

Even though we are armed with this alarming information, many people still do not fully understand this chronic condition that plagues more people than almost any other disease in America. Thus, the purpose of this paper is to provide readers with a general overview of the history, human anatomy, symptoms, causes, statistics, diagnosis, and treatment regarding arthritis and its many forms to help elucidate its mysteries. In addition, I will discuss the discrepancies that exist between people living in the 1st world and 3rd world countries. This analysis will help us better understand why arthritis is more inclined to strike people in certain demographics.

Throughout history, handicapped and disabled people have been down upon as mentally weak or deliberately crippled by God for their moral failings. A stigma was placed on such victims in the past. Instead of receiving the treatment they needed, many were neglected or placed in homes for the "feeble minded". Unfortunately, with limited scientific knowledge prior to the 20th century, these victims could do little to ease the pain. Most could not partake in the daily activities they used to enjoy. Instead, they were bedridden or reduced to hobbling along with canes or other walking devices. A significant percentage of those handicapped sufferers were likely afflicted with arthritis. Luckily, science and medicine has developed rapidly in the past few centuries, thus enlightening people on the truths of this illness.

Arthritis translates directly from the Greek roots arthro-, joint, and –itis, inflammation.[2] This is exactly what arthritis is, a chronic malady that causes mild to severe inflammation in the joints of patients, leading to painful sensations that differ depending on the extent of the damage. Joints are places throughout the body where 2 bones are connected together by different means. There are 3 types of joints: fibrous, cartilaginous, and synovial. Fibrous joints are immovable since they connect bones via the connective tissue known as collagen. The most obvious example of fibrous joints is skull sutures, which form as the bones in the head fuse throughout the stages of infancy. On the other hand, cartilaginous joints are made of cartilage, which acts as a cushion between bone to bone contacts. They are slightly mobile compared to fibrous joints.

Two examples of cartilaginous joints in the human body are the sternum and vertebral discs in the spinal column, which make up most of the cartilaginous joints in the body. The most common class of joints is called the synovial joints.

There are many different types of motions that synovial joints can perform: gliding, angular, rotational, pivot. Gliding joints are found inside the spine, wrist and ankle. They do exactly what their name suggests; they allow for a smooth gliding motion between bones with limited movement. On the other hand, angular joints, commonly known as hinges, connect long limbs to each other. Two examples of these types of joints are the elbow, where the humerus joins the ulna, and the knee, which joins the tibia to the femur are two examples of these types of joints. Rotational joints are ball and socket models that permit the greatest range of motion due to their mechanical structure. The hip and shoulder joints are the only rotational joints in the human body. Pivot joints are even rarer and can only be found in the elbow and neck vertebrae. They allow for a limited twisting motion without any angular displacement.[3]

The synovial joints are where arthritis strikes, often with devastating consequences. There are over a hundred different forms of arthritis, but most of them attack in the same manner. The disease progresses when the cartilage in the affected joint is degenerated. This can happen from wear and tear of the joint. The term for this condition is known as osteoarthritis. If the synovial membranes in the joints are inflamed as a result of an auto-immune condition, called rheumatism, then the destruction of cartilage can also result in joint stiffness and pain. To understand why inflammation leads to the lysis of cartilage, it's important to understand its structure and function.

Cartilage is a soft, connective tissue that lacks nerves and blood vessels. It consists mostly of chondrocytes, cells that build and maintain the cartilage in joints. This matrix is comprised mostly of proteoglycan and collagen. Proteoglycan consists of a protein known as aggrecan surrounded by carbohydrates. It serves to filter the movement of molecules throughout the extra-cellular matrix. Collagen is the main source of connective tissue in humans and abundant is throughout the body. During joint compression or motion, the synovial membrane is squeezed and releases its fluid into the cartilage to smooth out the grinding. When pressure is released on the joint, the fluid is replenished.[4] Non-rheumatic people do not feel pain when their joints are compressed because cartilage is avascular and aneural. As time passes by, the cartilage in their joints may wear down but it is immediately repaired by chondrocytes in their joints. Unfortunately, people afflicted with arthritis are not so fortunate.

During inflammation of the synovium, the cartilage is degraded by a specific enzyme known as Matrix metalloproteinase. MMP is widespread throughout the body and plays a major role in the growth of tissue via the proliferation of body cells. Unfortunately, MMP also has the capability to completely lyse the cartilage in joints. Normally, MMP is inhibited by the body's regulatory and feedback mechanisms. These Matrix metalloproteinase inhibitors (MMPI's) are found in the synovial fluid. They come in contact with MMP in the synovial membrane and prevent them from reacting with the cartilaginous matrix. However, people suffering from osteoarthritis and rheumatism do not properly inhibit MMP in the affected joint regions. When the synovium is inflamed, MMP is released directly onto the cartilage, thereby avoiding the inhibitors. They begin to break down cartilage rapidly before the chondrocytes can rebuild it.[5] Ultimately, the cartilage becomes jagged. As a result, it can no longer serve as a proper cushion between two bones. The subsequent bone on bone grinding causes pain because bones are innervated.

The two most common types of pain associated with arthritis are dull pain, and sharp pain. Dull pain is a low intensity degree of pain, often associated with annoying, "aching joints." The discomfort that dull pain causes is often spread throughout the entire joint region, and persists as a result of inflammation in the general area. Arthritic patients constantly feel dull pain regardless of their activities. On the other hand, sharp pain comes about when a person moves or applies weight on his or her joint. The person experiences a painful stabbing sensation that can oftentimes be excruciating. The main cause of this type of pain is the bone on bone grating found in advanced stages of arthritis. Oftentimes, the grinding will lead to deformation of the bones and creation of bone spurs known as osteophytes.

As previously stated, there are well over a hundred different types of arthritis. The most prevalent forms are osteoarthritis, rheumatoid arthritis, and psoriatic arthritis. Osteoarthritis accounts for over 50% of all cases in America.[6] This is the type of arthritis that most people know about; joint pain due to the wear and tear of the limbs. This condition usually develops as people age. The proteoglycan and collagen content of the cartilage decreases, while the percent composition of water increases. The chondrocytes are not able to maintain the cartilaginous matrix, and thus the joint slowly degenerates. In certain situations, some people develop osteoarthritis at a relatively young age from the constant overuse of specific joints. Long distance runners and tennis players can quickly succumb to osteoarthritis in the knees due to the constant high pressure pounding of the joints. Other people who constantly type on a computer keyboard can also develop this form of arthritis in their fingers and wrists. Once osteoarthritis begins its onslaught, there is little the patient can do to stop the disease's progression.

The most common clinical procedure for diagnosing osteoarthritis is to physically evaluate the joints and take x-ray images. Physicians will usually feel the area around the fingers, wrists, elbows, toes, ankles, knees, and jaws to determine if there is swelling or sensitivity. They will also move the limbs around to test the joint's functional range of motion. If there are noticeable signs of pain, inflammation, or loss of motion, then it is likely that the patient is afflicted with arthritis. X-rays are often taken to observe the joint area; they reveal if the cartilage structure has been damaged, or if the bones are deformed.

