Foreword

The 15th Annual Science Symposium was held on May 14, 2009. Students enrolled in Organic Chemistry from Paradise Valley Community College (PVCC) participated in the event. Each contributor was responsible for selecting and researching their topic and preparing a paper. A few orally presented their project to their peers. This booklet contains each of those papers.

As an instructor and faculty advisor for this symposium, I want to thank and congratulate each participant for their effort, courage and dedication. By participating, these individuals perpetuate this event annually. I am both proud and honored to present the work of these individuals.

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### Table of Contents

**Zyvox and Its Role in the Treatment of MRSA**  
by Monte Lewis

**An Analysis of Apomorphine**  
by Daniel Linville

**The Duragesic Patch for Chronic Pain**  
by Bradley S. Loewy

**Herbal Medicine: Acupuncture**  
By Golshan Majidi

**Thyroid Cancer: Diagnosis, Effects and Treatment**  
by Brandon Martinez

**Embeda™**  
by Makenzie Nye

**Noninvasive Cataract Treatments**  
by Raul Ochoa

**Genetically Modified Food: Is All Food Created Equal**  
by Chris Robinson

**Life and Pain: Living With And Treating Fibromyalgia**  
by Nicole Marie Runge

**The Discovery of Chaos Theory and Its Growing Application**  
by John A. Russell

**Rheumatoid Arthritis**  
by Maryam Rasouli Servati

**Understanding Interstitial Lung Disease (Interstitial Pulmonary Fibrosis)**  
by Megan Smith

**General Anxiety Disorders**  
by Mahtab Taghipour

**Solar And Wind Powered Homes**  
by Paul Waweru

**X-ray Emission and Characteristics**  
by David J. Wolfe
Zyvox and its role in the treatment of MRSA

Monte Lewis

April 17, 2009
Abstract

Zyvox is the brand name of the medication linezolid currently manufactured by Pfizer Pharmaceuticals. Zyvox, part of a new class of antibacterial medications known as oxazolidinones, is used primarily for the treatment of gram-positive, multi-drug resistant bacterial infections. Among the many indications Zyvox is used for, the treatment of MRSA (methicillin-resistant staphylococcus aureus) is very important. Zyvox works to neutralize MRSA and other bacteria by ceasing their process to replicate at the RNA level.

Zyvox and its role in the treatment of MRSA

Zyvox is a medication manufactured by Pfizer pharmaceuticals. Generically known as linezolid it is part of a new class of antibiotics that target multi-drug resistant bacterial infections. This new class of drug is known as oxazolidinones and Zyvox was the first of its kind available. Zyvox has been indicated to treat many different infections: Enterococcus faecium, Streptococcus pneumonia, Streptococcus pyogenes, and others (Pfizer, 2005). Perhaps its most important treatment, however, is for infections caused by MRSA (methicillin-resistant staphylococcus aureus). MRSA is an expanding issue in the world today as reported cases continue to rise. MRSA, which is generally known for being acquired in a clinical setting, is seeing an increase of cases that are community-acquired. Zyvox is often the last chance, the magic bullet, to solve MRSA and other infections of its type. There are many benefits to Zyvox but there are some issues as well.

Staphylococcus Aureus has been present in society long before any medication was available to treat it. Only four short years after penicillin was introduced and was effective for treating staph infections, resistant strains of staphylococcus aureus were found. In 1959, methicillin was introduced and was effective against these and other penicillin resistant strains. However, it was only two years later that strains of staph resistant to methicillin were discovered. This was the beginning of MRSA as we know it today. (Dunbar, 2009)

Dunbar (2009) asserts that the reason that we see strains of bacteria such as MRSA has to do with external selection pressure. If a bactericide is introduced into the environment, then only the bacteria that have mutated to resist these agents will grow and prosper. Penicillin and its derivatives were touted as ‘super-drugs’ after their creation and they were prescribed for patients suffering from almost any ailment. The downside to this was not apparent for several years. Patients prescribed an antibiotic when it was unnecessary harbored bacteria within their system as all humans do. With a large enough population of humans taking antibiotics all around the year, the bacteria were put into a kind of evolutionary ‘crucible’. The bacteria were subjected to these medications time and time again and were able to develop natural defenses against them. It is no wonder that this kind of bacterial metamorphosis occurs still today with the United States alone taking over fifty million pounds of antibiotics every year.
Today MRSA is delineated into two categories: HA-MRSA (hospital-acquired) and CA-MRSA (community-acquired). Most people are familiar with HA-MRSA and in fact, until recently, it was the only type of MRSA that most doctors were concerned with. HA-MRSA’s prevalence came from the fact that since hospitals are sterile places, there were no other competing bacteria that could affect MRSA’s ability to grow and infect. Since MRSA itself is resistant to the bactericides used, it could prosper in many hospital settings. Add to this patients that are bed-ridden, many with wounds, and MRSA becomes a clear and present danger in these settings (Dunbar 2009).

CA-MRSA is becoming a real problem in recent times, however. Dunbar (2009) states: approximately 33% of all people that carry CA-MRSA on their skin or nasal cavities never know. This creates a large amount of carriers who unknowingly are spreading the bacteria around the community. The Centers for Disease Control and Prevention (2008) state that 25-30% of the population are colonized by staphylococcus aureus in their noses. Figures for MRSA however are approximately one percent. MRSA can present as a skin infection that appears as a pimple or boil. They can show as red, swollen and painful and have pus or other drainage. More serious infections may cause pneumonia.

It is possible for a MRSA infection to recur after it has been cured, so the CDC (2008) stresses constant prescribed care for the condition as well as a hygiene regiment. “Keep your hands clean by washing thoroughly with soap and water or using an alcohol-based hand sanitizer. Keep cuts and scrapes clean and covered with a bandage until healed. Avoid contact with other people’s wounds or bandages. Avoid sharing personal items such as towels or razors.” These tips may help to curb the spread of MRSA both within the community and on the patient themselves.

Treating MRSA infections is difficult. It requires very potent medications that can overcome the resistances that the staph bacteria have developed. Fighting MRSA can be a losing battle as even amputation or excision of the infected area does not stop the infection from surging back to the new wound site. There have been quite a few drugs effective in the treatment of MRSA, but with the invention of Zyvox, a new and very effective weapon for fighting MRSA can be brought to bear.

According to Pfizer (2005), Zyvox is a synthetic antibacterial agent of the oxazolidinone class. The full chemical name for the drug is given as (S)-N-[[3-[3-Fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. It has an empirical formula of $\text{C}_{16}\text{H}_{20}\text{F}\text{N}_{3}\text{O}_{4}$ and its molecular weight is 337.35. A representation of the chemical structure of Zyvox is shown below.
Zyvox is metabolized in the body by oxidation of the morpholine ring. This results in two inactive open-ring metabolites which are both carboxylic acids. They are: the aminoethoxyacetic acid metabolite (A), and the hydroxyethyl glycine metabolite (B) (Pfizer 2005).

Not all of the medication administered to a patient is metabolized, however. Pfizer’s documentation (2005) goes on to state that examination of the urine of patients that are under Zyvox therapy show 30% of the dose appears as linezolid - the parent drug, 40% of metabolite B and 10% of metabolite A. Examination of the feces shows virtually no linezolid, 6% metabolite B and 3% metabolite A.

While Zyvox can be given as intended for mature adults to the elderly without any alterations, pediatric patients do present issues. The drug, after being administered to patients ranging from 1 week to eleven years old experiences a shorter half-life and the patient’s exposure to the drug from a single dose is shortened due to the high rate of metabolism of the parent drug within the small child. As the age of the patient increases, the behavior of the medication within the body approaches the average for a normal mature adult. While it has been shown that females distribute the drug within their bodies as less volume, the buildup of the drug within their bodies does not exceed levels known to be well tolerated and so no adjustment of dosage by gender is necessary (Pfizer 2005).

Patients on Zyvox must be careful not to intake foods with high tyramine content (e.g. fermented, spoiled, aged or cured foods). When this occurs, a significant pressor response has been observed (a sudden increase in systolic blood pressure). Additional pressor responses were seen when Zyvox was taken in combination with pseudoephedrine HCl (Sudafed) and phenylpropanolamine HCl (Dexatrim) (Pfizer 2005).

Studies performed on lab animals have determined sexual and pregnancy side-effects. While it did not affect the fertility or reproductive performance of adult female rats, sexually mature male rats that were exposed to the drug as a juvenile displayed mildly decreased fertility through much of their sexual development. In rats, mild fetal toxicity was observed with
decreased fetal body weights. Zyvox and its metabolites are excreted in the milk of lactating rats, thus it is not recommended that mothers breast feed while on Zyvox (Pfizer 2005).

Oxazolidinones (a class of compounds containing 2-oxazolidone in their structure) were first described for their utility for treating plant diseases in 1978. Antibacterial properties of this class of compound were discovered six years later. Zyvox emerged in 1996 and was approved by the FDA in 2000. The oxazolidinones have been the only new class of antibiotic that have been discovered and successfully implemented over the past 40 years (Klajn, 2005).

Zyvox works against bacterial infections by inhibiting protein synthesis. The mechanism in which it obtains this effect is different from other antibacterial medications. According to Pfizer (2005), “Linezolid binds to a site on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is an essential component of the bacterial translation process.” This mechanism, which prevents the 30S and 50S subunits from binding together, interferes with the binding of the transfer RNA within the bacteria which ceases the entire process of protein synthesis. Being denied the ability to replicate proteins within the bacteria renders it inert (in the case of enterococci and staphylococci) or kills it completely (in the case of streptococci) (Pfizer 2005). Because the mechanism used is unique, this makes cross-resistance between Zyvox and other classes of antibacterial agents unlikely (Plosker, G., & Figgitt, D, 2005).

The LEADER program (Linezolid Experience and Accurate Determination of Resistance) was founded in order to monitor and assess the resistance of multi-drug resistant strains of bacterial infection to linezolid by Pfizer Pharmaceuticals. In their 2007 report they found that Zyvox was 100% effective against oxacillin-susceptible staphylococcus aureus and 99.9% effective against oxacillin-resistant staphylococcus aureus. The numbers for the other indications of Zyvox were never lower than 97.8%. This gave an overall susceptibility rate of 99.56% of the surveyed population which shows that while Zyvox is still working for a grand
majority of the patient population, there do exist resistances to it within current strains of bacteria. In fact there were two linezolid-resistant strains of MRSA found and identified in medical centers in both Texas and Ohio (Castanheira, Mariana, Jones, Ronald N., Mendes, Rodrigo E., & Ross, James E. 2008). More recently, in the summer of 2008, an outbreak of linezolid-resistant MRSA was found in Madrid, Spain. Twelve such cases were presented in the intensive care unit of Hospital Clinico San Carlos. Six of the patients thus infected died from underlying complications. All of the linezolid-resistant strains of MRSA were contracted within the hospital (Smith 2008).

Zyvox has been shown to be more effective than vancomycin in the treatment of complicated skin and soft tissue infections caused by MRSA. Patients within the study conducted that took Zyvox had an 88.6% microbiologic cure rate while patients that were on a vancomycin treatment plan saw only a 66.9% cure rate. It was also shown that Zyvox patients spent an average of five fewer days in the hospital on intravenous treatment due to the availability of Zyvox to be taken as a pill ("MRSA Skin Infections Treated More Effectively with Zyvox" 2006).

Hospitals have found that treating MRSA with Zyvox has been beneficial, not only to the patient’s welfare but also to their bottom line. Zyvox is one hundred percent bioavailable, that is to say, it can be given orally or via intravenous injection at the same dosage with the same exact effect. The reason that this is such a benefit to the cost-analysis of using the medication is that a patient may change from I.V. Zyvox to oral Zyvox and be discharged from the hospital without any intermediate steps within the medication dosing procedure. Other antibacterials, such as vancomycin, need to be given intravenously to affect the body. Either the hospital must keep the patient a few extra days to complete the IV drug treatment, or switch them to another medication that can be taken orally and then observe them to ensure that everything is proceeding normally. (Plosker, G., & Figgitt, D., 2005)

There are drawbacks to Zyvox as well, however. Adverse effects appear in 21.7% of patients according to a study (Plosker, G., & Figgitt, D., 2005). This is significantly higher than other drugs used to treat MRSA. Diarrhea, nausea and headaches were the most common adverse effects, but others were reported. Anemia, leucopenia, thrombocytopenia, lactic acidosis, optic and peripheral neuropathy, convulsions, and serotonin-like syndrome have all arisen in patients receiving Zyvox. While the number of adverse effects reported are much higher than other antibacterials that are used to treat the same infections, they were mild to moderate severity and subsided very soon after the patient ceased taking the drug. During those studies, Zyvox was never associated with the death of a patient (Falagas, M., & Vardakas, K., 2008).

The FDA has recently released a report (2007) that links the use of Zyvox in the treatment of seriously ill patients with intravascular catheter-related bloodstream infections with patient death. In a study, patients with this condition received Zyvox, vancomycin, oxacillin, or dicloxacillin. It was shown that patients with gram-negative bacterial infections, a mixture of gram-positive and gram-negative, or no infection at all had a higher rate of death when treated with Zyvox. Patients that had all gram-positive bacterial infection showed no increase in mortality when treated with Zyvox. The FDA has stated that Zyvox is not approved for the
treatment of catheter-related bloodstream infections, catheter-site infections, or for the treatment of infections caused by Gram negative bacteria.

Another negative aspect to the treatment of MRSA with Zyvox is the personal cost that it incurs. Caldwell (2003) makes the point that insurance carriers won't pay for the strongest and newest forms of antibiotics until other, less expensive options have been tried. Due to this, some patients must be hospitalized to receive intravenous medications, and most have to take one or more forms of oral medication while applying a topical ointment and washing themselves thoroughly several times a day. Some patients must have surgery to remove dead skin. Since Zyvox is new, the chance of an insurance company authorizing payment for a patient without prior authorization given from a doctor with a statement of medical need is slim to none. Add to this the hefty retail price tag of the medication and the cost of Zyvox becomes a very real barrier to those that may need it. A call to my local Walgreens showed that the usual and customary cost of a thirty day supply of Zyvox (twice a day as is most prescribed) costs $5,166. Without insurance, the cost of this medication seems almost insurmountable.

Pfizer has developed a patient assistance program to provide many of its medications at low or no cost to those in financial and medical need. The program that covers Zyvox is known as the Pfizer RSVP program (Pfizer RSVP 2008). This program provides assistance for six medications, Zyvox being one of them. While this seems to be a very helpful organization set up by the drug manufacturer, the reality is that qualification for the program is very narrow indeed. In order to qualify for assistance with paying for prescription Zyvox a person must meet the following criteria: Patient must be at or below the federal poverty level and have either: no insurance, insurance that will not cover Zyvox, or insurance that covers a small part of Zyvox (threshold determined on a case by case basis); patient must also be a US resident. For reference, the federal poverty level for a married couple is $14,570 or in other terms – one person working a $7.00 an hour job. While there are, indeed, many people in our country that do fit those guidelines, it leaves an extremely large gap between the incredibly needy and the financially able - all of whom may need this medication.

Recently, the FDA has given tentative approval for Mylan Pharmaceuticals to develop and produce an Abbreviated New Drug Application (a generic) for linezolid. A generic version of Zyvox on the market would help those who are financially unable to obtain Zyvox, however, the process for a drug to pass from tentative approval to available to the general public is very long and could possibly be halted for many reasons. Also, if the drug’s expense is so high now, the difference between the price of the name brand and the generic, while still a savings, would still be abnormally high.