X-rays are a form of electromagnetic radiation that, because of their relatively short wavelength and high frequency, have the ability to penetrate through soft human tissue made out of "light" elements such as carbon, oxygen, and hydrogen. However, denser elements such as calcium in bone can effectively reflect the radiation that bombards them. In x-rays, the reflected electromagnetic waves appear white, which is why bones are white while soft tissue generally appears darker.[7] This radiation can be extremely harmful to the human body, so a technician must exercise the necessary precautions when generating x-rays. It is best to take as few images as possible, with a short duration of exposure, at a safe distance from the patient.

In the meantime, some people will also undergo magnetic resonance imaging (MRI) scans. MRIs work by using magnets that are attracted to hydrogen ions throughout the body. Electromagnetic pulses are emitted by the MRI machine into the patient; the resulting change in the proton gradient alignment produces an exothermic reaction that gives rise to images on film.[8] While x-rays often display only one picture from a certain angle, MRIs take dozens of images of the same area from different depths and varying points of view. Specialized radiologists will examine the multiple images on film and determine the integrity of the cartilage and bone structure. The enormous MRI devices are much more advanced than x-rays, and less harmful because they do not emit x-ray radiation. However, there are some risks

associated with using MRIs. Since they function by using extremely strong magnets, a person with certain metallic or magnetic transplants such as pacemakers in their body cannot undergo MRI scans. Otherwise, the machine would rip the device straight out of their body and kill the patient, which would not be beneficial to anyone

Additional tests are available to patients for diagnosing arthritis. Blood tests can be performed to rule out or confirm cases of rheumatoid arthritis, a form of joint disease that results from an autoimmune attack on the body. Specifically, the erythrocyte sedimentation rate (ESR) is a test measures the rate at which red blood cells settle into the bottom of a blood tube after an hour; this test helps determine the signs of inflammation in the body. Almost 100% of patients suffering from rheumatoid arthritis display a significantly elevated rate - almost 100 millimeters per hour - while the sedimentation rate in a healthy person steadies at roughly 1 mm/hr.[9] Unfortunately, high ESRs are found in non-arthritic victims with other diseases such as cancer or other inflammatory infections. However, if a person has been diagnosed with some form of arthritis, and displays a very low ESR, then the physician can safely rule out rheumatoid arthritis.

Oftentimes, arthritic victims will display narrower joint spaces on their x-ray or MRI film, because the cartilage is reduced in volume or completely destroyed. Bone spurs can also be spotted by radiologists. They form on the subchondral spaces in the ends of the bones. These osteophytes form from bone deformation because the surfaces of the bones are exposed to each other without the protection of cartilage and synovial fluid. Osteophytes restrict a joint's range of motion when they rub against each other; it is analogous to tightening a door hinge and coating it with sandpaper instead of loosening the screws and filling it with grease. Eventually, more osteophytes form as more cartilage and synovium is lost. This effect compounds upon itself so that as more cartilage is lost, more osteophytes are formed, and the joint gradually loses its range of motion until there is little to no movement left between the bones. In extremely severe cases, patients who have not properly exercised their joints will find that their bones begin to fuse. Unfortunately, they must also worry about the pain associated with joint preservation. When arthritic patients rest their joints, the pain is temporarily alleviated, but if they are moving their joints or bearing weight on them, the pain sharply increases. Therefore, the patients face a serious dilemma; they can either preserve the life of their joints by letting them function normally at the cost of moderate to intense pain, or they can let their joints decay and possibly fuse, but experience little pain throughout the ordeal.[10]

Official statistics recorded by the National Health Interview Survey (NHIS) have revealed startling details regarding arthritis in the U.S. In a 2003-2005 survey, 21.6% of all American adults were afflicted with one of the many forms of joint disease. The data clearly showed evidence which supported the notion that the prevalence of arthritis among the U.S. population increases drastically with age. 7.9% of adults ages 18 – 49 were diagnosed with the disease. 29.3% of men and women between the ages of 45 – 64 also had arthritis. Finally, an astounding 50% of senior citizens reported being diagnosed with joint disease by their doctors.[11] Even though this data seems plausible because many people expect to succumb to arthritis as they age, there are important discrepancies. Arthritis in fact does not strike victims indiscriminately; the NHIS divulges information that shows us how certain groups of people are more prone than others to acquiring the disease. Worldwide studies have been conducted documenting the prevalence of arthritis in other countries, but due to the small sample sizes and other logistical factors, we cannot draw concrete conclusions from them. However, better methods of epidemiology in the future will most likely produce more accurate results.

Most people believe that arthritis results mainly from the overuse of joints and the wear and tear of cartilage via constant physical activity, but the NHIS data reveal results that appear counter-intuitive. Almost 20 percent of physically active people reported arthritis, whereas a much higher 25% of inactive men and women had the disease. These paradoxical results can be attributed to the assumption that many of the physically inactive people were overweight or obese, whereas the physically active respondents were generally underweight or normal weight. If we take a look at the data again, we see that 16.3% of normal or underweight people had arthritis, 21.7% of overweight Americans reported the disease, and a resounding 31.6% of obese men and women were diagnosed with joint disease.[12] The ranges of these data are much greater than that of the data representing physical activity levels. Therefore, it is safe to conclude that obesity is more likely than intensive physical activity to cause of arthritis.

Unfortunately, obesity is an epidemic in America that is one of the leading causes of chronic disease in this nation. A person is classified as obese when his or her body mass index (BMI) is greater than 30. This value is determined by taking the mass of the person in kilograms, and dividing it by his or her height squared, BMI = kg/m^2. [13] Fortunately, Americans are increasingly aware of the obesity epidemic they currently face, so preventative measures in the future should stem the affliction rates of arthritis as well.

The reason obese people are more likely to develop arthritis is because they bear more weight on their joints. Cartilage, with the help of synovial fluid helps cushion the bones of a joint. Typically, the cartilaginous complex starts to decay as people age, because the chondrocytes cannot rebuild cartilage as fast as it's being broken down from daily wear and tear. With the added stress from obesity, the cartilage decay in arthritic patients is accelerated in the spine, hips, knees, and sometimes ankles. This is the reason why arthritis strikes Americans in much higher numbers than people of other nations. As previously stated, Americans are more obese than their counterparts in the rest of the world; this contributes substantially to this discrepancy. Increasingly sedentary lifestyles in developed nations have led to the development of significant health problems.

Modern advancements in medical technology have provided patients with the option to choose from a wide array of available remedies for arthritis. Since there is no cure for the disease, victims must contemplate the different short and long term treatment plans that they need to follow in order to delay or halt the progression of the arthritis. Medications, surgery, physical therapy and even diet and weight loss regimens are options that patients need to keep in mind to help prolong the life of their joints, and maintain or increase their joint mobility in order to carry on with daily activities.