Zyvox has been touted as a ‘wonder-drug’ and a sure-fire defense against many of the multi-drug resistant ‘super-bugs’ that have been developing in recent decades. While Zyvox certainly has many upsides, there are serious complications that Zyvox can cause both physically and financially. With the outbreak of linezolid-resistant strains of MRSA seen in the last two years, it is becoming clear that bacteria is undergoing further metamorphosis in order to survive its demise by this drug. Care must be taken by health providers to prescribe this medication only when necessary to ensure that those who do not have the need for it obtain it. This can result in more resistant strains through unnecessary use and possible death for the patient in the case of
catheter-related infections. It is clear that Zymox is effective for treating MRSA and other indications, but that will only stay true if health professionals take the time and effort to make sure that proper dosing and prescribing occurs.
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An Analysis of Apomorphine

By: Daniel Linville
Abstract

This paper will discuss the drug Apomorphine as well as its branded equivalents, Apokyn and Uprima. Some topics will include; history, chemical make-up, and approved uses, such as poison control and Parkinson’s disease treatment. A new experimental use for erectile dysfunction will also be discussed.

Apomorphine has been in use for many years within the medical community. It is a non-narcotic derivative of morphine. The IUPAC (International Union of Pure and Applied Chemistry) name for apomorphine is as follows, (6a$\delta$)-6-Methyl- 5,6,6a,7-tetrahydro- 4$H$-dibenzo [de, $g$] quinoline- 10,11-diol. The molecular formula of apomorphine is $C_{17}H_{17}NO_2$. Apomorphine has a molecular weight of 312.79 (RxList, 2008). It was first synthesized in 1869 by Matthiesen and Wright. Its original use was not really promoted until the 1930’s as an emetic. An emetic is a substance that induces vomiting when administered orally or less effectively, by injection (Clinical, 2006).

Apomorphine was extensively used to treat acute poisonings. It wasn’t until the discovery of ipecac syrup that Apomorphine outlived its usefulness to induce vomiting. This was mainly because Ipecac was much safer than the very fast and strong acting apomorphine (Clinical, 2006). It is important to note that although apomorphine lost support as an emetic for humans it is still used in veterinary medicine for poison control.

In 1951, Apomorphine was discovered as a possible useful treatment for Parkinson’s patients, although nothing was truly understood of how or why it helped. However, the strong reaction of its former primary use made it less than a desirable medication at the time. It wasn’t until the 1960’s that research discovered apomorphine possessed dopamine receptor agonist properties. A dopamine agonist is a compound that activates dopamine receptors in the absence of the dopamine ligand. Dopamine agonists activate signaling pathways through the dopamine receptor and trimeric G-proteins, which ultimately leads to changes in gene transcription (Clinical, 2008). The image on the top of the next page is that of a dopamine molecule.
Apomorphine is a morphine decomposition product by the process of boiling with concentrated acid (MedHelp, 2009). It is for this very reason that it has the name apomorphine, "apo" meaning from. It does not actually contain morphine or its skeleton, or bind to opioid receptors (MedHelp, 2009). Therefore, apomorphine acts next to nothing like its cousin morphine. The image below shows the morphine molecule. In the boiling process the hydrogen atoms released by the acid bond to both the epoxide and a hydroxyl group. This allows for water molecules to form which are a good leaving group. The remaining structure is that of a diol with four rings, one of which containing nitrogen.

Besides the emetic effects and use in Parkinson's treatment, apomorphine has been tried for a variety of uses including psychiatric treatment of homosexuality in the early 20th century (Mcfaddinn, 2004). Most experimental uses failed. Currently, apomorphine is used mainly in the treatment of Parkinson's disease as well as for erectile dysfunction in Europe under the name of Uprima. It was also successfully used in the treatment of heroin addiction (Mcfaddinn, 2004). With any use of apomorphine, it is not uncommon to have an anti-emetic such as domperidone administered alongside. In the
treatment of erectile dysfunction, it is believed that dopamine receptors in the hypothalamic region of the brain are the main target. However, dopamine receptors in the penis facilitate an erection as well, but do so far more weakly than those in the brain (Mcfaddin, 2004). As a side note, apomorphine is colorless as a liquid but stains green. Therefore, care must be taken to avoid splashes on clothing. Apomorphine does not remain stable for more than 24 hours in a plastic container, so syringes are discarded if not used within 24 hours.

It wasn’t until 1970 that clinical trials were first reported for use with Parkinson’s disease (Koerner, 2009). Although, it’s emetic properties and short half-life made oral use less than viable. A later study found that combining the drug with the antiemetic domperidone improved results significantly. Therapeutic use in Parkinson's disease is effective because of the drug's strong dopaminergic action. The effects come about rapidly within about 3-20 minutes but only last for a very brief duration (Koerner, 2009). This means that apomorphine is not a replacement for current Parkinson’s drugs, but rather a tool to make life a little more manageable. While apomorphine can be used in combination with Levedopa, the intention is usually to wean patients off of this, as by this stage they will probably be experiencing a great deal of dopa-induced dyskinesias and "off" periods (Clinical, 2006). Dyskinesia refers to the effects of diminished voluntary movements and presence of involuntary movements, similar to a tic. In regard to Parkinson's disease it is more commonly a jerky, dance-like movement of the arms or head (Clinical, 2006).

In the treatment of erectile dysfunction apomorphine goes by the trade name of Uprima (FDA, 2004). It is its mode of stimulating dopamine in the brain which is believed to enhance the sexual response. It was found to be of poor effectiveness in a large-scale study by researchers at the UK's Drug Safety Research Unit and University of Portsmouth and discontinued in the UK in January 2006. Around 65-70% of doctors felt it was ineffective, with 60% of over 11,000 patients discontinuing in month 1 and a further 23% in month 2. The average age was about 61 (Mcfaddin, 2004). Apomorphine has been reported to be an inhibitor of Beta amyloid fibril formation, and therefore may have another potential therapeutic application for Alzheimer's disease (Clinical, 2006).

When Uprima was launched in Europe as the first medical treatment for sexual dysfunction after Viagra, it was suspected that it could repeat the success of Viagra (Mcfaddin, 2004). This turned out to be not the case. Unlike Viagra, apomorphine and other dopaminergics exert their pro-sexual effect not upon the erectile organ but upon the brain. Apomorphine provokes erections not by interfering with the blood supply to the penis, but rather the neural wiring necessary for arousal (Mcfaddin, 2004). This means that apomorphine is not for the man that has physical impotence, but rather for the man that may have a neurol abnormality. This could very well explain the poor results of earlier drug trials. Apomorphine or Uprima is not effective for men that physically can’t sustain an erection. The fact that apomorphine is a potential pleasure drug is the only real link to its parent, morphine (Mcfaddin, 2004).

It has long been documented that most Parkinson's medications have sexuality-enhancing side effects. It must to be noted however, that the sexuality-enhancing side effects hold true for many but not all dopamine-enhancing Parkinson's medications (Koerner, 2003). Whether or not a dopamine agonist enhances sexual functions seems to
depend primarily on the dopamine receptor and sub-receptor sites it targets. Dosage for a pro-sexual effect is difficult to determine for all dopamine agonists. This is the case because a dosage that is too high will inevitably result in nausea (Koerner, 2003). This too might have been the reason for such poor results with Uprima trials. This nausea can be so bad that the last thing one would think about is sex. This particularly is a problem with apomorphine, which is commonly used to induce nausea.

Uprima has so far not been approved for marketing in the US. If a FDA endorsement is to be obtained for its marketing in the US as treatment for erectile dysfunction, the primary concern will be to keep the nausea side effect at bay. As of right now, the makers of Uprima have already made minor violations by hinting in a press release that the FDA is going to approve Uprima (FDA, 2004). With apomorphine, nausea can be reduced if it gets into the bloodstream quick enough. This means Parkinson's patients will use an injectable apomorphine. Parkinson's is a serious condition; a matter of life and death, and in such a case, patients can be expected to tolerate injections. But as treatment for non-life-threatening conditions like lack of libido or erectile dysfunction, injection medications have always lost interest from possible consumers. Tap Pharmaceuticals, the makers of Uprima, are trying to get around the problem. Their solution is packaging the drug as sublingual, and by keeping the dosage per tablet as low as 2 or 3 mg per sublingual tablet (Mcfaddimn, 2004). With these small doses of apomorphine, the likelihood of nausea will be negligible. However, so will the pro-sexual effect. It is important to remember that Uprima is not for sale in the U.S. yet, so people in other parts of the world, for the most part, make up their own dosage strengths as they see fit.

Apomorphine hydrochloride appears as minute, white or grayish-white glistening crystals or as white powder that is soluble in water at 80°C (RxList, 2008). As the injectable medication Apokyn, it appears as a clear, colorless, sterile solution for subcutaneous injection. Apomorphine in any application must be kept at room temperature and within glass vials if in liquid form to avoid decomposition. As Apokyn, each milliliter of solution contains 10 mg of apomorphine hydrochloride and 1 mg of sodium metabisulfite in water for injection (AHFS, 2007). In addition, each milliliter of solution may contain sodium hydroxide and/or hydrochloric acid to adjust the pH of the solution and 5 mg/mL of benzyl alcohol as a preservative (AHFS, 2007). Below is the structure of the injectable Apokyn.

![Apomorphine structure](https://via.placeholder.com/150)

**Apokyn is indicated for the acute, intermittent treatment of hypomobility** (Clinical, 2006). Hypomobility refers to the loss of control of bodily movements. These times of loss of control are known as "off" episodes associated with advanced Parkinson's
disease. Common symptoms would include muscle stiffness, slow movements, or difficulty starting a movement. Apokyn as shown through trials to be able to improve the ability of patients to control movements when it is used during an "off" episode (MedHelp, 2008). This may help a patient walk, talk, or move around easier. Rarely there has been reported motivation for apomorphine abuse related to the attempt to avoid all symptoms of all "off" events when "off" events occur frequently (MedHelp, 2008). A second, rarely reported, motivation for apomorphine abuse is a psychosexual reaction related to the stimulation of penile erection and increase in libido (McFadden, 2004). The consequences of such overuse have shown an increase in possible side affects which will be discussed later. It is important to note that when Apokyn is used in Parkinson’s patients, it is vital to avoid direct intravenous injections. Serious adverse events such as intravenous crystallization of apomorphine can occur in this instance. This will ultimately lead to thrombus formation and pulmonary embolism (RxList, 2008).

As a dopamine agonist, apomorphine carries the same risks as similar drugs in this class. Dopamine agonists may cause orthostatic hypotension at any time, especially during dose escalation (Clinical, 2006). In addition, Parkinson's disease patients may have an impaired capacity to respond to an orthostatic challenge. It is for these reasons that Parkinson's disease patients being treated with dopaminergic agonists ordinarily require careful monitoring for signs and symptoms of orthostatic hypotension, especially during times of dose escalation. Unlike most of its brethren, apomorphine's pharmacokinetics are rather different in nature. Apomorphine hydrochloride is a lipophilic compound that is rapidly absorbed (Clinical, 2006). In most cases, time to peak concentration ranges from 10 to 60 minutes following a subcutaneous administration into the abdominal wall. After subcutaneous administration, apomorphine appears to have bioavailability equal to that of any intravenous administered medication. Apomorphine exhibits linear pharmacokinetics over a dose range of 2 to 8 mg following a single subcutaneous injection of apomorphine into the abdominal wall in patients with idiopathic Parkinson's disease (Clinical, 2006). It is not yet clear on how apomorphine is metabolized, but it is cleared out of the body very quickly. Below is a graph of motor scores from a pool 550 patients tested with apomorphine in the form of Apokyn. The graph basically shows the faster motor skills timing initially after injection and the gradual drop off. With most patients apomorphine only lasts for about an hour and a half. This is just enough time to get them past an "off" episode (RxList, 2008). With that said though, it is more evidence that apomorphine is no where near a viable permanent fix for Parkinson’s symptoms.
Like most medications, apomorphine has a list of pre-conditions that may make apomorphine unsafe to use for certain individuals. Apomorphine in Apokyn contains a sulfite called metabisulfite. Sulphites can cause severe, life-threatening allergic reactions in some people, especially in people with asthma (RxList, 2008). Also, Apokyn or just apomorphine in general should be avoided by people being treated with certain drugs to treat nausea and vomiting or irritable bowel syndrome. These medications include; ondansetron, granisetron, dolasetron, palonosetron, and alosetron, which are also called 5HT 3 antagonists or blockers (RxList, 2008). Also vasodilators and sleep medications should be avoided while on any apomorphine treatment (AHFS, 2007). People that take this type of drug together with apomorphine can have severe low blood pressure and lose consciousness. It should also be mentioned that apomorphine has not yet been studied in children. Some other certain conditions that potential patients should be wary of include; frequent dizziness, fainting spells, low blood pressure, asthma, liver problems, kidney problems, heart problems, have had a stroke or other brain problems, have a mental problem called a major psychotic disorder, drink alcohol, or are pregnant (RxList, 2008).

As with all drugs there are also certain side effects that accompany the desired effects. Some heart problems such as, shortness of breath, fast heart-beat, or chest pain are some signs of a major side effect that should be reported immediately (MedHelp, 2008). Due to the nature of apomorphine, some patients may experience severe nausea or vomiting and may require the use of an anti-emetic such as Tigan (Clinical, 2006). Sometimes sleepiness or just falling asleep during the day can happen (RxList, 2008). This sort of effect is one reason why any person on apomorphine, or most drugs for that matter, should not drive or operate heavy machinery until they know how it affects them. As stated earlier there is a risk of dyskinesias or falling from prolonged use of apomorphine. A very common side effect to apomorphine treatment is dizziness which may or may not accompany nausea. This is due to the fact that apomorphine lowers blood pressure. High doses of apomorphine such as 10 mg can cause a drastic drop in blood pressure (Clinical, 2006). A way patients combat this nausea is by not standing up too quickly. A more minor side effect is that of hallucinations. Hallucinations refer to seeing or hearing things that are not real. Depression is also another possible side effect or even frequent headaches (RxList, 2008). Besides the side effects from the medication there are also possible injection site reactions that can occur. This refers only to the Apokyn product for Parkinson's disease where it is only given as an injection. Some of
these types of reactions include; soreness, redness, bruising, and itching at the injection site. Changing the injection site with each injection, and putting ice on the injection site before and after injections are ways of getting around these potential problems (RxList, 2008).

As was shown, apomorphine is by no means a new kid on the block of medicine. It is however, being developed in ways that would have never been fathomed in the late 1800's when it was first synthesized. With so much more of the brain now being understood, new doorways are being opened for old medications such as apomorphine. Apomorphine is only one of some of the older medications that have found a new niche in modern day medicine.
Bibliography


The Duragesic Patch, for Chronic Pain

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Organic Chemistry 236
Dr. Hank Mancini
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Abstract:

The topic of this paper will be the Duragesic patch. The Duragesic patch is a relatively recent product that the drug companies created for those patients who are experiencing chronic pain. For those who read this a chronic pain patient is someone who is in pain all day and every day. They are usually victims of serious injuries or cancer patients. The topics of the paper will include; how this patch functions, to what chronic pain patients actually say about the patch. It will also cover the chemical make up and synthesis of Fentanyl, all the way to opioid receptors.