The most common method for patients to combat arthritis is to take pain relief medication. Advil (ibuprofen), Alleve (naproxen), and Aspirin (acetylsalicylic acid) are non-steroidal anti-inflammatory drugs (NSAIDS) that work by reducing pain and inflammation of the patient's joints when given in high doses. Specifically, NSAIDS function by inhibiting cyclooxygenase, an enzyme that helps form a class of biological compounds called prostanoids. Even though prostanoids are beneficial to the body in certain ways, they also instigate inflammation during auto-immune attacks of the body. [14] The effectiveness of NSAIDS will vary because patients will respond differently to the drugs based on their biological makeup and the severity of the arthritis. Side effects include the formation of stomach ulcers. This occurs because cyclooxygenase protects the gastrointestinal muscles, so when the NSAIDS inhibit the enzyme, that protection is diminished. Unfortunately, these NSAIDS do not stop joint destruction; they merely provide temporary pain relief.

Instead of issuing over the counter medications, physicians can prescribe disease-modifying anti-rheumatic drugs (DMARDs) that may help stop the disease's progression, especially in rheumatoid arthritis, which is caused by an auto-immune response. Enbrel (Etanercept) was developed in the late 1990's, and it continues to be one of the most popular rheumatoid arthritis drugs on the market today. Enbrel is a tumor necrosis factor (TNF) inhibitor. TNF proteins are essential to the immune system because these molecules kill dangerous cells throughout the body. [15] Unfortunately, they are the main cause of inflammation in rheumatoid arthritis. Since this particular DMARD was invented only recently, scientists are still unsure about the long-term consequences of its prolonged use. However, it is certain that Enbrel arrests the progression of rheumatoid arthritis by suppressing the body's own immune system. Therefore, it is recommended that elderly people and cancer and AIDS victims are not subject to this form of medication.

A study evaluating the efficiency and effects of Enbrel was published in 2006 by Swedish rheumatologists. The clinical study group comprised of 549 arthritic patients who previously displayed no signs of improvement when taking other arthritis combating medications. All test subjects received two 25 mg subcutaneous injections weekly. Statistics revealed that there was a significant decrease in the number of people afflicted with joint swelling and pain, 72% and 71% respectively. The short term consequences of bi-weekly injections included rash at the injection site and infections. Several patients died, but from unrelated causes. There were a few reports of patients developing breast and lung cancer, but the small percentage was consistent with the general population; it's almost certain that Enbrel was not a contributing factor of cancerous growth. The study concludes that the DMARD Etanercept provided great benefits to many of its patients, and that the efficacy rate and safety of the drug was excellent.[16]

Cortisone steroid injections are also available for patients. Cortisone is naturally produced by the adrenal glands; it provides temporary relief when released into the bloodstream. Typically, these injections are used to treat tendonitis and lower back pain. However, in the case of rheumatoid arthritis and osteoarthritis, doctors can inject the corticosteroid directly into the joint space to reduce the inflammation of the cartilage. Corticosteroids are more potent than NSAIDS because in addition to reducing inflammation by inhibiting cyclooxygenase, they also block phospholipase A_2, an enzyme that's used in the lipoxygenase pathway of the inflammation process.

To pinpoint joint cavities located deep within the body, such as the hip and shoulder sockets, the surgeons will usually implement a technique known as fluoroscopy. [17] This procedure involves bombarding the patient with a constant source of x-rays against a fluorescent screen in order to obtain real-time images of the internal body structures. Of course, fluoroscopy is harmful to the patient depending on the duration of x-ray exposure during a prolonged operation, so the risks must be properly balanced with the benefits of the procedure. However, it is generally better to properly inject cortisone into the intended location when using fluoroscopy, as opposed to injecting into the wrong spot during a "blind" insertion.

Oftentimes, physicians advise patients against receiving multiple cortisone shots because there are potential side effects. Even though it may seem counter-intuitive, inflammation is part of the body's natural healing process. Corticosteroid injections may provide temporary pain relief as a result of reduced inflammation, but they will have deleterious effects on the joints in the long term. According to a study performed on rabbits, multiple intra-articular cortisone injections resulted in damage to the meniscus and a

decrease of proteoglycan in the cartilaginous matrix.[18] Therefore, it can be concluded that continually injecting human patients with corticosteroids will also lead to further cartilage destruction and progression of disease in the joint. It is recommended that people only receive 2-3 injections during their lifetime. The steroids usually only provide relief for a few weeks to several months, so alternate treatments must be found.

In addition to injecting cortisone into a joint, the physician can also draw out fluids to take a biopsy of the surrounding tissue. This can provide information regarding the patient's disease, and may help lead to a more accurate diagnosis and treatment plan. A similar method of making incisions into the joint for the purpose of extracting tissue is known as arthroscopy. A tiny fiber-optic camera known as an arthroscope is inserted into the joint to help display a live-feed video of the joint anatomy on a computer screen. A second incision is usually performed to create a space to stick the medical instruments into the joint. Often, the joint cavity is filled with a saline solution to expand the viewable space. There are several purposes for performing an arthroscopy on a patient.

The main goal of arthroscopy is to diagnose a specific type of degenerative joint disease. The arthroscope enables surgeons to carefully observe the joint to see which structures are damaged, and if there is loose debris. These floating pieces of cartilage can cause severe pain to the patient if left untreated. If the physician decides that it is necessary to remove cartilaginous debris from the joint, then he will perform arthroscopic surgery. Removal of the debris is a generally safe procedure with few risks. Of course, infections are possible as with all incision based surgeries, but the prevalence of infections among people undergoing arthroscopies has been very low.[19]

In recent decades, physicians have started performing a type of surgical operation that may increase the cartilage in the joints of arthritic people. This technique, known as joint distraction, utilizes a bizarre looking contraption known as an external fixator. It is a two-part metallic device that is attached to the two bones encompassing the joint via several thin screws that are drilled through the skin. When first introduced into the medical field, this surgical procedure was used to help stabilize bone fractures in victims who could not benefit from wearing a cast. However, throughout the decades, it has become a popular form of treatment for victims of arthritis as well. In the case of joint distractions, the external fixator is aligned with the body parallel to the limb, while a large screw connects the two pieces together. By reversing the screw every day for a set period of time, and leaving the fixation in the body for a few months, the two components will pull apart the bones and slowly decompress the joint. Since most of the pressure from the patient's body weight is placed on the external fixation instead of the joint, then it's possible for the articular cartilage to regenerate in the joint cavity.

Several risks exist while patients are bearing their external fixations. The most common problem is the possibility of acquiring infections at the sites where the pins pierce the skin. It is essential that the patients painstakingly clean and dress their wounds daily, because if an infection sets upon the wound, then the entire device must be removed before the joint is successfully distracted; they will have suffered intense pain without gain. For people with external fixations of the hip, knees, or spine, the problem of moving around without bumping into other objects is also a problem. These bulky devices can protrude up to about 6 inches from the body, so patients will experience discomfort when performing certain actions such as sitting or lying down. Another issue is aesthetic; it's rare for people to see others walking around with huge metal contraptions projecting out of their limbs, so most pedestrians would stare at these victims and cause unwarranted shame. However, it's best for the device wearers to live with their

stigma for only a few months in the hopes of regenerating their joints.

In order for the external fixation to accomplish its goal of healing the diseased joint, the patients must make commitments on their own part as well. They must use a continuous passive motion (CPM) machine for as long as the external fixator is attached to their body. The orthopedic surgeon Dr. Robert Salter first invented the device in the 1980s; since then, it has become a crucial component of the post-surgical recovery regimen. CPM machines work by moving the limbs back and forth in a 2-dimensional reference frame around a joint without having the recuperating patients exert their own strength. The patients usually stay strapped onto the machine for several hours a day. The most common CPM machines move the knee and hip joints; they are analogous to large, cushioned braces. The device helps maintain range of motion in the joint, and it can also help stimulate cartilage growth. This occurs because the joint moves without pressure on it, so the synovial membrane can release nutritional fluids easier into the cartilaginous matrix. In addition, blood flow to the area is increased, so the overall health of the joint is maintained following major surgery.[20]

Unfortunately, joint distractions are not always successful. A study performed from 1979 through 1982 involved 80 patients who were subjected to hip joint distractions via external fixations. Forty two of the people evaluated experienced signs of joint improvement or cartilage regeneration. These patients were all under 45 or were diagnosed with milder forms of arthritis. On the other hand, 4 people over the age of 45 displayed joint regeneration. However, 24 of the victims showed no signs of improvement; most were over the age of 45 and some had severe inflammatory arthritis. This led to the conclusion that joint distractions were more successful with younger patients with non-severe cases of arthritis, whereas elderly people and those in the advanced stages of arthritis received little to no benefit from the procedure.[21]

The next option available to arthritic patients who have lost most or all of the cartilage in their joints is partial or complete resurfacing (arthroplasty). The modernized form of this surgical procedure is less invasive than a total hip replacement; instead of completely replacing the femur head and part of the pelvis, the surface of the bones is layered with an almost frictionless cobalt-chromium metallic complex.[22] Resurfacings performed as early as the 1980's often failed due to crude technology and techniques. Back then, there was a high possibility that metal ions could be released into the joint and damage the affected area. However, as medical technology progressed throughout the decades, the success rates and lifespan of the resurfaced joints have greatly increased.

Clinical trials were performed and evaluated from 2000 through 2006 with two different techniques of resurfacing technology. Prior to an investigatory meeting on arthroplasty in 2003, a group of 292 patients were given 292 hips made out of a form of plastic known as polyethylene. After that meeting, a group of 614 patients received a total of 727 hips that comprised of cobalt-chromium-molybdenum on cobalt-chromium. Ultimately, the metal-on-metal resurfacing techniques resulted in higher survival rates for the joints, and fewer complications. According to the study, 7.2% of the polyethylene femoral necks fractured, while only 0.8% of the cobalt-chromium necks ended with the same result. Revision rates of the two types of resurfacing dropped from 13.4% to 2% with the implementation of the new metal technology. Ultimately, these promising results can grant hope to arthritic victims; better technology in the years to come will reduce the need to undergo total joint replacement or receive multiple resurfacings.[23]

If all else fails, complete joint replacement surgery oftentimes is the last resort for patients with arthritis. People need to

undergo these surgeries because the cartilage is nonexistent, and the bone surfaces have been so deformed from grinding that it is no longer possible to resurface them. Luckily, recent advancements in medical techniques and chemical materials have led to increased survival and success rates for the artificial joints of the 21st century. Currently, joints are replaced with cobalt-chromium alloys, similar to resurfacings. However, there is a major difference between the two types of operations; we will use the hip joint as an example. During a resurfacing, the surgeon will reshape the femoral head with a metallic cap that will act as the new joint surface. In a replacement, the entire femoral ball is removed from the rest of the bone, and a new metallic head is anchored into the femur. The lifetime of these artificial joints can range from 10 to 20 years, but in the future it is possible that it can be extended to 30+ years. It is best to avoid total joint replacements until later on in life, because undergoing multiple hip replacements is generally not desirable. Fortunately, the recovery time for joint replacements has significantly reduced due to increasingly smaller incisions through the muscle.

Another form of long-term treatment that arthritic patients can pursue is intensive physical therapy. The first purpose of this exercise regimen is to maintain muscle strength to reduce pressure on the joint, or to recover from muscle incision during surgery. The second benefit of physical therapy is to help maintain or increase range of motion in the diseased joints. Depending on which joints are affected and the extent of the disease, physical therapists will formulate unique training plans for their patients to help with their rehabilitation. In the case of a person with hip arthritis, a typical workout would include the following muscle strengthening exercises: warming up on a stationary bicycle or treadmill, straight leg raises and heel slides on a table, hip abduction with rubber tension bands, hip adduction against a small medicine ball, squats against a wall, standing knee raises etc. In the meantime, the physical therapists can also apply heating pads in order to loosen the muscles and ligaments before manually stretching out the patient's limbs.

One of the most important types of treatment that arthritic patients can receive is hydrotherapy; there are many forms of hydrotherapy, but most involve training swimming pools. When patients walk or swim in water, their joints experience very little pressure from body weight. This occurs because the force of buoyancy nearly equals the force of gravity, so people can float or barely touch the pool floor. This medium provides the perfect atmosphere for patients to exercise their muscles against water resistance and work their joints. Treading water is one of the best full-body exercises that people can perform without weight bearing; it makes it easier for the synovium to release fluid into the joints to help lubricate and possibly rejuvenate the cartilage.

An ongoing study beginning in January 2009 and ending in December 2010 will compare the effects of Kneipp hydrotherapy and physical therapy among three groups of patients. This form of hydrotherapy involves water affusion – alternating between hot and cold water massages to the joint area.[24] The theory behind the treatment is that this will increase circulation in the area, so that more nutrients are brought into the joint space. Furthermore, hydrotherapy should boost the immune system of the patients.

For this experiment, 180 people with osteoarthritis in the hips or knees were apportioned into three sections of 60 each. One group received only hydrotherapy, a second group received only physical therapy, and a third group got both hydrotherapy and physiotherapy. The researchers expect that the third group of patients will show a greater improvement than the other two cohorts.[25] An original clinical trial consisting of 30 patients was monitored in Germany under the same conditions, but with the small number of test

subjects, the results were not statistically reliable. Since there are 180 patients in the current trial, the results should prove more acceptable. After the end of the study period, the patients will be evaluated for reduction in pain, increase in mobility, and increase in quality of lifestyle. Pain will be measured by the Lequesne index, while quality of life will be rated according to the German Arthritis Impact Measurement Scale (AIMS2).[26]

The purpose of this experiment is to discover new, cost-effective methods of long-term arthritis treatment.[4] Until recently, buying over-the-counter NSAIDs and prescription DMARDS was the only continuous treatment plan for arthritic patients. However, these medications resulted in many detrimental side effects including gastro-intestinal irritation and reduced immunity. According to the authors of this study, Kneipp hydrotherapy will prove to be a cheap and convenient alternative to taking risky medications. In the meantime, other areas of arthritis research have developed in recent years.