The Duragesic patch is a transdermal system that provides a constant dose of Fentanyl for seventy-two continuous hours straight by releasing it into the body fat and then into the blood stream. The patch is a rectangular transparent unit that works by incorporating a protective liner and four functional layers. These four functional layers are: starting from the layer closest to the skin are; a backing layer composed of a polyester film, a drug reservoir of Fentanyl and alcohol gelled with hydroxyethyl cellulose, a ethylene-vinyl acetate copolymer membrane that controls the rate of Fentanyl delivery to the skin surface, and finally a Fentanyl containing silicon adhesive. (1)
As you can guess transdermal Fentanyl patches are distributed by other manufacturers as well. One such brand is called Mylan. Mylan is unique because with this brand the medication is infused in a fabric mesh. This creates an advantage to the brand because the Fentanyl in the fabric mesh can be cut to change the dosage. This future has made it prominent in Nursing homes and rehabilitation facilities. This is not because it is more convenient but because the Mylan style prevents patients from overdosing by cutting the medication out and swallowing it. (8)

As previously mentioned, the Duragesic patch releases a drug called Fentanyl. Fentanyl is a class two drug which means it can only be given out by a doctor’s prescription. It is a class two drug because Fentanyl is one of the strongest opioids that we know about.

Fentanyl also called \( N \)-phenyl-\( N \)-(1-phenethyl-4-piperidinyl) propanamide was first synthesized in 1959 by Paul Janssen by using a four step process. Dr. Paul Janssen first started with some 4-piperidinone hydrochloride and phenethyl bromide and reacted it with a PTC catalyst and some heat to get \( N \)-phenethyl-4-piperidinone or NPP intermediate. Dr. Janssen then treated the NPP intermediate with aniline and followed by a reduction with sodium borohydride affording 4-anilino-\( N \)-phenethyl-piperidine or ANPP. Finally ANPP and propionic anhydride are added together drop wise to form the amide product or Fentanyl. This last step of the synthesis was an endothermic reaction so Paul had to keep the reaction between 30-60°C (4)
Fentanyl like any other compound has a boiling point and a half life. Fentanyl's boiling point is 87.5 °C or 190 °F and it has a half life of three to twelve hours. (4) Fentanyl also has a steady and constant absorption rate when it is inside the body. This is great to know because it allows doctors and pharmacists to more accurately prescribe the dosages of the Duragesic patch. In the case of the Duragesic patch it had an average absorption rate of 2.3 micrograms per hour giving. (7)

As you can see Fentanyl has a rather unique and highly distinctive chemical composition. This is especially obvious when you run an Infrared spectrometer, NMR spectrometer, and a mass spectrometer. The reason why it would be very obvious is because the molecule of Fentanyl has several distinct groups. The first one that will stick out is that it has two mono cyclic aromatic rings that will appear on both an Infrared spectrometer and an NMR spectrometer. The second group that will appear is a carbon oxygen double bond in the compound seen once again the Infrared spectrometer. Next you have an amine group or a nitrogen group that is attached to the mono cyclic aromatic ring that will appear on the Infrared spectrometer and a mass spectrometer. Also in Fentanyl is a heterocyclic ring with nitrogen group in it that will appear in the Infrared spectrometer. Finally you have a few alkane groups or carbon groups in the molecule that will appear in the Infrared spectrometer and the NMR
spectrometer. Overall, all these features make the obvious distinction from Fentanyl and all other chemical compounds.

The Fentanyl inside the Duragesic patch is considered an opioid because of the method it uses to reduce severe pain. The way that the pain is reduced is that Fentanyl blocks certain target neural pain receptors. These pain receptors are more commonly called opioid receptors. Opioid receptors originally came to pharmacologists' attention in the 1960's. Through a series of binding tests in which they tagged the opioids with radioisotopes to track them in the body they discovered where the receptors were located. As it turned out the receptors are membrane homogenates located inside the brain. (3) Since then, many more opioid receptors have been identified and separated into four different categories. The first category and the first type of opioid receptors to be located are called the mu (µ) receptors. Then there are also the delta (δ) receptors, the kappa (κ) receptors, and finally the Nociceptin receptors. (3)

For the purposes of this paper we will be focusing on only the mu (µ) receptors because that is what the opioid Fentanyl affects. The mu (µ) receptors are located in the brain and also the spinal cord. (3) More recently though pharmacological studies have revealed that the mu (µ) receptors are made up of seven transmembrane-spanning domains that each contains twenty or more amino acids. (6)
As mentioned before Fentanyl affects the mu (µ) opioid receptors. Fentanyl does this by inhibiting the neurotransmitter in the mu (µ) receptors as shown and described below.

As shown up above with this general diagram, the mu (µ) receptor will increase the K⁺ channels movement but decrease the Ca²⁺ channel movement. Overall, this will interrupt and occupy the mu (µ) receptor stopping a majority of the pain signals from reaching the brain. This is because the K⁺ channels are responsible for increased K⁺ neurons in the brain. These neurons are most likely the mechanism for inhibiting neurons in the nervous system. Then the diagram also shows a decrease in the Ca²⁺ channels which are responsible for the movement of Ca²⁺ neurons. The Ca²⁺ neurons are responsible for inhibiting neurotransmitter release. So with the K⁺ and the Ca²⁺ channels being affected the way there are you can see why an opioid like Fentanyl works so effectively.(6)

Now Fentanyl is not the only opioid out there but it is the one that is most commonly used for patients in chronic pain. This is because unlike morphine or oxycodone, Fentanyl is extremely potent. Common doses for the Duragesic patch are 25
micrograms per hour, 50 micrograms per hour, 75 micrograms per hour, and 100 micrograms per hour. But you would need between 60 mg to 135mg of oral morphine just to equal the 25 micrograms per hour dose. (1)

### DOSE CONVERSION GUIDELINES

| Oral morphine | 60-134 | 135-224 | 225-314 | 315-404 |
| IM/IV morphine | 10-22 | 23-37 | 38-62 | 53-67 |
| Oral oxycodone | 30-67 | 67.5-112 | 112.5-157 | 157.5-202 |
| IM/IV oxycodone | 15-33 | 33.1-56 | 56.1-78 | 78.1-101 |
| Oral codeine | 150-447 | 448-747 | 746-1047 | 1048-1347 |
| IV hydromorphone | 1.5-3.4 | 3.5-5.6 | 5.7-7.9 | 8-10 |
| IM meperidine | 75-165 | 166-278 | 279-390 | 391-503 |
| Oral methadone | 20-44 | 45-74 | 75-104 | 105-134 |
| IM methadone | 10-22 | 23-37 | 38-62 | 53-67 |
| Recommended DURAGESIC® Dose | 25 mcg/h | 50 mcg/h | 75 mcg/h | 100 mcg/h |

(1)

Though the Duragesic patch is a great product with Fentanyl in it there is a small problem with the system itself. Patients who have had experience wearing the Duragesic patch have had a problem with how the patch distributes the drug. Since the Duragesic patch is tested to release the Fentanyl at a temperature of 98.7 °C if the patient’s skin becomes hotter or colder the patch will not distribute the Fentanyl at the desired ratio. So if the patient was sick or the sun was shining down on where they had there Duragesic patch the Fentanyl would be distributed at a much faster rate then it was designed be. On the other hand if the patient was swimming or was cold for a long period of time, the Duragesic patch would distribute the Fentanyl at a slower ratio. This would leave the patients in extreme pain because they would not be getting the medication they would need to sufficiently block the pain receptors.

In conclusion, I personally think that the Duragesic patch is a great break through in pharmacology. Its ingenious transdermal design to give a constant and balanced distribution of Fentanyl for patients in chronic pain is amazing. Even though no one person will have the same results on the Duragesic patch and its small problems it is still
a great distribution system for Fentanyl. I also think that it is wonderful because I have seen first hand the difference that it can make in peoples lives that are in chronic pain. These changes have been from barely being able to get out of bed in the morning to going back to work.
Bibliography


Herbal Medicine

Acupuncture

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Organic Chemistry 236
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April 24, 2009
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Abstract

Herbal Medicine is the use of herbs to their medicinal. Also known as Herbalism or Botanical Medicine. Herb produced by plants and contain chemical nature that effect upon human body. Herbal medicine has many treatments. Acupuncture is one of the traditional medical techniques that manifest in the traditional medicine of China, Japan and other Eastern countries. Acupuncture is a method of remedy, which is inserting needles into the body to reduce pain.

How do we know the acupuncture is good for the body, and how would it effect on the human body to relief the pain, and that would be its effectiveness that is by (self-testing) it.

Introduction

Herbs and medicinal plants have a very long history in remedying disease. Acupuncture is the oldest way of medicinal that relief pain. The most important epoch in the history of Acupuncture has been in the Monarchy of yellow emperor (2697-2597).

Acupuncture text is Nei Ching Su Wen and it means (The Yellow Emperors Classic of Internal Medicine), and was the earliest document that was discovered on Chinese medicine. Acupuncture discovered 5000 years ago from china, at this time we have over 3,000,000 practitioners, however, since 20th century the number of people who is studying acupuncture is steadily growing, and many herbalist working and practicing on this method of remedy, which is help to treat the diseases and illness.

Acupuncture Methods

Acupuncture treatment is the oldest system since the ancient times. Traditional Chinese Medicine has based on beliefs that effect of one part of body on the other part of body. Some people believe this style of treatment is in actual, a myth. As it mentioned Acupuncture treatment consists of inserting needles at specific points on the skin, which are close to end of nerve. This has two effects - First it stimulates specific nerves which transmit electrical impulses via the thin, tubular bundle of nervous tissue, which is spinal cord and brain, to the illnesses area. Secondly, it Instigates release of chemical natures from center of brain to the diseased area for pain relief.

There are different method of acupuncture, but they have same concept:
1. Moxibution: To warm the acupuncture point and instigate the small circle of the needle inserting point and limpid current of blood
2. T.E.N.S: usinf electricity to acupuncture needles
3. Cupping Therapy: placing the cups on the skin as vacuum to suck out the blood.
4. Soft laser Therapy: turning on the laser and hold it on the specific point on the skin.
5. Ultrasonopuncture: using high frequency of sound instead of needles.
GETTING THE NEEDLE

1. Diseases of Head and Neck, like migraine headaches.
2. Diseases of limbs and musculature:- like muscular pains, rheumatoid and osteoarthritis, low backache, slipped disc with sciatica.
3. Diseases related to digestion, like irritable bowel syndrome, gastritis and constipation.
4. Diseases related to respiratory system, like chronic bronchitis, and bronchial asthma.
5. Diseases related to cardiovascular system, like angina pain and high blood pressure.
6. Diseases related to genitourinary system, like bed wetting in children, frequent urination, enlarged prostate.
7. Diseases related to gynecological system, like irregular menses, leucorrhoea etc.
8. Diseases related to sexual disorders, like Impotence, Azoosperma.
9. Diseases related to eyes, like optic atrophy & blurred vision.
10. Diseases related to ear, nose & throat, like sinusitis, carache, tonsillitis, laryngitis & nerve Deafness.
11. Diseases related to skin, like Acne, chronic eczema, psoriasis, skin rashes & falling hair.
12. Diseases related to nervous system, including paralysis, polio, epilepsy and coma.
13. Diseases related to psychiatric disorders (including stress related disorders), like insomnia, anxiety, mania, depression, anxiety, schizophrenia and behavior disorders.
14. Acupuncture also cures addictions, like smoking, alcohol and other addictions.
15. Acupuncture is also helpful in Diabetes and overweight.
16. Laser Acupuncture is extremely useful for cosmetic problems like black circles under the eye, Wrinkles and for tightening the facial muscles.
17. Preventive Acupuncture is also given for patients with family history of Diabetes, Hypertension, Asthma etc.

How do we know the acupuncture is good for the body, and how would it effect on the human body to relief the pain, and that would be its effectiveness which is by “self-testing” it.
Treatments

There are some treatment of using acupuncture that will help the mechanism of the body to collate with the diseases. Quit smoking, losing weight and migraine are some treatment of acupuncture. It is really hard to find the cause of the using this method to remedy diseases, because you have to observe the body response, as using the method, so it would be by experienced.

Quit Smoking

Many people had trouble after they quit smoking, that means the new balance because of quit smoking doesn’t built up in their body. So Acupuncture helping you to balance your body with the new situation after quitting. There is some good reason that people choose this method to quit smoking:

1. Easy to use.
2. Very safe
3. Very high quitting rate: up to 95%.

Losing weight

Actually the acupuncture is not treatment of weight control, but it will helping to make it easy to lose, and also the patients have to change their lifestyle. As it mentioned the acupuncture is inserting needles into specific point of body, also in the ear, relaxing effect that can release the overeating to make fat. So the acupuncture rebalance the system of the human body that working fast or slow in some case. There are some treatment of losing weight and other disease:

- Mouth: for the impulsive eater who may also smoke a lot and talk a lot
- Stomach: for the person who eats even after they’re full or who’s constantly nibbling
- Hungry: for general appetite control
- Lung: for food addictions, and people who love chocolate, sweets
- Shenmen: a calming point, for the psychology overlay for anxiety, anger, frustration, insecurity
- Endocrine: for water retention that’s responsible for some of the weight gain
- Adrenal and Ovary: if weight gain is due to menopause or P.M.S.
- Spleen: for sugar imbalances and hormonal disturbances
- Kidney: for water retention, and nervous system and hormonal imbalances
- Thyroid: for slow metabolism

Migraine

This method of acupuncture should be long term goal, that means the patients have to continuing this method during the headache. Acupuncture can have profitable effect on autonomic nervous system.

Side effects

Actually not. Acupuncture methods are safe method of pushing the body forward to Progress improvement of function. Most people feel the pain, like a pinprick, during needles insertion. Sometimes a blunt ache around the needles insertion area. Other problems could be by from making mistakes by the acupuncturists.

Some acupuncturists have seen on their patients a original sign worsening for couple days after an needles treatment. Sometimes other changes in, sleep, bowel or emotional state may be triggered, it should not cause, as they are indications that starts working of acupuncture.
Conclusion

Acupuncture was the oldest way to cure the people who had diseases or illness. Since the basis of acupuncture is based on thousands of years of observations. Many resources tell us the effectiveness of acupuncture but unfortunately, few of these informations are well structured. However, innumerable pretensions have been made for the effectiveness of acupuncture treatments. Due to the fact that acupuncture is the natural curing of the human body and has less side effects than other treatments, this method seems to provide less damages and more benefit. However, acupuncture is a modern method in all of the world, and most people believe that this phenomenon works on the human body, and in future of the medical world, this way would be good help and natural heal for the patients who are fighting with their illness.

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Thyroid Cancer: Diagnosis, Effects, and Treatment

Brandon Martinez

April 24, 2009
Thyroid cancer occurs when mutations of thyroid cells cause the cells to grow and multiply quickly, this results in a tumor and can spread to other cells. Thyroid cancer has adverse affects on the body because of the great importance of the thyroid gland which affects nearly every part of the body. Thyroid hormone is involved in basal metabolic rate, body heat production, blood pressure regulation, tissue growth regulation and development, and skeletal, nervous system, and reproductive system maturation and development. While not much is known about the specific cause of thyroid cancer, the treatment of thyroid carcinomas has proven to be rather effective. The following research discusses the function of the thyroid, types of thyroid cancer, risk factors, diagnoses, and treatment.