The popularity of Glucosamine supplements has exploded in the past few years. Glucosamine is a sugar that's used in the formation of Glycosaminoglycan, which in turn connects with certain proteins to form proteoglycan; this protein complex is used to create articular joint cartilage.[27] Pharmaceutical companies have advertised that the products can reduce the loss of cartilage in arthritic joints, or even regenerate it after continuous consumption. In theory, Glucosamine should increase the production of cartilage and inhibit metalloproteinase; thus it can act as a matrix metalloproteinase inhibitor. However, these products are not FDA approved, so many researchers have questioned the reliability of these "medications". Multiple studies were published regarding the efficacy of Glucosamine complexes.

In particular, one experiment in 2009 evaluated the effects of Glucosamine sulfate treatments on patients with knee arthritis. 60 people were split into two groups of 30; the first group orally received 1500 mg Glucosamine daily for 12 weeks, while the second group received a placebo powder that appeared identical to the real medication. The study measured subjective and objective data from the patients. Tolerability to the Glucosamine supplement and changes in pain levels were reported by the patients. Blood tests evaluating the "erythrocyte sedimentation rate, C-reactive protein, glucose levels, creatinine, complete blood count, and electrolytes" were also used to provide concrete statistical data.[28]

According to the results of the experiment, patients given Glucosamine orally experienced significant decreases in pain levels when stationary and when moving. Furthermore, NSAID consumption decreased in the experimental group, because the alleviation in pain reduced the need to take the anti-inflammatory medications. There were also signs of increased mobility in the knee joints. These results have shown that Glucosamine may indeed be a viable, long-term treatment alternative to other NSAID and DMARDS. However, due to the relatively small size of the examined group, more research will need to be conducted in the future to help solidify the beneficial effects of Glucosamine supplements.[29]

Proper diet and weight loss regimens have also been integral to preserving the health of a patient's joints. As previously noted, obesity is one of the leading contributions to the onset of osteoarthritis. For every extra pound of body weight a person carries, an extra 6 pounds of pressure are placed on the hip joints. The ratio is even greater for the knees and ankles, since they are further down in the body, and thus carry more weight. Obesity is endemic in America; if the nation as a whole cuts down on the excess fat, then there will be a significant decrease in all types of medical maladies, including heart disease, diabetes, and of course, arthritis.

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Anthropocentricism and the Synthesis of Human Beings

David Sanchez

Traditionally, vulnerability, free will, and emotion are universally accepted values deemed essential to the conception of the human condition; thus, as its name suggests, the *human condition* is encapsulated solely within the confines of a corporeal entity assumed to pertain to the species *Homo sapiens*. The capacity to clone animals has enabled the possibility of synthetically and scientifically reproducing these strictly humanistic values under the guise of genetically identical replicas. Questioning the ontological ramifications of such a revolutionary practice is of utmost importance. Are these genetically identical replicas entitled to the same privileges of *natural* human life due to their commensurate human-like qualities (i.e. genetic makeup, emotional response, and semblance) or are they codified to a level of inferiority, and thus blatantly subjugated, due to their scientifically *synthetic* nature?

In the book Never Let Me Go by Kazuo Ishiguro, the narrator Kathy articulates her status as a thirty-one-year-old "carer," or nurse who specifically takes care of human clones whose sole purpose is the provision of organs to naturally conceived humans. Kathy details her atypical childhood experiences at her primary educational institution, Hailsham, where she was often left perplexed by the idiosyncratic rules and regulations set forth by the institution and it's "guardians." Unbeknownst to all its students, Hailsham wasn't a school for the gifted or talented; rather, Hailsham served as an experimental institution where the only criterion for attendance was belonging to the class of human clones. These human clones were subjected to abstract tests by these "guardians" in an attempt to find an inherent sense of the human condition in order to facilitate their social acceptance. Unfortunately, this progressive institution ultimately failed in accomplishing this endeavor. The story ends with Kathy's realization that her struggles to uncover the truth behind Hailsham were done in vain as she could never escape her inevitable fate as an organ-donating clone. Kathy would "complete," or essentially die as a result of complying with her societal niche as an organ donating clone.

If synthetic clones were introduced into mainstream "natural" society, would entitlement boundaries shift? Ishiguro's account of the future offers a bleak answer to the prospect of privilege between natural and synthetic beings. For one, the institutional "guardians" were all accorded a complete degree of freedom and personhood; something as rudimentary as shopping outside the boundaries of their elementary institution was permissible only for the "guardians." Conversely, the imposed dynamic for clones stymied societal progression. Their code for dress was stringent. They were only allowed to talk amongst themselves. Long term relationships were disparaged, meaningless sex was covertly encouraged. The clones had their life predestined without much room for breaking convention.

The underpinnings of this story recapitulate notions of "political" docility expounded upon by Michel Foucault in the piece titled "Docile Bodies" from the book Discipline and Punishment: The Birth of the Prison. Foucault elaborates how the promise of

peace, as a form of utilizing "politics" to instill order and subservience, is "no doubt a real force, an ever-threatening sword…it was a technique and a body of knowledge that could project their schema over the social body (186)." Parallel to these militaristic descriptions Foucault offers, utilization and optimization of the social body on a collective scale by means of disciplinary action (via the educational institution) through the vehicle of promulgating certain knowledge, or what Foucault refers to a "politics," was meant to produce efficacious organ donors who feared resistance and accepted institutional repression. Hailsham was antithetical to this notion as a lenient, experimental institution with an egalitarian vision that failed to subvert Katy's, Tommy's, and Ruth's inquisitive minds and, consequently, rebellious behavior (i.e. perusing pornography magazines). However, the uncovering of Hailsham's failed endeavors and its subsequent downfall substantiated a particular set of "truths" that effectively subordinated the soon-to-be organ-donors into compliance and acceptance of their prospective reality. Kathy's inability to escape her predetermined organ-donating future after finding love with Tommy was not going to delay her donations; furthermore, she came to accept her inability to procreate. The "political" promise held in this regard was static social order, the hierarchy of clones and humans didn't change. Compliance, through subjection, equates to order.

It is important to note how this particular stratum of subjection relates only to those who are clones as the role of organ-donation was imposed upon them since their creation. This moment of creation, where strictly human genetic information was utilized to create an organism possessing the same *human condition*, is continually devalued in society as only useful for the propagation of other naturally-conceived human species; this demonstrates an underlying sentiment of anthropocentrism. Thus, the subjection of the clones also helps to the perpetuate a hierarchal class structure that shackles the organ-donating clones to a predestined future and ensures repression by means of lack of entitlement to freedom. In Ishiguro's prospective world where clones and humans coexist, the synthetic entities remain subservient to those who willfully synthesized them and willfully deny them rights. This begs the question: would these postulated social disparities stop our civilization from creating synthetic beings (i.e. clones created through the avenues of medicine) merely as a means to an end?

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Malaria: A Worldwide Epidemic

Julie Webb

An ongoing worldwide concern revolves around the number one infectious disease killer on the planet. Threatening two billion people and killing two million people annually, malaria serves as a compelling case study for the impact of infectious disease on the human population. The parasitic protozoan *Plasmodium* that causes malaria has been around for millions of years, but more recent human influences on ecology along with cultural changes have made this disease endemic to a large portion of the world. In looking at the history of malaria and the way in which human actions have shaped its development, we must, as always, look through an evolutionary lens. As Williams posits, "…there is no kind of medical problem for which a knowledge of our evolutionary past and the continued action of natural selection cannot provide an important aid to understanding" (Williams, 2001). Why have certain 'genetic antimalarial' diseases persisted in human populations? Why have attempts to attack the vector or the parasite behind the disease failed? The forces of evolution are vital in understanding and explaining this complex story.

We can start with a small scope to see how this disease works. Mosquitoes serve as the vector that carries the parasite *Plasmodium* from human host to human host. *Plasmodium falciparum* and *Plasmodium vivax* are the most common strains of the parasite, with *P. falciparum* being more dangerous and accounting for about 93% of worldwide cases in 2008 and the majority of deaths (WHO Report, 2009). When the mosquito bites the human, the parasite enters the body and rapidly travels to the liver. It resides there or can remain dormant for months and reproduces before entering the bloodstream and the red blood cells where it runs throughout the body. Because the plasmodium goes through multiple phases of growth and lives within the red blood cell, this parasite is good at avoiding the immune system. Symptoms of malaria include fever, chills, vomiting, convulsions, and brain damage resulting from cerebral malaria. The disease spreads when another mosquito bites the infected individual and then in turn bites another human, thereby continuing the cycle.

With this background in mind, we should begin by analyzing the origins of this pathogen. About 50 million years ago, the ancient *Plasmodium* genus began to infect ancestral primate species as part of a complex two-host life cycle. These Plasmodia had already evolved a vector-borne technique, whereby they took advantage of the increased transport opportunity provided by blood-feeding insects to travel more easily between hosts and eventually also reproduce inside of the insect. Around 40-50 million years ago, mosquitoes seemed to have become the vector of choice. Studies of evolutionary molecular biology show that simian origins 25-50 million years ago account for three of the four plasmodium species that infect humans. Different forms of malaria then evolved within apes over the past 10 million years and then either developed in the early hominids from an arboreal existence, or jumped the species barrier to early humans through sporadic zoonotic infection (McMichael, 2001).

From these origins long ago, how did malaria come to be endemic? Human patterns of settlement and culture and interaction with the environment over the more recent history help to explain how the population became dense enough to provide a reservoir of hosts for malaria to thrive. The Holocene interglacial epoch that began about 10,000 years ago marked the beginning of warmer temperatures and was followed by the beginning of agriculture. At this time, people began to settle into farming communities and living in larger villages. Although malaria was present in humans before the dawn of an agricultural lifestyle, the accelerating deforestation and fostering of pools of still water on the landscape coupled with larger populations living together caused malaria to become a major infectious concern in the past few thousand years. More recently, the rapid increase in human mobility due to international sea trade has facilitated the spread of the disease. European conquests of colonial times brought *P. vivax* into Latin America, while the slave trade later brought the more malicious *P. falciparum* from West Africa into the Americas (McMichael, 2001). In the course of just a few hundred years, malaria became a truly worldwide endemic due to human action and technological development.

While humans and their cultural patterns have affected disease patterns and the environment, conversely, infectious disease is one of the major environmental agents of natural selection that has acted upon human populations over time. This tenet helps explain the reason why we see various diseases involving hemoglobin structure persisting in certain populations and regions of the world. Because "malaria is an ancient affliction of humankind…co-evolution has therefore brought about some mutual biological adaptation" (McMichael, 2001). As humans have coevolved with this disease over time, it has served as a powerful influence that generates selective pressures for certain randomly-occurring mutations to survive. Essentially, humans in malarial regions have developed various defenses against the disease. By taking an evolutionary approach, we can see that the overlap of the distribution of sickle-cell traits with endemic malaria areas is not coincidental.

A sickle-cell case study serves as the best-known example of a natural 'genetic antimalarial.' The sickle-cell trait involves a single base mutation at the DNA level that changes a single amino acid sequence, thereby changing the shape of the protein. This mutation changes the hemoglobin structure so that the red-blood cells are sickle-shaped and cannot properly carry oxygen or clot. People that are homozygous for this gene suffer from symptoms such as bacterial infections, blocked circulation, organ degeneration, and painful joints. Many of these people die during childhood without proper medical care. Heterozygotes, on the other hand, have a mixture of the normal hemoglobin A and the abnormal hemoglobin S and suffer no symptoms or only mild anemia. "In red cells of sickle-cell heterozygotes, infection by the malaria triggers sickling, and the sickled cells are subsequently destroyed by the patient's body. Those infected cells that survive provide a poor environment for the parasite's further growth" (Diamond, 1989). Heterozygotes therefore are resistant to malaria. People that are homozygous for the normal hemoglobin A therefore are prone to malaria, while people that are homozygous for the abnormal hemoglobin S easily fall ill or die from the disease.

The question, however, arises: If most homozygotes die of sickle-cell anemia, how has the sickle-cell gene survived? The answer is that the survival advantage conferred from retaining a large percentage of heterozygotes in a population under constant threat of malaria is a powerful enough force to maintain the deadly sickle-cell gene. It is the price paid for protection against malaria. This constant tradeoff is a balanced polymorphism that helps explain why in some parts of Africa—those most endemic for malaria—40% of the

population carries the gene as a heterozygote. The sickle-cell gene has persisted because it does more good than harm; the small portion of the population which dies from sickle-cell anemia is somewhat insignificant compared with the larger portion of the population which can survive malaria. In fact, the sickle-cell gene mutation did not just occur once and then distribute itself. It arose independently and at least five mutated versions have survived (Allison, 2002). Jared Diamond describes the general group of abnormal hemoglobin structure diseases that in certain forms resist malaria:
"These seem to me beautiful examples of how evolution works in our own species. Malaria…has been a prime target for natural selection. Mutations produced thousands of red cell abnormalities…Dozens did prove useful and have repeatedly arisen identically or with slight variations. All these useful antimalarials rose independently to high frequencies through natural selection" (Diamond, 1989).

Humans have also attempted to combat the disease by attacking the parasite through the development of antimalarial drugs and vaccines, or attacking the vector through the use of insecticides. While certain treatments have proved effective for particular intervals in time, socioeconomic and evolutionary factors have prevented these approaches from being successful in completely eradicating this disease. There is a wide-range of antimalarial drugs that have been used over the past decades, but drug resistance has become a major problem. With the short life-span of the plasmodium parasite, natural selection occurs rapidly. As a consequence, the few parasites which have a mutation that allows them to survive in the face of an antimalarial drug will propagate rapidly. The mosquitoes then carry and spread the drug-resistant parasites that survive. If brought to an area where only one type of antimalarial drug such as chloroquine is available, that drug soon becomes ineffective for many cases and the situation gets worse. Drug-specific mutations begin to accumulate and the very basis by which we are trying to control malaria is lost. The same is true for trying to get rid of the vector of the disease. Mosquitoes also have a relatively short life-span, so they too can evolve rapidly as selection acts upon mutations that provide resistance to insecticides like DDT, which used to be widely effective. Now in some areas, 80% of mosquitoes are resistant to DDT.