With approximately 37,000\textsuperscript{[5]} diagnoses in the United States in 2008, thyroid cancer had the least number of incidences out of the thirteen most common types recognized by the National Cancer Institute.\textsuperscript{[6]} Although thyroid cancer is not considered common when compared to other cancer types, the incidence rate is steadily on the rise and is about three times more common in woman than men.\textsuperscript{[9]} The reason for the rise is unknown. However, a combination of factors are thought to play a role in the increase such as improved diagnostic technology\textsuperscript{[5]} and an increase in therapeutic radiation treatments, which are thought to contribute to the formation of cancer cells.\textsuperscript{[3]} While not much is known about the specific cause of thyroid cancer, the treatment of thyroid carcinomas has proven to be rather effective. The survival rate for thyroid cancer patients is over 95%, and the rate continues to increase despite the fact incidences are increasing.\textsuperscript{[9]} The following research discusses the function of the thyroid, types of thyroid cancer, risk factors, diagnoses, and treatment.

The thyroid is an extremely important gland which affects nearly every part of the body. The thyroid is a butterfly shaped endocrine gland in the front of the throat, on the trachea, beneath the larynx. It is the largest endocrine gland in the body and is made up of two lobes connected by tissue called the isthmus. The thyroid is composed of follicles. The follicles of the thyroid are formed by epithelial cells. These cells produce thyroglobulin, which attach to iodine atoms in the colloid. Thyroid hormone comes from thyroglobulin colloid. The thyroid also contains C cells which produce calcitonin. The thyroid affects nearly every cell in the body through the secretion of thyroid hormone. Thyroid hormone has a number of effects on different systems in the body. It is involved in basal metabolic rate, body heat production, blood pressure regulation, tissue growth regulation and development, and skeletal, nervous system, and reproductive system maturation and development. It also plays a minor role in maintaining calcium levels in the blood through calcitonin.\textsuperscript{[4][2]}

Thyroid hormone synthesis begins with thyroglobulin. Thyroglobulin is synthesized on ribosomes then transported to the Golgi apparatus. From the Golgi apparatus the thyroglobulin moves into the lumen of the follicle in the thyroid where it combines with the colloid. Iodide ions are then collected by the follicle from the blood through active transport. Once in the follicle the iodide is oxidized, converted into iodine, and moved into the colloid. Iodine is then attached to the amino acid tyrosine and form monoiodotyrosine (T1) and diiodotyrosine (T2), depending on the number of iodines attached. Within the colloid T1 and T2 are combined into T3 and T4. The combining of two diiodotyrosines results in T4 while a diiodotyrosine and a monoiodotyrosine produce a T3. The colloid containing T3 and T4 is endocytosed and combines with lysosome. Lysosomal enzymes then cleave the T3 and T4 from the thyroglobulin colloid and T3 and T4 diffuse through the follicle wall and are released into the bloodstream. The main product of this
process is T4. Some T4 is converted into T3 before being released into the blood stream but this conversion happens mainly in the cells which the hormones target, such as the liver.\[4\]

Synthesis and release of thyroid hormone

While thyroxin or T4 is more abundant in the body, triiodothyronine or T3 is the more active of the two hormones. T4 is converted to T3 by deiodination. Thyraxonine and triiodothyronine are vital to normal growth and maintenance of normal metabolic and neurological activity in the body. T4 is transported throughout the body by attaching itself to thyroxine binding proteins and plays an important part in diagnosing problems with the thyroid. In patients with hyperthyroidism T4 levels are normally elevated while patients with hypothyroidism typically show lower levels of T4. T4 is now being thought of as a prohormone to T3. T3 is thought to be the metabolically active hormone. T4 and T3 both bind to tissue receptors but T3 is much more active and binds more eagerly.\[1\][2]

Another hormone released by the thyroid is calcitonin. Calcitonin is produced by the C cells of the thyroid and helps control calcium (Ca\(^{2+}\)) levels in the blood. Calcitonin lowers calcium levels in the blood and is therefore has the opposite function of parathyroid hormone. Calcitonin inhibits release of calcium from the bony matrix as well as stimulates calcium uptake into the matrix. Calcium levels must be maintained a strict levels because calcium ions are
crucial for important bodily functions such as nerve impulses, muscle contraction, and blood clotting.[4]

The thyroid gland also consists of small glands on its posterior side called parathyroid glands. The parathyroid glands are made up of chief cells which secrete parathyroid hormone. The parathyroid glands are small and are hidden from view. For this reason the parathyroid glands were actually accidentally discovered during total thyroid removal. Some patients who had their thyroids removed recovered without incident. Other patients however suffered from severe pain and muscle spasms and consequently died. These deaths lead to the discovery of the parathyroid glands and the function of the parathyroid hormone. PTH is the most significant hormone in controlling the calcium levels in the blood. PTH raises calcium levels in the blood by stimulating the skeleton, the intestine, and the kidneys. Once PTH is released it acts on the skeleton to release calcium ions into the blood from the bony matrix, increases reabsorption of calcium by the kidneys, and increases calcium absorption in the intestines from food. If the parathyroid glands are accidently removed during thyroid removal surgery the effects on the body can be lethal. This results in hypocalcaemia or low calcium levels, which cause loss of sensation, muscle twitches, and convulsions. These symptoms can worsen, resulting in respiratory paralysis and eventually death.[4]

Because of the significance of the thyroid gland and its hormones it is important to understand complications affecting the thyroid, one of which is thyroid cancer. There are several types of thyroid cancer. The identification of the type of thyroid cancer in a patient is important for the specific treatment that patient is to receive. Because of the importance of the thyroid gland itself the treatment received by the patient is equally as important.

The most common type of thyroid cancer is papillary thyroid cancer. Papillary thyroid cancer is also the most successfully treated type of cancer and most people are cured through surgery. Papillary cancer accounts for about 10,000 cases of thyroid cancer each year in the United States. This particular cancer forms in the follicular cells of the thyroid. The most common diagnostic tool used to identify papillary thyroid cancer is a fine needle aspiration biopsy. In this procedure fluid is removed from the thyroid lump and the cells from the fluid are examined for specific characteristics. One characteristic of papillary cancer is an optically clear nuclei. Normal thyroid cells have a dark nucleus but papillary cancer cells have characteristic clear spots within the nucleus. Another characteristic of papillary cancer is called "nuclear grooving." This is where a groove becomes visible within the nuclei. Papillary fronds may also be visible when looking at the cells from the biopsy. Fine needle aspiration biopsies are over
they have to be removed as well. If there is a recurrance of the cancer the cancer nodules can be removed again by surgery, or if the entire thyroid has already been removed radioactive iodine treatment can be used.\[3\][8]

The second most common type of thyroid cancer is follicular thyroid cancer. Follicular thyroid cancer is generally more aggressive than papillary thyroid cancer but the cells still grow slowly and treated successfully if diagnosed early. Like papillary thyroid cancer follicular thyroid cancer begins in the follicular cells. Follicular cancer is one of the more trying types to try and diagnose because unlike papillary cancer there are no characteristics that can be easily identified by fine needle aspiration. It is difficult to differentiate between a follicular cancer cell and a nodular goiter which is a benign condition. Because of this, surgery known as a “diagnostic lobectomy” is used to diagnose follicular cancer. In this procedure one of the lobes of the thyroid is removed in order to identify the follicular cancer cells. Once the lobe is removed the entire capsule surrounding the nodule is examined for follicular cancer cells. If the nodule is found to be benign the patient keeps the remaining lobe and can function without the use of hormone drugs. If cancer is found in the lobe the rest of the thyroid is surgically removed. Like papillary cancer, follicular cancer can be cured surgically. Unlike papillary cancer, follicular cancer tends to spread to different parts of the body. While papillary cancer mainly only spreads to the lymph nodes, follicular cancer tends to spread to the lungs or bones. For this reason early diagnosis and removal of the follicular cancer cells is important to prevent the spread of the cells which would cause more serious complications.\[3][5]

Medullary thyroid cancer is much less common than papillary and follicular cancer. It also differs from the other two cancers by where it originates. Medullary thyroid cancer originates in the C cells in the thyroid. Cancer is the C cells can cause higher levels of calcitonin to be produced which would serve as a red flag for medullary cancer. There are four different types of medullary cancer, sporadic, MEN 2A, MEN 2B and familial. Sporadic medullary cancer is not hereditary and cannot be passed on to a patient’s children. MEN associated stands for multiple endocrine neoplasia. These are tumors passed from generation to generation which affect endocrine, or hormone secreting glands. MEN 2A patients have thyroid cancer as well as tumors that affect the adrenal gland and the parathyroid glands. MEN 2B patients also have thyroid cancer and tumors affecting the adrenal gland but not the parathyroid glands. Symptoms of MEN 2B include bumps on the tongue (mucosal neuromas), under the eyelid and in the stomach. Familial medullary thyroid cancer is passed on through genetics but is not coupled with tumors of other endocrine glands the MEN 2A and 2B. Papillary and follicular thyroid cancers affect more women than men but medullary thyroid cancer affects both equally, as well as a wide age range. Medullary thyroid cancer can be diagnosed from taking cells from the nodule via fine needle aspiration and staining the cells for calcitonin. Blood tests can also show the increased level of calcitonin associated with medullary cancer. Once it is determined a patient has the medullary type of cancer it is important to look for tumors in the adrenal and parathyroid glands associated with MEN 2A and MEN 2B types of medullary cancer. Family history also plays an important role when diagnosing medullary type cancer because some types are hereditary. DNA testing can also be used for early diagnosis of medullary cancer. The DNA test can detect the changes in genetic mutations which cause the cancer to form. If diagnosed early enough medullary cancer can be cured completely. With early diagnosis most medullary cancer can be removed by surgery. If the cancer spreads to different organs throughout the body the patient can be treated with radiation and chemotherapy but this will not cure the cancer. If this happens the
cancer will most likely become lethal. Radioactive iodine also does not work for medullary cancer like it does for papillary and follicular cancers.\(^3\)

Anaplastic thyroid cancer is the least common type of thyroid cancer and also the most aggressive. It also begins in the follicular cells like papillary and follicular thyroid cancers but spreads quickly and is not easily controlled. The cause of anaplastic thyroid cancer is unknown but one theory is that it develops from other types of thyroid cancer and grows wildly. Like papillary and follicular cancers, anaplastic thyroid cancer affects more women than men. Anaplastic cancer cells are usually the easiest to identify when diagnosing. Patients also complain of symptoms such as hoarseness and difficulty breathing, where the other types usually don’t have related symptoms. In most patients a large mass can be seen growing in the front of the neck as well. Coarse needle biopsy is used instead of fine needle because the anaplastic tumor is more solid than the other cancers. A small piece of thyroid tissue may also need to be removed to make an accurate diagnosis. After identification of an anaplastic tumor a CT scan may be run to see how much the cancer has spread and to see if it has spread into the lungs. Unfortunately once diagnosed, there are not many options for treatment of anaplastic cancer. If the cancer is diagnosed early enough a patient might have a chance to have the thyroid gland removed and be cured of the cancer. More commonly, the cancer is identified at a stage in which the gland is inoperable and the only options are radiation and chemotherapy to try to attempt to shrink the tumor, but this obviously will not cure the patient of the cancer. The survival rate for anaplastic thyroid cancer is only 5%. Most patients die only months after being diagnosed.\(^3\)\(^5\)

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{normalthyroid.png} \quad \includegraphics[width=0.5\textwidth]{anaplasticthyroid.png}
\caption{Normal Thyroid \hspace{1cm} Anaplastic Thyroid Cancer Cells}
\end{figure}

It is not entirely clear what causes thyroid cancer. Cancer of the thyroid occurs when mutations of thyroid cells cause the cells to grow and multiply quickly this results in a tumor and can spread to other cells. While it’s not known what causes these mutations there are a number of certain risk factors thought to contribute to the growth of these cancerous cells. One of the main risk factors thought to contribute to thyroid cancer is exposure to radiation. Patients who have been exposed to high levels of radiation are at greater risk to develop papillary or follicular thyroid cancers. It is thought that one of the factors leading to the increase in incidence rate of thyroid cancer is past exposure to high doses of radiation. Doctors used to use x-rays to treat things such as acne and enlarged tonsils which exposed patients to large doses of radiation to the face and neck area. There is also the theory of people who were exposed to radiation from radioactive fallout from things such as atomic weapons testing, nuclear power plants, and atomic weapons plants. Other factors contributing to thyroid cancer include family history. Family history is related specially to medullary type thyroid cancer. Medullary thyroid cancer is thought to be passed on by a mutation to the RET gene passed from generation to generation. People with a family history of goiters and colon growths are also at risk as well as people with a personal history of goiters or thyroid nodules which turned out to be benign. Women are three times more likely to develop thyroid cancer than men in the United States. Thyroid cancer increases in
incidence with age as well. Anaplastic thyroid cancer occurs more frequently in people over 60 years old and thyroid cancer in general occurs more frequently in people older than 45. The most intriguing possible risk factor for thyroid cancer is iodine when considering the relationship between the thyroid gland and iodine. The thought is too much iodine in a person’s diet increases the risk of developing papillary thyroid cancer. Too little iodine in a person’s diet is thought to increase the risk of developing follicular thyroid cancer.⁶²

Thyroid cancer can be diagnosed in a number of ways depending on symptoms, medical history, and the type of thyroid cancer present. A simple physical exam can help identify problems with the thyroid. A doctor can feel the area in the neck of the thyroid as well as the lymph nodes in the neck for nodules and swelling. If an abnormal nodule or swelling is felt in these areas further diagnostic tests can be run in order to determine if the nodule is benign or malignant. A blood test run on a patient can determine if the thyroid is working properly. These blood tests check the levels of thyroid stimulating hormone, T4 and T3 levels, as well as the level of calcitonin present if a patient is believed to have medullary thyroid cancer. An ultrasound is used if nodules are too small to be found by a simple physical exam. The ultrasound uses sound waves to create an image of the thyroid. This image can show size, shape, and makeup of nodules present in the thyroid. Another diagnostic tool used is the thyroid scan. A patient ingests a radioactive material which shows up on a scan. There are nodules that take up more of the radioactive substance than the thyroid (hot nodules) and nodules that take up less of the substance than the thyroid (cold nodules). Cold nodules are potentially cancerous nodules. A biopsy is the most accurate way to identify thyroid cancer cells. There are several ways to do a biopsy of the of the thyroid tissue which are dependent upon the type of thyroid cancer present. Fine-needle aspiration is the most common type of biopsy in which a needle is used to extract cells from the nodule on the thyroid. These cells are then examined by a pathologist for specific characteristics. This is the most common diagnostic tool used to identify papillary thyroid cancer. A coarse needle biopsy is needed if the nodule is too thick or hard for a fine-needle aspiration. In a coarse needle biopsy a thicker needle is used to account for the hardness of the nodule. Nodules formed in anaplastic thyroid cancer are identified using coarse needle biopsy. If it is not possible to identify the cancer cells using a needle biopsy, a surgical biopsy of the thyroid tissue is needed. In a surgical biopsy a small piece of thyroid tissue or possibly an entire lobe is surgically removed then examined for thyroid cancer cells. A surgical biopsy is needed if follicular thyroid cancer is suspected because the follicular cancer cells are not easily differentiated like papillary cancer cells.⁶²