To work on eliminating malaria, we need effective, safe, available, affordable, and acceptable antimalarial drugs that will lead to effective diagnosis and treatment of this disease. The richer nations of the world that have achieved malaria eradication happen to be in areas that were not particularly endemic. Sub-Saharan Africa is suffering the worst from this infectious disease. About 85% of malaria cases occur in this region and the socioeconomic status of these countries and others in South-East Asia and the Eastern Mediterranean continue to perpetuate the problem because medical care is inadequate and antimalarial drugs are not readily available (WHO Report, 2009). There is also a lack of proper resources or motivation to research new avenues. "These drugs are all we have available now to treat malaria. It is difficult to see where the next generation of antimalarial drugs will come from…there is little pharmaceutical industry interest in developing new antimalarial drugs; the risks are great, but the returns on investment are low" (White, 1996). Weak economic growth and GDP hurts the quality and availability of medical care and vice-versa; the fact that so many people are sick and dying from malaria and disrupting families hinders economic growth.

Not surprisingly, drug resistance is a serious concern. "For years the medical community combated the disease with chloroquine—a cheap, effective drug that did much to alleviate the situation. But chloroquine resistant malaria emerged and spread over the next few decades. Today resistant strains flourish in Asia, Africa, and South America"

(Wong, 2000). Not only does this issue serve as a blow to poorer nations trying to eradicate, treat, or ease the effects of the disease, but the major problem of cheap counterfeit drugs creates even more problems. The drugs often cause more harm because they contain too little of the active ingredient to be effective, but enough of it to cause drug resistance (Peeples, 2009).

The current outlook for malaria and its elimination in the endemic regions of the world is somewhat grim. So far, the human genetic antimalarial improvised evolutionary responses, like sickle-cell trait, have proven more consistently protective against malaria than the development of drugs, vaccines, or insecticides (McMichael, 2001). If we look through an evolutionary lens and recognize the patterns of resistance prevalent among the parasite and mosquitoes, we can try a new approach, such as universally switching antimalarial drugs every few years to avoid the development of resistance. Such experimentation on a global level would require jumping huge socioeconomic and political hurdles, and would require much coordination on the international level. Perhaps the sequencing of the mosquito and plasmodium genomes will provide insight into new routes of attack.

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Prospective Approach to Cancer Treatment: Targeting Telomerase and p53 Inhibitors

Aransiola Fakorode

Background:

Cancer is a genetic disease that ignores growth regulatory factor such as density-inhibition, cell-to-signaling, and intermembrane signaling molecules. Cancer can be caused by cytoplasmic and non-cytoplasmic factors such as UV radiation, carcinogenic chemicals, and mutation at the cellular level. Understanding how cancer cells form and function in the tissues requires the knowledge of DNA replication, which begins with the unwinding of the DNA helix by the helicase enzyme. Two complementary strands of DNA, lagging and leading strand, are synthesized in different directions. Leading strand transcription proceeds from the 5' to the 3' end of the strand. The 5' end consists of repeating sequences of G bases, which will later become an important factor in the protection of the matured m-RNA from enzyme degradation in the cytosol. During each consecutive replication of a lagging strand, the 5' end of the nascent strand becomes shorter until the point that the cell will have to manipulate the gene sequence to extend the 5' end region. A result of this intrusion in the genome is either a mutation in the lagging strand or apoptosis (cell death). (Peng et al, 433).

The 5' UTR region is referred to as the telomere. The enzyme telomerase extends the 5' UTR by detecting the G sequences in the pre-mRNA and using its RNA, the telomerase RNA (TERC) (Goldman et al, 17119) as a template for the extension of G region in reversed direction to the synthesis of the 5' to 3' leading strand. However, the somatic or non-gonad cells have deactivated telomerase, which means that cellular aging caused by the shortening of the telomere is inevitable. The synthesis of the leading strand goes in the 5' to 3' direction without any distortion. In other words, the DNA polymerase III adds DNA molecules to the 3' OH group of each DNA segment's starting at 5' end of the RNA primer. As a result of this strict rule, the lagging strand is synthesized as Okazaki fragments, short nucleotides of RNA particles. Unable to complete the last 5'UTR region on the pre-mRNA strand, the enzymes do not perform the rest of the function leaving the 5' end to be shortened during replication.

Introduction

The onset of cancer development occurs after the disruption in cellular regulation by external factors such as UV radiation or carcinogenic agents (Campbell et al, 376). The oncogene, which codes for cancer, is the mutated version of the proto-oncogene that controls cell cycle and cell regulation at the cellular level. Proto-oncogene is the "unmodified" (King) and natural version of the oncogene in the cell that initiate cell growth and division in the human genome. A proto-oncogene may be converted to an oncogene by amplification of the "protein product" (Campbell et al, 374), point mutation in the genome, and integration or insertion of retrovirus gene products into the genome (King). One of the most important oncogenes in the genome is the ras oncogene, which contains

a G-protein that receives and relays signals to kinase enzyme pathways. The ras gene requires a GTP molecule (Luo et al, 836) to act as a co-factor in stabilizing the ras protein. At the point of signal transduction, a mutation in the ras oncogene may result in a "hyperactive" (Campbell et al, 376) ras protein that controls the cell cycle in the absence of extrinsic regulation factors. Oncogene expression may occur if the proto-oncogene mRNA becomes too short as result of point mutation preventing the binding of micro-RNA (mi-RNA). The mi-RNA hydrogen bonds to mRNA needed in protein translation at the 3'UTR end preventing the attachment of the ribosome subunit (Christine Mayr et al, 673-680). In addition, hyperactive ras protein may result from a mutation in the protein that prevents the hydrolysis of the GTP molecule after signal transduction; thereby leaving the protein in an immortal active state (Luo et al, 835).

When a situation such as the mutation in ras gene occurs in the cell, tumor-suppressor protein such as the p53 binds to a p21 gene that codes for a p21 protein, which acts as a traffic signal for cells undergoing transcription and replication. Mutation in the p53 may change the conformity of the p53 molecule; thus, becoming unable to act as a transcription factor for the p21 gene (PubMed). The p21 protein initiates the dephosphorylation of the ras protein by binding to the cdk2 protein that stimulates the cell-cycle and cell division. It can be hypothesized that cdk2 is one of the proteins produced during the G-protein-coupling kinase-phosphorylating pathway (Hydbring et al, 61). In cancer cells, the p53 inhibitor is deactivated, resulting in uncontrolled cell division. At the same time, telomerase is switched on in cancerous somatic cells like colon or epithelial cancers with the net result of cell accumulation—tumor. Factors that deactivate the p53 and other cell-regulation inhibitors remains unknown but scientists hypothesize that the same factor that hyper-activates a ras protein deactivates cell-cycle inhibitors. Telomerase compared to the ras gene influences the expression, multiplication of cancer cells, and their resistance to chemotherapy and anti-cancer drugs. Telomerase is a ribonucleoprotein(RNP) that consists of three parts: Telomerse Reverse Transcriptase (hTERT) (Hydbring et al, 58), Telomerase RNA (TERC), and dyskerin. TERC and TERT functions in the extension of G' cap of the pre-mRNA molecule after transcription as described above. The lagging strand of the DNA molecule, in which the 5' G strand has been extended, folds the G' region through weak hydrogen bonding between the guanosine molecules; thereby forming the shape that earns it the "G' cap" name that protects the fragile gene in the middle region of the m-RNA from cytosolic enzyme degradation. Dyskerin is a "pseudouridine synthase" (Beth et al, 10859) that serves as a co-enzyme in stabilizing and maintaining the telomerase complex (Kalpana et al, 2332). Dyskerin facilitates the tight binding of the telomerase to the telomere G' or C' strand allowing faster reverse transcription of the TERC template.