Accurate diagnosis of thyroid cancer is important when considering treatment as well is the specific stage the cancer is in when diagnosed. The stage the cancer is in depends on the size of the cancer nodules which have developed as well as the spread of the cancer to different sites in the body. The most common site of spread of thyroid cancer is the lymph nodes, but spread to the lungs and bones occur as well. When thyroid cancer spreads it is known as metastatic thyroid cancer. Although the cancer metastasizes and spreads to different parts of the body the cancer is still thyroid cancer and is treated as so. Different tests are used to identify the stage the cancer is in. An ultrasound can be used to detect the spread of thyroid cancer to areas near the thyroid, such as the lymph nodes. A CT scan is used to view the possible spread of the cancer cells to areas of the neck, lymph nodes, as well as the chest. An MRI can be used to show spread to the lymph nodes as well as other areas, and a chest x-ray can detect spread into the lungs. Another technique used to detect the spread of the thyroid cancer is a whole body scan. This works by ingesting a small amount of radioactive substance which travels throughout the body and will be
taken up by thyroid cancer cells present in other parts of the body. A full body scan is run
looking for uptake of the radioactive substance to identify which parts of the body the cancer
cells have spread to. \[6\]

Once diagnosed, there are a number of treatment options available to thyroid cancer
patient. Specific treatment depends on the type of thyroid cancer, size of the cancer, age, and the
stage or where else in the body the cancer has spread. The treatments of thyroid cancer include
surgery, thyroid hormone treatment, radioactive iodine therapy, external radiation therapy, and
chemotherapy. Depending on the type of thyroid cancer and the stage of the cancer the treatment
can be limited to one or a more likely a combination of several treatments. The most common
treatment for people with thyroid cancer is surgery. The surgery involves the removal of the
entire thyroid are part of the thyroid and depends on the type of thyroid cancer as well as the
stage of the cancer. A total thyroidectomy is total removal of the thyroid gland through an
incision in the neck. All types of thyroid cancer can be treated by total removal of the thyroid
gland. Most of the time a small amount of thyroid tissue is left behind to avoid damaging the
parathyroid glands or the larynx and the remaining thyroid tissue is destroyed by radioactive
iodine treatment. If the cancer has spread into the nearby lymph nodes they can be surgically
removed as well. A lobectomy is partial removal of the thyroid gland. This treatment can be used
on people with follicular or papillary types of thyroid cancer. The cancer can be completely
removed by removing only one lobe but sometimes lobectomy patients return to have the
remainder of the thyroid removed. Since the thyroid, which contains the cells which create
thyroid hormone, is removed a thyroid hormone treatment is coupled with removal of the
thyroid. Pills which act as thyroid hormone must be taken for the rest of the patient’s life. If the
parathyroid glands are also removed the patient must also take a calcium supplement as well as
vitamin D pills to make up for the loss of parathyroid hormone. Another risk of surgery on the
thyroid is the risk of damaging nerves or muscles surrounding the thyroid. Specifically if the
larynx is accidently damaged during surgery the patient will have voice problems. \[6\]

Thyroid hormone treatment is virtually always attached to thyroid surgery. Thyroid
hormone treatment is the replacement of natural thyroid hormone by taking pills which act as
synthetic thyroid hormone. It is particularly important to take the correct dose of thyroid
hormone. If too much thyroid hormone is taken, heart rate can increase, as well as chest pains,
cramps, weight loss, diarrhea, and feeling hot and sweaty. If the dosage of thyroid hormone is
inadequate the symptoms include weight gain, feeling cold, fatigue, and dry hair and skin. \[6\]
Synthroid® is the number one prescribed thyroid hormone drug in the United States. Synthroid®
is a name brand for levothyroxine sodium tablets. L-3,3',5,5'-tetraiodothyronine sodium salt is
the synthetic form of T4 and is identical to the T4 produced by the thyroid gland. Levothyroxine
sodium acts as T4 in the body and is converted to the active form, T3, by specific cells in the
body. \[8\]

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\]

L-3,3',5,5'-tetraiodothyronine sodium salt [levothyroxine (T\text{4}) sodium]

Radioactive iodine therapy is another treatment available for papillary and follicular
thyroid cancer. Radioactive iodine is used to kill thyroid cells as well as thyroid cancer cells after
surgery without damaging other cells in the body. Unfortunately anaplastic and medullary thyroid cancer cells do not respond to radioactive iodine. Radioactive iodine is an iodine isotope, I^{131}, which releases radiation for medical use. I^{131} is ingested either as a liquid or a capsule and travels through the bloodstream where it eventually travels to the thyroid or thyroid cancer cells present in the body. Once radioactive iodine is taken up by thyroid cells or thyroid cancer cells the cells are killed. People who receive radioactive iodine treatment try to avoid contact with other people because they are emitting radioactive material. It is also important for people receiving this treatment to drink a lot of water as well as eat hard and sour candies. This helps combat the dry mouth caused by the treatment as well as avoid the loss of sense of taste.\textsuperscript{[6][7]}

External radiation therapy or radiotherapy is a localized treatment for thyroid cancer cells that are unresponsive to I^{131} therapy. It is also used to treat cancer which has spread to other parts of the body such as the bones. This type of therapy uses high-energy rays to target and destroy cancer cells. The treatment is normally administered several days a week for a few minutes at a time. Another alternative treatment is chemotherapy. Chemotherapy is mainly used as treatment for anaplastic thyroid cancer. Chemotherapy is this use of chemicals or drugs to kill cancer cells. The chemicals travel through the bloodstream and can target cancer cells throughout the body. The risk of chemotherapy is the affects the dosage or type of chemicals used to kill the cancer cells have on the other cells in the body.\textsuperscript{[6]}

In conclusion, I feel this topic was interesting to research not only for the scientific knowledge gained, but because of my direct experience with people who have fought the battle against thyroid cancer, and won. The most intriguing part for me was learning how such as small gland regulates a wide range of functions within the body. In most thyroid cancer cases, the entire gland is removed and the individual must endure hormone therapy for the rest of their life. So not only does your body have to adjust, the individual must adapt to a new lifestyle where every day begins with a pill. Statistically, thyroid cancer may not be the most predominate type of cancer, but for those who have traveled the road to recovery, it is a type of cancer they are reminded of every single day. Modern medicine is constantly advancing, and with a 95% recovery rate for thyroid cancer cases, it should exhibit a glimmer of hope in the race for a cure.
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Abstract:

Embeda™ is a new drug by King Pharmaceuticals that is taking a giant step towards preventing opioid abuse. It is a morphine analgesic that has a sequestered core containing opioid antagonists so if crushed or chewed the abuser will not receive the same euphoria as they normally would with a regular tablet. This technology is sure to revolutionize the manufacturing of new medications and significantly cut down on opioid abuse.

Methods and Materials:

According to the Journal of the American Medical Association (JAMA) “Opioids are a family of related drugs that relieve pain. All of the opioids (sometimes called narcotics) are chemically related to opium, which is a substance collected from the poppy plant. Opioid drugs include opium, codeine, fentanyl, heroin, hydrocodone, methadone, morphine, oxycodone, paregoric, and sufentanil. When prescribed by a doctor, the pain-relieving properties of opioids are used during and after surgical procedures, for the pain of childbirth, for injury, and for other pain problems. Although opioid medications have helped millions of individuals with pain, these drugs can be used inappropriately.”

When ingested, opioids bind to opioid receptors, which relieve pain, give off a sense of euphoria, suppress the respiratory system, and give a degree of sedation. These affects fuel many addicts’ addictions.

Opioid abuse is a large growing problem around the world. “Drug abuse” in general “is a pattern of inappropriate drug use that leads to recurrent problems in fulfilling obligations, impaired physical functioning, conflicts with family and friends, and legal problems. Drug abuse may progress to dependence (sometimes called addiction), manifested by a strong desire to continue the drug despite the increasingly severe problems it causes, tolerance (a need for larger amounts of the drug to get the same effects), and withdrawal symptoms if the drug is stopped” says JAMA1. Opioid withdrawal for addicts starts hours after the last dose. Three to four hours after, the addict can start to feel anticipatory fear, cravings, and compulsive drug seeking behavior2. Which escalates around eight to twelve hours later to early withdrawal symptoms such as watering eyes, sweating, listless behavior, anxiety, restlessness, and stomach cramps2. After twelve to sixteen hours they can experience restless sleep, nausea, vomiting, excessive dilation of pupils, anorexia, cold clammy skin, fever, chills, and compulsive drug seeking behavior2. At 48 to 72 hours they hit the peak intensity of the withdrawal where their heart starts to race, they can experience hypertension, hypothermia, muscle spasms, nausea, vomiting, dehydration, compulsive drug seeking behavior, and possible cardiovascular collapse2. Even after six months they can still experience stimulus driven cravings, anorexia, fatigue, hypotension, and bradycardia where the heart slows down to less than 60 beats per minute2.

Prescription medications are widely abused because people think that prescription medications are safer to use than illicit drugs because they are legal with a prescription and they know family and friends that take them. Taking a medication that was dispensed by a pharmacist sounds a lot safer then going and buying a hard drug on the street where one does not know how it was made, who it was made by, or what was put
in it. As well, the new widespread phenomena of online pharmacies have made getting prescription medication extremely easier than going into a pharmacy where one can verify an individual's identification. This also includes ordering medication from other countries that do not have the same stringent rules on requiring prescriptions for certain medications. According to the Drug Enforcement Administration (DEA) on opioids "in spite of regulatory controls, drug abusers obtain these and other prescription medications by diverting them from legitimate channels in several ways, including fraud, theft, forged prescriptions, and via unscrupulous health professionals."³

With 11.4 million people in the US using prescription pain relievers non-medically, including a 542% increase in new abuse among teens from 1992-2002, this is clearly an expanding problem⁴. It is claimed that opioid abuse costs Americans over $484 billion annually from things such as loss of wages, abuse of health care system, car accidents, and crime with the associated criminal justice system costs⁵. Opioid abuse can also lead to death. From 1985 to 1995 in Arizona alone there were 2,625 deaths due to drug poisoning⁶. The majority of the deaths accruing from morphine and morphine derivatives were suffered by the Hispanic and American Indian races⁷.

Addicts that abuse the regular morphine extended release capsules break open the capsules and crush the pellets inside making a fine powder. With that they can intake the powder several ways, whether it be snorting it through the nostrils, mixing it with a liquid and injecting it intravenously, or putting it into a liquid to dissolve and drink it. This then gives the addict the euphoria or "high" almost instantaneously. This also gives off a much bigger "high" then if were taken normally because it is designed to slowly release over time and when the time release capsule is tampered with the entire drug is released all at once giving a much higher dose than was intended. This enhances the danger of over dosing because addicts are already taking a much larger dose than they should be at once and after time their bodies become immune to the high dose and they keep increasing the amount to get that same feeling. This can eventually lead to such a high dose at once their bodies will not be able to handle it.

King Pharmaceuticals which bought the rights to Embeda™ from Alpharma Pharmaceuticals is trying to put a stop to these epidemics. They say "an estimated 50 million Americans live with chronic pain, a serious, under treated public health problem. Opioids provide effective pain management and are especially useful in treating appropriately selected patients with moderate to severe chronic pain who have not responded adequately to other pain management therapies. However, the misuse, abuse and diversion of prescription opioids have escalated along with increased legitimate use in pain management. In fact, 70 percent of people who have abused opioids obtained the drugs from friends and relatives (by stealing, buying, or accepting them). As a result of the increasing misuse, abuse and diversion of prescription medicines, especially among young adults, patients and physicians may be reluctant to initiate opioid therapy for pain relief. Therefore, there is a need for products that deliver effective pain relief while minimizing the potential for misuse, abuse and diversion."⁸ "EMBEDA™ is a long-acting Schedule II opioid analgesic" that "contains extended-release morphine pellets, each with a sequestered core of naltrexone, an opioid antagonist. The formulation is designed to work such that if taken as directed, the morphine would relieve pain while the sequestered naltrexone would pass through the body with no intended clinical effect. If EMBEDA™ pellets are chewed or crushed, naltrexone is released and rapidly absorbed,
reducing the feeling of drug liking and euphoria. This means EMBEDA™ may reduce misuse or abuse when tampered with by crushing or chewing." The overall idea of the drug, as well as the chemical structure of morphine sulfate and naltrexone are depicted below.

Morphine sulfate
(5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol
Naltrexone
17-(cyclopentylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6-one

An agonist is a drug that binds to a receptor and alters the activity. It mimics the chemical that makes the receptor function, or essentially acts to “turn on” the receptor. Morphine is a full agonist, that is, it binds to the opioid receptor and activates it to its full capacity. It copies the effects of endorphins at the mu-opioid receptor thru the central nervous system.

An antagonist drug does the opposite of the agonist. It binds to the receptor to block or weaken the agonist mediated responses.

EMBEDA™ is not the first drug to use the agonist/antagonist formulation to try to deter drug abuse. Talwin generically known as pentazocine was another narcotic that was widely abused in the late 1970’s and early 1980’s. It was combined with an antihistamine called tripelennamine which was blue in color. The street name for this combination was “T’s and Blues”. The abuser would get a euphoric effect after injecting the two, similar to heroin but at a lower cost. This helped it become widespread as well as the fact that doctors first believed it could not be abused. Drug addicted doctors also abused the drug because it was not a schedule II medication therefore it could be prescribed in large quantities without being picked up on by monitoring systems. The extensive abuse became so bad the manufactures were considering pulling it off the market. In a last ditch effort to save the medication they tried reformulating it with an antagonist naloxone and came up with a drug now known as Talwin NX. Naloxone is an opioid antagonist that is not absorbed well through the oral route. So when taking Talwin NX as intended (orally) the patient would not absorb the naloxone and only receive the effects of the pentazocine. However, if the medication was to be crushed and injected the naloxone would compete at the receptor site with the pentazocine reducing the opioid affect.

Talwin NX proved to be successful looking at the Drug Abuse Warning Network emergency room system (DAWN). DAWN is a public health surveillance system that monitors: 1) Drug-related visits to hospital emergency departments (EDs) and 2) Drug-related deaths investigated by medical examiners and coroners (ME/Cs). Pentazocine went from being mentioned in the system 2,700 times in 1981 down to 1,550 times in 1983 when Talwin NX was introduced. Then it continued to fall to only 500 mentions by 1987. This paved the way for other drug companies to attempt making deterrent forms of medication.
Pain Therapeutics, Inc. is another company striving towards making abuse deterrent drugs. They have teamed up with King Pharmaceuticals in launching their investigation of a drug called Remoxy®. “It is an extended-release oxycodone capsule in a high viscosity, hard gelatin capsule” that “cannot be fragmented even with freezing, oxycodone cannot be extracted by dissolution” and stirring in high concentrated alcohol just releases a fraction\textsuperscript{13}. They are in the process of getting it FDA approved to start marketing it. In addition, they are beginning research on two other deterrent drugs named PTI-202 and PTI-721 but have not released any information other than the two will be instrumental in helping alleviate opioid abuse\textsuperscript{13}.

Acura Pharmaceuticals is another company pairing with King Pharmaceuticals as well in a study of another deterrent drug called Acurox. It is an oxycodone hydrochloride tablet that contains niacin. It is “designed to deter misuse and abuse by intentional swallowing of excess quantities of tablets, intravenous injection of dissolved tablets and nasal snorting of crushed tablets”\textsuperscript{14}. It has a gel forming agent that, supposedly, if tampered with will inhibit its ability to be extracted and injected intravenously as well as the ability to snort it through the nasal route\textsuperscript{14}. The niacin acts to deter the intentional oral overdosing by inducing niacin flush. Niacin, which is used to reduce high cholesterol, in large quantities results in what is called a niacin flush\textsuperscript{15}. It causes the small capillaries in the body to expand and blood flow to increase which means the body has to start working harder to pump the blood and results in increased heart rate\textsuperscript{15}. Also the skin starts to flush or redden and eventually the body starts to send histamine to the cells which then causes the person to itch\textsuperscript{15}. The overall experience is unpleasant and sometimes scary to people who do not understand what is going on. This will help deter abuse after the addict experiences it just one time.

EMBEDA\textsuperscript{TM} appears to be one of the first of many deterrent drugs soon to hit the US market after Talwin NX’s success. Phase III of the drug’s 12-month open-label safety and efficacy study results were released in January 2009 “The results showed that EMBEDA\textsuperscript{TM} provided continued pain relief for up to 12 months in opioid-tolerant patients with chronic, moderate to severe, non-malignant pain. Findings also showed that EMBEDA\textsuperscript{TM} was safe and well-tolerated for long-term chronic pain therapy.”\textsuperscript{7} While Embeda\textsuperscript{TM} is an investigational new drug, the FDA has put a Priority review on its
investigation and an article released by MSNBC on March 13, 2009 claims its US release will be sometime this year.  

Conclusion:

I used to believe people addicted to drugs were a basic stereotypical image of drug addicts; dirty, uneducated, unemployed, thieving, manipulative, etc. Now working in a pharmacy, I see, first hand, that I was completely wrong. It could be anyone; moms, doctors, lawyers, teenagers, and so on and so forth. I have heard horror stories from family members that say their loved ones had great lives and after being injured and taking a narcotic analgesic became addicted. This shocked me at how ignorant I had been to the thought of the type of people that abused drugs. As well as how big of a problem prescription drug abuse actually is.

I think the idea to start creating deterrent drugs is a much needed step forward for our medical community. I have high hopes for EMBEDA™'s success for the sake of our society.

After researching this medication, I found it to be not only exciting, but also fascinating in its design to attempt to halt its abuse. It has encouraged me even more so now, that I am going into a field that I will love. I am excited for the day when I will get to research medications and find new ways to make contributions to the medical field.
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Noninvasive Cataract Treatments
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4/24/2009
Abstract

Surgery to correct cataracts is a controversial debate in the optical community. Historically, cataracts were solved with surgery. The debate lies in the dangers of invasive treatment: not every one is a healthy candidate for and surgery can lead to other complications. For those who are detected early or know of prevalence in their family history healthy changes in medication, diet, or lifestyle can change the severity of cataracts.

Causes

Cataracts are defined as a slow but progressive degeneration of the lens in the eye. This can be visibly seen a white cloudy formation over the eye. As most cases of cataracts do not cause physical pain they can become a life-altering condition in which impaired vision and sensitivity to light becomes a daily struggle. Many cataract patients do not notice early symptoms, and mistake of oncoming cataracts as they view as a headache perhaps from lack of proper prescription lenses. There are a wide variety of causes for the formation of cataracts ranging from diabetes to family history, age, and even smoking (1).

Surgery is a common treatment for all stages of cataracts, but if treated early enough and with proper care there are a number of non-invasive treatments that can help one suffering with cataracts avoid invasive surgery.

It is important to understand how cataracts actually form in the lens of the eye itself. Within the eye lies the outer most layer of the cornea which acts as a line of defense towards foreign agents what which with the aid of the tear ducts, which secrete a solution that helps keep the eye clean and hydrated in order to function properly (2). The lens in conjunction with the cornea serve to bend and focus light to help focus objects from a range of distances, the pupil according dilates in order to allow the correct amount of lighting into the eye for further focusing (2). This visual information is now dissected between size, shape, color, and distance and sent through the optical nerve to the brain for processing and reaction. This entire complicated process is handled within the blink of an eye. Within the lens of the eye, cataract damage is formed; the main source is oxidative damage (3). Oxygen free radicals that go unbalanced begin to remove electrons from cells lying in the cell membrane and begin to cause damage, as this process continues cloudiness forms as a sign of cell damage in the lens. Another contributing factor can be advanced glycation end products or AGE’s (3). In other words a surplus of sugars begin to attach to proteins in the lens changing their overall structure. The lens being a naturally flexible organ overtime due to AGE’s begin to become rigid and have less of an ability to focus light causing a discomfort in sight and cataract formation. AGE’s can be linked to diabetes where the body has an inability to process sugar normally. Smoking is linked to cataract development as an accelerant; habitual smokers increases oxidative stress in the body that occurs in the eye (4). While most causes of cataracts can be linked to heredity,
diet, and lifestyle choices. Another cause of cataract development can be trauma to the eye; when trauma to the eye occurs such as scratching the cornea or a bacterial infection or change in the lens structure may occur (1). Trauma can weaken an eyes defensive as it attempts to repair damage caused to blood vessels allows the lens to become or susceptible to oxidation or other forms of damage to develop a cataract. An optometrist or ophthalmologist currently has an arsenal of options for non-invasive treatments to choose from in addition of surgery.

Disability

There are three main types of cataracts all defined with the same result just depending where the cloud-like structure begins to form. A subcapsular cataract forms in the back of the lens and is commonly linked with diabetes and high levels of steroids. Nuclear cataracts occur right in the center of the lens and is commonly linked to the oxidation brought on by aging. A cortical cataracts form in the cortex and instead of a gradual overlapping of cloudiness causes more of a spoke formation (4). All three forms of cataracts begin with small signs of blurred vision that could be confused with a headache or high stress, but as time continues these vision problems increase. Congenital cataracts are defined as when a child at birth shows classic symptoms of cataracts with out developing symptoms over time. If left untreated congenital cataracts could lead to what is commonly known as “Lazy Eye” or where the pupil begins to lose focus of its main point of sight. More options exist for young children, as they have not settled completely into their distinct vision yet. Nuclear cataracts do have a defining symptom that distinguishes from the other two, a temporary improvement in near vision also referred to as “second sight” occurs in the early stages of symptoms (6). Within time all three forms of cataracts the cataract begins to grow in an outwardly fashion slowly reducing the available field of vision. A heightened sensitivity to light begins to form, which is especially dangerous for nighttime driving as oncoming headlights will become almost unbearable and a distraction. Colors being to lose their definition and far objects begin to lose recognizable shape all together. Basically it is comparable to viewing out of a dirty, cloudy glass that only becomes worse with out treatment.

Many people with cataracts will denounce early symptoms as it usually occurs in one eye at first being able to use the other more dominantly. The problem with this is that the eyes are created to work in junction together, one can function with out the other but the strain created on this “healthy” eye will in time allow the eye to become over time in a sense tired requiring if not already having a harsh prescription. Also assuming for one eye to take over will slightly reduce the peripheral vision allowed. A good way to test your own peripheral vision is to extend both your arms out until you can barely see your own fingers while looking forward that is your field of sight. Now conduct the same with only one eye and that becomes your new field of the sight, the difference is what could seem minimal but necessary for activities such as driving. Treatment of one cataract eye as opposed as letting the symptoms increase and spread to both eyes is a risk. Early detection is key.
Surgery Complications

An overwhelming number of sources list surgery as the first and best option for cataract treatment. Many claim that cataract surgery creates the fastest results and its postoperative healing period is minimal while those noninvasive options require months of time to expect any sort of results. While surgery does provide a high result of success there are some factors that allow it to be not the best choice at first. Just like any other surgery not all patients are ideal candidates for the procedure. They may not be able to meet some or all physical requirements, whether it may be high blood pressure or a weakened physical presence as which maybe be present for those elderly patients. Another factor could be that of an emotional level, a cataract surgery is entirely performed while the patient is awake and many may fear the process in first person view. Those suitable for surgery then undergo the procedure that consists of an outpatient procedure where the patient is placed down while applied with a sedative and an incision is made into the lens. After the incision it is the surgeons job to remove as much of the cataract as possible with out changing the integrity of the eye and replaces the removed area with an implant (6). The implants act as a filler for the removed area and assist slowly as the eye returns to its near normal state. An alternative to an implant would be contacts or prescription lenses. What a prescription lens does is bend the light before reaching the lens allowing a much less amount of strain on the eye allowing it to heal in a quicker time period. A common misconception is that surgery after cataracts will produce clear sight immediately. Many patients opt for glasses as the contact lens may provide too much of a discomfort post surgery. However surgery followed by contacts is the preferred treatment for congenital cataracts as the child has a higher tolerance to withstand change and would not require an implant, as the contact would help to achieve a successful recovery. One study in Toronto showed that using contacts rather than an implant was no difference in progress and parents opted for a contact rather than an implant (7).

While cataract surgery’s success is most partly due to the fact of its lack of invasiveness as compared to other procedures, complications do occur and range from something as small as inflammation to complete vision loss. While about most to all damaged cells are removed during the initial surgery a small percent remain to still cause some blurred vision. About twenty percent of all procedures exhibit some type of post surgery vision blurriness (6). An additional procedures involving a laser is a solution as no further incisions is required to make, the only problem is that this secondary procedure has complications of its own such as retina detachment. Another complication involves the implant dislocation. Dislocation of the implant may occur and could affect vision where you constantly see the implant or even have double vision. Double vision is an eyestrain and could lead to chronic migraines. Improper post surgery care could also lead to a number of issues. A patient in the following days after surgery is required to administer topical antibiotics and refrain from any strenuous activity as heavy activity could lead to bleeding and pressure build
up in the operated eye possibly leading to glaucoma. In weighing out the whether or not to elect surgery as an option, surgery should be at best a last option.

Diabetes onset Cataracts

Both type one and type two diabetics who do not regulate their glucose levels run into a cluster of complications ranging from the heart, kidney, blood vessels, limbs, and eyes (8). Cataracts derived from diabetes are one of the most common ocular complications along with glaucoma. The high levels of unprocessed sugar in the body begin to alter certain protein structures in organs such as the eyes. In the case of cataracts glycation occurs in the lens of the eye where blood flowing from the optic nerve enters the retina and lens altering its flexibility and causing a cloudy lens, a common trait of cataracts. If treated early observance of a diabetes glucose levels could help alleviate cataract symptoms. These include from life style changes adding routine exercise, keeping a regular record of glucose levels, medication as prescribed by a physician, and diet modification (98). Additionally, unhealthy habits such as smoking and excessive drinking and eating of unnecessary foods should be reduced if not stopped. It is vital to stay in a healthy presence during treatment in order to gain an advantage over illnesses such as cataracts. The objective to modify diet is to intake foods low in sugar but still maintain the vital vitamins and minerals needed as recommended in a daily diet. Foods containing antioxidants can help reduce not only with a surge in glycation in the eye but help reduce oxidation in the lens. There exists a vast amount of natural foods containing antioxidants. Some common antioxidants include:

- Flavonoids/Polyphenols
  - Soy, Red wine, Concord grapes, Pomegranates, Cranberries, and Tea
- Lycopene
  - Tomato and tomato products, Pink grapefruit, and Watermelon
- Lutein
  - Dark green vegetables such as kale, broccoli, kiwi, Brussels sprout and spinach
- Lingnan
  - Flax seed, Oatmeal, Barley, Rye (9)

Along with foods containing antioxidants there is a wide assortment of supplements that contain essential vitamins and antioxidants. Dietary regimen is a healthy natural option in the treatment of cataracts and is the option of choice those trying to avoid costly procedures.

Nu-Eyes™

Nu-Eyes, also known as N-acetylcarnosine is a topical application is distributed in the form of drops. Currently not yet listed on the food and drug administrations database as approved, has clinical studies overseen in Russia with impressive results.
According to BioNational Pharmaceuticals the components of Nu-Eyes are:

- N-Acetylcarnosine 1.0% (approved by IVP)
- Glycerin (lubricant) 1.0%
- Carboxymethylcellulose sodium (lubricant) 0.3%
- Sterile Water (Ophthalmic Grade Isotonic Solution, pH 6.3 to 6.5) buffered with Potassium Phosphate
- Dibasic and Potassium Phosphate Monobasic
- Purified Benzyl Alcohol (Preservative)

Application for Nu-Eyes is just that like other common eye drops where once tilts their head back and without blinking applies a drop in the center of the eye and immediately closes to ensure maximum application. Clinical studies have shown that using the appropriate dosage in a time span of six months and on have shown significant reducing in ocular opacity and removal of what is known as halos around the iris, of clinical studies twenty-six patients who were not given the placebo showed 90% improvement. Of those 88.9% showed an improvement to glare sensitivity and 41.5% had an overwhelming over all improvement (10).

Additionally, N-acetylcarnosine is effective as a result of the natural carnosine found in the eye as a powerful antioxidant and opposes glycation. Carnosine (beta-alanyl-L-histidine) C9H14N4O2 is naturally found not only in the eyes but also in the brain, nervous system, skin, and muscles. It has been linked as our bodies own form to slow down the aging process. As the human body ages the natural levels of enzymes and reactions slow down, a link between our own aging process and levels of carnosine could show a pattern of cataract cases amongst the elderly population. Why Nu-Eyes exists as acetylceronasine is that as an eye drop diluted solutions of carnosine alone are not able to bypass the lipid layers of the eye to reach the lens and other structures needed in repair or balance in the eye, carnosine alone would be broken down by tears and outer layer of the eye to anayl and histamine which later breaks down into histamine that which causes allergic reactions (3). Improper application of carnosine would only cause an allergy than repair. Additionally different forms of application of carnosine would not ensure maximum deliverance to the eye as stated before that carnosine is also used by different systems of the body. To be able to be a successful topical eye drop Nu-Eyes adds acetyl group in order to pass through the outer layer and into the eye system itself to safely administer carnosine to the lens. This acylation of carnosine adds stability to its structure allowing it to not just apply all at one but become a time releasing agent to give small slow doses to the lens.

Conclusion

In a perfect situation cataract treatment would only be minor and be more focused on prevention but cataracts does on occur vision-altering basis. As more advances in chemical applications in cataracts rise, the utmost need for surgery could now be seen as a an secondary option. Surgery should not be an option that is omitted in cataract treatment, though it should be used with caution and as almost of a final option. No medical professional should discourage one option over another but rather list all possible
to the patient and help guide them to chose a path that is in the patient’s best interest. While the negative aspects and side affects of an invasive surgery are some to raise concern, as long as the patient is truly in need and other options have been explored it is critical to visit surgery as treatment. An option that I favor most is lifestyle changes. Lifestyle changes such as diet and exercise is one of the most basic treatments as it yields the potential of the natural sources around us. As time progresses we discover more in regards to advancements in both invasive and non invasive treatments but hopefully one day we arrive to a complete noninvasive treatment to cataracts. Just as important as the path of treatment is also patient responsibility, as much focus is placed on treatment so should be on awareness. It is this junction of education and future possible treatments that lay the success of noninvasive cataract treatment.
Bibliography


Genetically Modified Food:
Is all food created equal?

Prepared for
Dr. Hank Mancini
Instructor
Organic Chemistry 236

Prepared by
Chris Robinson
April 22, 2009
Abstract

When you hear the term “Genetically Modified Foods (GMFs),” what do you think? Most people probably assume this is something of the future. How could you possibly genetically modify food? Well, the truth is that our food, especially in the U.S.A., is genetically modified and has been for quite some time. This paper is going to demystify the foreign term “Genetically Modified” and give it meaning. We all need food for survival, but is all food created equal?