Results

Lou et al scanned the human genome for cancer cells' "vulnerability" (Lou et al, 845). It was hypothesized that tumor can be cured by reversing the damages caused by the oncoproteins. For this experiment, the colorectal cancer cell of line DLD-1 were initially used. A clone of the cancer cells with a mutated version of KRAS gene shows reduce kinase Activity. Microarray hybridization combined with viral RNA library screening technique was used to detect the presence of cell-cycle signaling factors, on which the Ras mutant cells depend. The weakness was found in the ras oncogene G-coupling pathways: NAE1, COP9 signalasome, PLK1, MCAK, and other ras pathway enzymes (Luo et al, 845). Lou et al also discovered specific drugs, such as paclitaxel and Velcade, that effectively targeted the genes that code for the ras supporting enzymes, and treatment with the drugs for more than 24hrs not only

prevented the proliferation of cancer cells, but also resulted in apoptosis (Lou et al, 844).

Xu et al targeted the telomerase binding to the telomere end using a "6-mer photo-controlled oligonucleiotide" (Xu et al, 635).

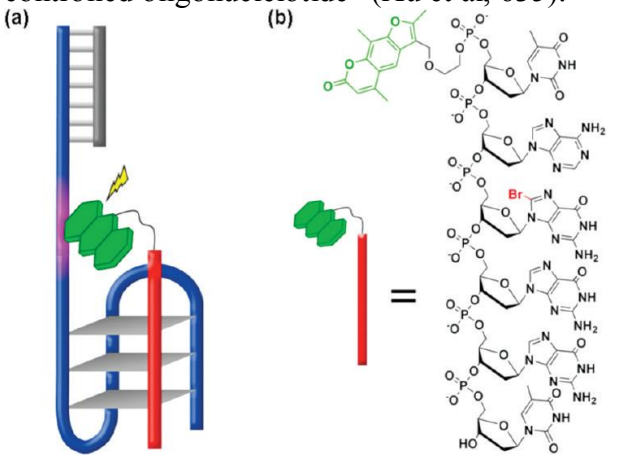

Figure 1: (a) The psoralen molecule above the photo controlled oligonucleotide absorbs photo radiation needed prevent the elongation of the telomere, and the G-Quadruplex molecules attached the psoralen molecule to the target telomere sequence. **(b)** The psoralen photo reagent is attached to the 5' end of the TAGGGT sequence on the 6-mer photo-controlled oligonuceotide (Xu et al, 632).

The 6-mer photo-controlled oligonucleotide functions using a "photo-linking" (Xu et al, 631) chemical compound such as psoralen that can bind to the TT pyrimidine bases in the telomere sequence (Xu et al, 631). A PCR reaction confirmed that telomerase activity was inhibited by the photo reagent oligonucleotide as half of the cancer cells were reported dead. The specificity of the photo reagent to cancer cells was also confirmed using human cells: The concentration and amount of radiation used to kill the hela cells were maintained, and the result showed that the photo reagent had no effect on fibroplast cells that lack telomerase (Xu et al, 634). In addition, alternative versions of photo-controlled oligonuceleotide were tested for efficiency and specificity, and Pso-ODN-2, an oligonucleotide with palmitic acid attached to its 3' end, produced significant outcomes.

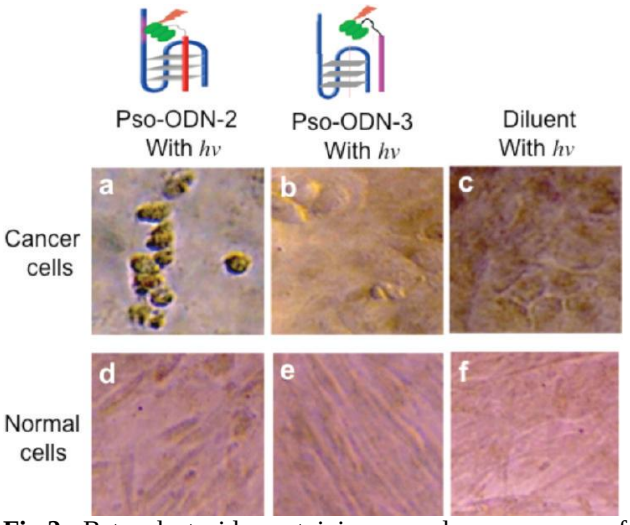

Fig.2: Betagalactosidase staining reveals senescence of cancer and normal cells in solutions containing different molecules of 6-mer photo-controlled oligonucleotide radiated with 365nm source (Xu et al, 635).

Discussion:

Cancer is one of the most complex of diseases that requires challenging research to find the most efficient way to treat patients without interfering with normal cellular processes. The discovery of genes that support ras mutant proteins shows that difficulty in research methods and drugs for cancer treatment results from protein-protein interaction at the genome level. The effect of mutation of KRAS gene in colorectal cancer cells portrayed cancer cells dependency on key mitotic cell cycle proteins, and a deregulation of one of these proteins will be insufficient as other proteins are still present to propel the wild type cancer cells through the cell cycle.

Cancer cells also exhibit higher level of telomerase activities if compared to the dermal fibroblast (somatic) cells that lack telomerase. Treatment of cancer cells with photo radiation technique that is specifically designed to bind and affect targets cells opened new therapeutic opportunities for patients with minimum or no side effects. The combination of Xu and Lou et al's approach to cancer treatment can facilitate the production of drugs that will simultaneously halt enzymes that promotes the transcription and translation of defective (cancer) genes, and the

migration of cancer cells to form malignant tumor.

Conclusion

The treatment of cancer requires further research into factors that activate telomerase and inhibit the expression of the p53 gene in cancer cells. Cancer treatment will progress if telomerase activity can be inhibited, and p53 gene activated. The use of advanced biotechnology techniques such as microarray and in-situ hybridization, gene cloning, and PCR has facilitated discoveries of gene-to-gene, protein-to-protein, or RNA-to-RNA interaction that promote the proliferation of cancer cells. There are many factors and genomic processes that conceives cancer in humans and focus on their vulnerabilities, weaknesses, and strengths will ascertain generic solution to cancer treatment.

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