Definition- What is a Genetically Modified Organism?

The World Health Organization (WHO) defines genetically modified organisms (GMOs), also known as Genetically Engineered Organisms (GEOs), as organisms in which the genetic material, DNA, has been altered in a way that does not occur naturally. Specific genes are chosen to be transferred into other organisms, which can be related or non-related species. The technology that allows genetic engineering falls under any of the following names: modern biotechnology, gene technology, recombinant DNA technology or genetic engineering. Another name for human made DNA is transgenic.

To breakdown all of this, we are now able to select specific genes, particularly desirable genes of interest and move selected genes into a different organism. By doing so, we can create a product for a special need or purpose. The primary focus in this paper is genetically modified foods (GMFs); however, biotechnology allows for the creation of GM products (current or those in development) such as medicines, vaccines, foods, food ingredients, feeds, and fibers. With the development of biotechnology over the past few decades, we have been able to develop numerous applications that will ever so increasing effect everyday life. Technological advances greatly impact the way people live their lives. Just like the Internet changed the way people communicate, the technology used to today to grow our food is no different.

History of Food Production & Food Preparation

In the 18th century, the only means of transportation were waterways or trail. There was no electricity; therefore oxen and horses were used and all sowing in the farm fields was done by hand. At this time, farmers made up 90% of the workforce, producing “cash crops” for economic survival.

In the beginning of the 19th century, the process of “canning” food began to preserve mass quantities of food by placing cooked food into sealed containers so the food wouldn’t spoil. At first there was much public skepticism about food safety; however this technique is still used today.

During the industrial revolution (1840-1860), over 3000 miles of railroad infrastructure was installed thus massively improving transportation. The development of the telegraph
revolutionized communication to once distant communities and dramatic increases in manufacturing brought labor-saving devices to rural farm communities.3

During the mid 1850s, the pasteurization of food products began. With this process, the production of pathogens was slowed down so that the food could safety be digested before the expiration date. Pasteurization stopped the spread of diseases, especially tuberculosis and undulant fever.11 Today we have several products that our pasteurized, especially dairy products.

Today, less than 1 percent of the United States population works in the agriculture field.4 The United States is no longer agriculturally dominant and we don’t rely on “cash crops” for survival. Currently, the U.S. and Canada produce 90% of the world’s transgenic crops.5 The main crops that have been genetically modified include corn, soybean and cotton; however, the following items are all derived from these crops: cornmeal, oils, sugars, etcetera.6 The farm is no longer a family struggling to meet ends, but rather a transfer to corporations focusing on bigger profits.

Overview of GM Crops

The initial objective for developing plants based on GM organisms was to improve crop protection. The GM crops currently on the market are mainly aimed at an increased level of crop protection through the introduction of resistance against plant diseases caused by insects or viruses and developed resistance towards herbicides.

DNA- Deoxyribonucleic acid

Just like the blueprints to a skyscraper in a downtown metropolis to the infamous secret family recipe that has been passed down countless generations, our bodies are just the same; we are all made up of genetic material called DNA. Our bodies contain 25,000 to 30,000 genes12. Nucleotides are the subunits that are linked to form the nucleic acids ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), which serve as the cell’s storehouse of genetic information.10 Our DNA holds all of our small unique pieces of genetic information coded within the double helix structure. The nucleotides represent the small building blocks and the helix represents the blueprint for the entire organism it builds.

*Appendix Tables 1-1.2
DNA is composed of several nucleotides which contain three components: a five-carbon sugar, a phosphate group and a nitrogenous base. There are two different types of bases purines and pyrimidines. Purine bases are named Adenine (A) and Guanine (G). Pyrimidine bases are named Cytosine (C) and Thymine (T). It's important to note that DNA contains deoxyribose sugar and RNA contains ribose sugar. The only difference between these two sugars is that deoxyribose has one fewer oxygen atom than ribose.\(^\text{10}\)

![Diagram of nucleotide structures and DNA structure](image)

**Table 1.1**

<table>
<thead>
<tr>
<th>Purine bases (two rings)</th>
<th>Pyrimidine bases (one rings)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenine (A)</td>
<td>Cytosine (C)</td>
</tr>
<tr>
<td>Guanine (G)</td>
<td>Thymine (T)</td>
</tr>
<tr>
<td>Uracil (U)</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1**

**Special Note:**
Uracil is found in RNA and replaced with Thymine (T) in DNA.

Friedrich Miescher discovered DNA in 1869 while extracting a white substance from human and fish cells in his lab.\(^\text{2}\) Close to a hundred years went by before we discovered that DNA was a three-dimensional double helix structure. James Watson and Francis Crick at Cambridge University, were able to build a model noting that the DNA structure was built of two chains of nucleotides representing the double helix.\(^\text{2}\) The double stranded helix structure contained a phosphodiester backbone. The phosphodiester backbone was made up of long polymers of nucleotides with each strand made up of repeating sugar and phosphate units joined by phosphodiester bonds.\(^\text{2}\)

**Recombinant DNA- Today's RNA**

Recombinant DNA is the backbone of biotechnology by allowing us to directly isolate specific genes and manipulate DNA. When using the Recombinant DNA technique, a single strand of DNA is produced from two different sources. These two sources can be from two totally unrelated species.
Restriction Endonucleases were first discovered by Paul Berg at the University of California San Francisco in 1973 and published in a paper titled “Construction of Biologically Functional Bacterial Plasmids In Vitro.” In 1978, the Nobel Peace Prize was awarded to Werner Arber, Daniel Nathans and Hamilton O. Smith "for the discovery of restriction enzymes and their application to problems of molecular genetics." This discovery led to a breakthrough on how to cut and paste DNA.

**Process of Recombinant DNA**

The term recombinant DNA is man-made human DNA from two different sources or species. Controversy has risen over man now playing God and manipulating DNA for desirable traits or genes. Since the completion of the Human Genome Project (HGP) in 2003 by the United States Department of Energy and the National Institutes of Health, all 25,000 genes in human DNA have been identified. Although the HGP is finished in identifying the more than 3 billion base pairs that make up DNA, researchers will continue to analyze for many years to come to fully understand all of the genetic information that makes humans tick. Before the HGP project, finding a particular gene was like finding an address for someone in New York City and you only knew their first name. Now after the completion of the HGP, genes are now easier to locate.

The process to make recombinant DNA consists of these 3 steps:
1. Locate genes that have desirable traits.
2. Remove the specific genes from their original DNA using restriction enzymes.
3. Place in new strands of DNA using a vector, or delivery vehicle.

**The Flavr Savr Tomato**

The main selling point behind genetically modified foods is the ability to stop using pesticides and to also create a longer shelf life. Calgene, now owned by Monsanto, created the first genetically engineered food to reach the market after approval by the Food and Drug Administration in May 1994. The goal of the Flavr Savr tomato was to increase shelf life and reduce the number of tomatoes lost by farmers during shipping. Calgene was able to accomplish this by inserting an antisense gene that interfered with the production of the polygalacturonase enzyme, which controls the ripening
process. This way the tomato spent more time ripening on the vine, preserving flavor and increasing shelf life to reduce losses. The Flavr Savr tomato had several benefits for commercial purposes of tomatoes, but not so much for consumers in the marketplace.

Calgene wanted to take their breakthrough technology to the marketplace with a bang. Calgene tried selling the Flavr Savr tomato as high priced gourmet produce with labels indicating that it was a GM product; however, high public skepticism and questions about nutritional value led to disaster. The public certainly did not want to pay more for something foreign and nutritionally deprived. Calgene also ran into production problems and after several attempts could never produce the tomato on a large scale. The Flavr Savr tomato was pulled from the market in 1996 and at the same time, Monsanto bought out Calgene. The Flavr Savr Tomato may not have had success as being the first transgenic crop, but this was the beginning of a whole new way to grow food.

Golden Rice- fortified with a β-carotene (Vitamin A)

Syngenta, another corporation like Monsanto that produces GM products has developed a variety of rice called Golden Rice. The key difference between regular rice and Golden rice is the increased production of β-carotene (Vitamin A). The target market for this transgenic crop is countries with high rice consuming diets, yet high vitamin A deficiencies. This primarily occurs in third world countries where a diet is not diversified to receive all of the necessary nutrients from multiple sources. The research and development of Golden Rice was made possible with combined efforts from Syngenta and The Golden Rice Project.

VAD- Vitamin A Deficiency

Vitamin A deficiency (VAD) is the leading cause of preventable blindness in children and increases the risk of disease and death from severe infections. Vitamin A deficiency is a public health problem in more than half of all countries, especially in Africa and South-East Asia, hitting hardest young children and pregnant women in low-income countries. VAD also leads to premature death. The goal of Syngenta with the Golden Rice Project was to curb this phenomenon by developing a method to increase the vitamin A intake in third world countries through food intake. The recommended daily amount of rice for a child 1-3 years of age is 300 μg per day.

The Golden Rice Project focused primarily targeting countries whose overall intake of Vitamin A, from all dietary sources, was the lowest. The countries with the highest Vitamin A deficiencies are Africa and South-East Asia. All of these countries typically consume less than 100 μg of Vitamin A per day.

The Golden Rice Project is currently testing its Golden Rice crops in the field. In September of 2004, the first Golden Rice crops were planted and the results were amazing. The crops produced in the field produced an average of 6 μg/g β-carotene. In the second generation of Golden Rice, a greenhouse was used and an average of 23 more times the variety original developed in 1999.
Presently several new techniques are being exercised to see which methods yield the highest amount of β-carotene per grain. The benefit of Golden Rice is its easy integration into the food supply; the Golden Rice variety can be easily hybridized to other breeds of rice. The downside is that for an adult to get all of their recommended daily intake of Vitamin A from Golden Rice they would have to eat 9 kg (~20 Pounds) of cooked rice! Obviously, no one would could possibly eat that much rice in one day; however, any effort to help increase Vitamin A intake can lead to substantial health benefits. For excellent health we need to utilize as many sources as possible to receive all the proper nutrients we need.

**Benefits of GM products**

After the industrial revolution, more and more people chose to work in factories instead of the family farm. Agriculture used to be the backbone of the U.S., but just like everything else, times change. As of 2006, there were 859,000 agricultural workers in the U.S., mostly in California, Oregon and Nevada. This makes up less than one percent of our entire population in the U.S.!

A result of technology is to get more products by doing less work; this is the case with biotech crops. The 10 year study of GM crops in the U.S. concluded that herbicide-tolerant cotton and corn were associated with increased returns, as were insect-resistant cotton and corn when pest infestations were more prevalent. Not only were the farmers receiving more for their money, they also had more time to spare. The study also stated the adoption of herbicide-tolerant soybeans is associated with increased off-farm household income, suggesting that farmers adopt this technology because the simplicity and flexibility of the technology permit them to save management time, allowing them to benefit from additional income from off-farm activities.

Another important benefit from the use of GM crops is the protection of the environment. Overall pesticide use is lower for adopters of GE crops, and the adoption of herbicide-tolerant soybeans may indirectly benefit the environment by encouraging the adoption of soil conservation practices.

**The First Decade of GM Crops in the United States**

The first biotech tomato became available to consumers in the United States in September 1994 after approval by the FDA. Since then, several different types of genetically modified products have been introduced and still used today. Much public controversy has risen over the labeling of such genetically modified products.

The USDA has to remain neutral since they promote the production of agriculture as well as regulate the production of agriculture. In 1992, the USDA president stated the agency’s policy on transgenic products by saying genetically engineered foods will not be treated differently from naturally produced foods, they will not be safety tested, they will not carry labels stating that they have been genetically engineered, nor will the government keep track of foods that have
been genetically engineered. The USDA has had a very laid back approach about the use of biotech food, unlike Europe. The main worry about the use of transgenic crops is losing control of everything and creating an irreversible problem. When transgenic crops are produced, they are in a controlled environment; however, Mother Nature is an uncontrollable environment, especially the spread of seeds and pollen when the wind blows. This is unable to happen in maize, or corn, but can happen to any other type of biotech product produced.

European Union (EU) trying to keep a Farmer’s Market

The European Union (EU) has been the leader in combating the use of technology in agriculture. This has been no easy task and some people wonder if the avoidance of biotech crops can be accomplished! In 1998, the EU required clear labeling put on all genetically modified soy milk; however, this wasn’t easy to track since the substance is lost when combined with other ingredients. Genetically modified soy is present in 60 percent of all the processed food sold in the supermarkets around the world. The truth is, people want to know what’s in their food and how their food is produced.

Labeling- GM or Non-GM?

The United States has experienced the greatest success in developing and applying transgenic crops into our food system. In most cases, genetically modified foods are unrecognizable because the changes are hidden in the genes and the manufacturers, mostly American firms, have successfully fought off labeling requirements as invitations to hysterical boycotts. Most of us don’t work in scientific fields, nor do we know much more about genetics than what’s published in Genetics for Dummies. The case in point is that most people can’t visualize the adoption of genes into our crops, and we can’t comprehend the consequences in modifying our food. Without knowing, we will always have fear, but by doing more, we gain knowledge.

As Americans, we are highly blessed with all of the government agencies we have in place. The United States Department of Agriculture (USDA) as well as the Food and Drug Administration (FDA) monitor and assist the safety of our food supply. Like any other government agency, they receive their equal share of critics questioning their methodologies. For example, the approval of bovine growth hormone, which raises cow’s milk production, was approved by the FDA in 1993 and has received little notice in the U.S. despite its extensive use. The American public highly relies on our government agencies to protect us from becoming mutants. Ten years after the first generation of genetically engineered (GE) varieties of major crops became commercially available, adoption of these varieties by U.S. farmers has become widespread. U.S. consumers
eat many products derived from these crops—including some cornmeal, oils, sugars, and other food products—largely unaware of their GE content.

Either way you look at the puzzle, no matter what side of the Atlantic you reside on, you have the right to know how your food was grown and if your food was modified.

Conclusion

We have discussed the process of how genetically modified foods are made, the benefits and the outcomes. I think genetically modified foods will continue to dominate the food supply without much impairment to our health. The USDA has allowed genetically modified food into our food supply for ten years without any severe problems, and without many people even noticing the difference. The track record shows that for the last ten years show no evidence of a problem occurring. My only concern is that we get ahead of ourselves and genetically modify something that creates an irreversible problem. Hopefully this will never happen and we will be able to enjoy the modern conveniences of genetically modified food.

We all want fresh products and this might just be as fresh as we can get them. Modernization has changed the way we live our lives. At this point, genetically modified crops provide us the benefit of capitalism, more profit for less work; we just don’t want to become too greedy that we kill ourselves. Literally.
References:


Appendix

Table 1:

<table>
<thead>
<tr>
<th>Component of DNA</th>
<th>Base: Can be any of 4 different bases. See table below</th>
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<tbody>
<tr>
<td>R–O–P–O–OH</td>
<td>deoxyribose in DNA (pentose: sugar with 5 carbons)</td>
</tr>
<tr>
<td>Phosphate Group</td>
<td>Deoxyribose sugar is found in DNA while ribose sugar is found in RNA</td>
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<tr>
<td>Cytosine (C)</td>
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Table 1.2

Example of Nucleotide with all 3 components
Life and Pain: Living With & Treating Fibromyalgia

Nicole Marie Runge

April 24, 2009
Abstract:

Fibromyalgia is a debilitating disease that is loosely understood and difficult to diagnose. Lyrica is a medication that has been approved to treat fibromyalgia in some patients with few side effects. The cause of fibromyalgia is unknown and treating it is a controversial topic in the medical field despite its new-found recognition as a clinical disease.

Introduction, fibromyalgia specifications:

What is fibromyalgia?

Fibromyalgia is a chronic disease that involves pain throughout the entire body as well as a great amount of fatigue. Most of the sufferers of fibromyalgia are women. In fact, as stated by the Pfizer Company itself, 80-90% of people that have fibromyalgia are women. This does not mean, however, that men and children are safe from the evil grasp of fibromyalgia. People experiencing the various symptoms of this disease are often suffering from other medical disturbances. Whether the fibromyalgia is brought on by the other problems a patient may be suffering from or vice versa is currently unknown.

What are the symptoms of fibromyalgia?

There are various and peculiar symptoms surrounding fibromyalgia. The most obvious is the unique and widespread pain. Other symptoms found by the U.S. Food and Drug Administration (FDA) is headaches, difficulty sleeping, painful menstrual periods, morning stiffness, difficulty remembering, and numbness in the extremities. Also, many people experiencing fibromyalgia may suffer from pelvic pain, depression, irritable bowel syndrome (IBS) or restless leg syndrome. Although there are no clinical tests available to diagnose
Fibromyalgia, medical providers can perform a physical exam to determine whether a patient does, indeed, have fibromyalgia.

How is one diagnosed with fibromyalgia?

The diagnosis involves the determination of what is known as “widespread pain”. This is determined by the 18 points on a person’s body (as depicted above) and whether the patient has pain in 11-18 points. According to the FDA, the patient must also have been suffering from this pain for at least three months. A common problem found with people in the medical industry is that there are, in fact, no other tests available to determine the diagnosis of fibromyalgia. This is part of what makes fibromyalgia such a controversial topic. Before the disease was determined to be a real disease it was often, and still is, misdiagnosed. Common misdiagnoses include lupus, mental instabilities, or side effects of stress. Also, there is no “fibromyalgia specialist”. This means that any medical provider can diagnose it.
What are the causes of fibromyalgia?

The cause of fibromyalgia is, unfortunately, unknown. However, there are many options that scientists have been researching to come to a conclusion on the actual causes. Some ideas they have been rummaging through, according to the FDA, are side-effects of a serious injury, a virus that may alter the way one's brain responds to pain, and emotional aches. One thing that adds to the controversy is that people with lupus, rheumatoid arthritis, and spinal arthritis can be more likely to be diagnosed with this disease as found by the FDA. The FDA also notes that scientists are looking into something called Substance P that is found in the spinal cord. They believe that persons suffering from fibromyalgia may have an "abnormal level of Substance P". Substance P is responsible for sending messages of pain to and from the brain. If the level of this is "abnormal" it can cause pain to feel much differently than it actually should to the patient. Because of this theory of the Substance P abnormality, researchers are also looking at fibromyalgia as a genetic problem meaning that there may be a gene(s) that can increase the likelihood of someone having it.

What are the treatments for fibromyalgia?

There are few medicinal treatments specifically for fibromyalgia. Only two have been approved by the FDA, Lyrica and Cymbalta. Cymbalta (duloxetine hydrochloride), a product of Eli Lilly and Co., was initially developed for depression diabetic peripheral neuropathy, and also anxiety. It was approved for fibromyalgia in June of 2008. The fact that it was initially for depression reinforces the belief that fibromyalgia may be a side-effect of stress or depression. Lyrica (pregabalin), a product of the Pfizer Company, was initially used to treat specific types of
seizures. It was approved for the use of treating fibromyalgia a year prior to that of Cymbalta. Both medications, according to the FDA, have shown researchers and doctors that they can significantly reduce the amount of pain that fibromyalgia sufferers experience. This allows them to live much more comfortable of lives. Other tactics used to treat this chronic disease is small amounts of exercise like jogging, walking, yoga, or even massage.

**Methods, a deeper look into Lyrica:**

![Lyrica Logo](www.lyrica.com)

**What is Lyrica?**

Lyrica is a drug marketed by the Pfizer Company. It was approved for and became the first medication specifically for the treatment of fibromyalgia in June of 2007, according to the FDA. Lyrica was initially released for other medical inconsistencies such as diabetic peripheral neuropathy, certain types of seizures, and pain acquired from altered nerves commonly from the painful disease known as shingles.

**What are the scientific details on Lyrica?**

The active ingredient in Lyrica is a compound known as pregabalin. Pregabalin is a crystalline solid that is white in color and is soluble in water. Lyrica also contains fillers or "inactive ingredients" such as lactose monohydrate, cornstarch, and talc as found in the medical pamphlet included with the bottle of the medication. Lyrica is dispensed in a capsule form in strengths of 25, 50, 75, 100, 150, 200, 225 and 300 milligrams of pregabalin. An example of a capsule of Lyrica and the chemical structure of it is illustrated on the next page. Its full
scientific name is \((S)-3-(aminomethyl)-5-methylhexanoic\) acid. It has an \(S\) configuration meaning it rotates in a counterclockwise manner. Another interesting aspect of this compound is the amino group found on the third carbon. Nitrogen is a common element found in medicinal products. Its longest chain consists of six carbons and it is a fairly simple compound that is used to medicate many problems. The shell of the capsule consists of gelatin and titanium dioxide.

![Chemical structure](image)

**How do they believe Lyrica works?**

The exact mechanism for how Lyrica works is not completely understood by scientists. However there are theories of what is happening when a patient with fibromyalgia begins taking Lyrica. The explanation given by the Pfizer Company explains that a person with fibromyalgia may be getting a greater amount of "electrical signals" being sent amongst the cells and Lyrica lowers the number of electrical signals causing the pain to diminish. This theory is depicted below:

![Lyrica mechanism](image)
The picture on the left is what it is thought to be like when a patient is not taking Lyrica and on the right is the effect of Lyrica. According to the patient information included with the bottle, the mechanism of the reaction involves pregabalin attaching to the “α2-δ site with high affinity”\(^3\). This occurs in the tissues of the nervous system. This is all that is known about the mechanism of pregabalin because it is still a mystery as to how it really works. They know some information from performing tests on animals such as mice\(^3\).

What are some side effects of Lyrica and what should be avoided?

Lyrica is a serious medication and is a class four drug. This means it is a highly monitored drug that can become habit forming\(^6\). Not only can it be habit forming but it can also interact with several medications a patient may also be taking. These medications include tranquilizers, medications for sleep, antihistamines, anxiety medications, and drugs to help or prevent seizures, as stated by the Pfizer drug Company in the patient information pamphlet\(^1\). Alcohol can also affect a person taking Lyrica because it can make the side effects more aggressive. Also, extreme activities and driving are not a good idea while on the medication because the side effects could compromise a person’s ability to control their actions and concentrate\(^3\).

Some side effects of Lyrica are more common than others. The main side effects that could be due to an interaction with something else are the possibility of weight gain involving diabetic patients or swelling in patients with heart problems\(^3\). Also sleepiness and dizziness are likely as well. Along with that is the possibility of eyesight difficulties which are the main reasons why driving while under the influence of Lyrica is a poor decision for a patient who is just beginning their treatment process with Lyrica. Allergic reactions may occur which makes it
important for a patient to read the drug information in the pamphlets. Some, almost minor, side effects of Lyrica include concentrating being difficult and dry mouth. Another caution within the pamphlet involves a patient’s history with drug abuse whether illegal or prescription drugs. It states that Lyrica may make a patient feel “high” and could lead to the abuse of Lyrica if they have a past with drug abuse.

**Results, living with fibromyalgia:**

Thorough investigations have shown that patients living with fibromyalgia can recover to a point that can allow their lives to get back in order. Fibromyalgia is debilitating and can leave a patient bedridden. This can cause the patient to lose their jobs and it is difficult on their families needing to care for them. Some patients are barely able to walk to their own mailbox and back without suffering from extreme pain. Patients have the advantage of not needing to visit a specialist to be diagnosed with fibromyalgia and can, in turn, receive the proper medications such as Lyrica or Cymbalta. Medication, however, is not the only option a patient who is suffering from fibromyalgia has. They can begin engaging in physical activities like exercise and walking or stretching to help their muscles cope with the pain they are experiencing. Recovery of fibromyalgia involves serious dedication on the patient’s part.

**Conclusion, fibromyalgia and Lyrica in a nutshell:**

Fibromyalgia is a highly controversial subject to discuss in a medicinal way. Is treating fibromyalgia with medication the best route to take? Personally, I believe there are better ways to help a patient than simply prescribing them medications. Studies done by the U.S. Food and Drug Administration (FDA) and the National Center for Chronic Disease Prevention and Health Promotion (CDC) have shown that patients suffering from fibromyalgia commonly have other
health issues on top of the fibromyalgia. They show that these patients are also suffering from other chronic pain disorders as well as anxiety and depression problems that are also being treated with medications. This alone can cause for a patient to be bedridden just because of the numerous medications they may be on. As a pharmacy technician I see these types of patients on a daily basis. Many are on multiple anti-depressants as well as tranquilizers and Lyrica. As shown above, it is dangerous to mix these medications and can amplify the side effects of all three types of drugs.

Some people believe that they need to resort to medications as their only option to feel better when many times these patients feel worse or do not feel at all. Fibromyalgia is such a floating type of disease that it can be quite easy for a doctor to automatically diagnose a patient with it because there are no tests to prove it aside from physical tests. I believe that Lyrica and other drugs meant to treat fibromyalgia are too serious of medications to be prescribing as an “easy-way-out” because a doctor may not be able to determine what is really happening within the patient. Also, increase stress and depression can cause a patient to feel “achy” all over their body which can be treated in other ways instead of medication. These patients just need to have the will power and drive to want to get better and their lives back to the way they should be as healthy individuals. I do believe, however, that Lyrica can help a patient but it should definitely be a last resort or an aide in the recovery process instead of a staple in it.
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The Discovery of Chaos Theory

and its Growing Application

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4/24/09
Abstract

Chaos theory is a fairly recent discovery in the field of mathematics and physics that has made theorists rethink their previously held notions about the physical world. Discovered by a mathematician and meteorologist Edward Lorenz, chaos has had a sizeable impact on the analysis of systems, especially in the prediction of long-term results, and currently appears in many fields, from meteorology to military leadership.

Chaos Theory

“Twentieth-century science will be remembered for just three things: relativity, quantum mechanics, and chaos.” While the world has passed the twentieth century and advanced into the twenty-first, this statement, made by the “most passionate advocates of the new science [chaos]” (p. 6) in the prologue of James Gleick’s book Chaos: Making a New Science, has been echoed in many science articles and publications since, and puts chaos theory among the ranks of the greatest scientific discoveries in recent history. Considering the wide-spread and growing range of fields that chaos has been found to have application in, this statement may well be warranted.

Chaos theory has an extensive history, and one that is important to know in order to be able to understand its far reaching implications and the impact it had on the scientific community. The “discovery” of chaos can be dated to 1890, but it wasn’t until nearly a century afterward that chaos began to grow in popularity and become more widespread.

Lorenz’s Experiment: These curves represent the two trials for which Lorenz put his weather program through. The two curves are initially in-synch and close together but gradually fall out of phase until they bear absolutely no resemblance to each other. The experiment demonstrates how sensitive a dynamic system is to initial conditions – the difference between the starting values of each run (curve) is only .000127. (Image from Gleick)

Prior to when chaos theory appeared, science was grounded in determinism, the belief that “every event or action is the inevitable result of preceding events and actions,”
which are called “initial conditions” (Trump). This scientific “philosophy,” which dates back to ancient Greece, essentially states that “every event or action can be completely predicted in advance, or in retrospect” (Trump). The scientist who was able to put determinism at the core of modern science was Isaac Newton, who changed everything when he came up with his set of three simple laws. Newton’s three laws of motion, expressible in just a couple sentences, could predict the behavior and motion of “an astonishingly wide variety of systems to a very high degree of accuracy” (Trump). Because it has proven to be a highly accurate and effective way to look at the world, determinism still remains at the heart of modern physics today.

There is one small problem with determinism, however. According to deterministic principles, if one knew the starting conditions and forces acting on a system, one would be able to predict the exact behavior that the system would exhibit. The catch is that one has to know the exact initial conditions of a system in order to make an exact prediction of its future behavior. Getting exact initial conditions is impossible, because no instruments exist today that can make exact, or infinitely precise measurements. “One way to understand this fact is to realize that in order to record a measurement with infinite precision, [an] instrument would require an output capable of displaying an infinite number of digits” (Trump). The lack of infinitely precise initial conditions didn’t prove to be a problem for scientists, at first. The reasoning was that “close enough” measurements could be obtained, which would only create a microscopic level of error or “noise” in experimental data. More accurate measurements could subsequently make the obtained data all the more accurate, in a direct relationship: “in studying the motion of a rocket, for example, one could know the final position of the rocket ten times as accurately by specifying the initial conditions at launch ten times as accurately” (Trump). In the late nineteenth century, the lack of infinitely precise starting data began to raise issues. While working with astronomical data, a physicist named Henri Poincare first discovered the limitations of deterministic thought, and in doing so, got his first glimpse of chaos.

By studying certain mathematical equations, Poincare found that in most cases, increasing the accuracy of the starting data increased the accuracy of the final results. His important discovery, however, was the number of cases where the system being examined didn’t obey the “shrink-shrink” rule of increased final accuracy with more precise initial conditions. Poincare, working on calculations involving astronomical systems of three or more bodies, noticed that these systems responded in vastly different ways depending on their starting data, and that even minuscule inaccuracies in the initial conditions would result in vastly different outcomes. Unless the initial conditions could be determined to infinite accuracy, Poincare reasoned, then it would be impossible to make accurate predictions about the behavior of the system.

It wasn’t until about 70 years later, towards the latter stages of the twentieth century, that chaos theory would truly emerge, and receive far more attention from the
scientific community. A mathematician and meteorologist named Edward Lorenz discovered something very similar to Poincare, and devise a name and set of graphs that have become famous and are always associated with chaos.

Lorenz had invented a computer program that modeled a weather system. The system, based on twelve equations, didn’t actually model the world’s actual weather, but predicted what a weather system might actually be like. “One day in 1961, he wanted to see a particular sequence again. To save time, he started in the middle of the sequence, instead of the beginning. He entered the number off his printout and left to let it run” (imho.com).

Lorenz was startled by the results when he came back to his computer an hour later. “Instead of the same pattern as before, it diverged from the pattern, ending up wildly different from the original. Eventually he figured out what happened. The computer stored the numbers to six decimal places in its memory. To save paper, he only had it print out three decimal places. In the original sequence, the number was .506127, and he had only typed the first three digits, .506 (imho.com).

“Chaos is the study of the behavior of dynamic systems, which are highly sensitive to initial conditions: Suppose we have to points \(X_0\) and \(X_1\), on a circle, which represent the correct starting value and a very close to correct value for a variable in the model of a system \(T\). We assume that the difference between the two numbers is represented by the distance between the points on the circle, given by the variable \(d\). To demonstrate the importance of infinite accuracy of initial conditions, we iterate \(T\). After only one iteration, \(d\), or the distance between \(T(X_0)\) and \(T(X_1)\), has doubled. Iterating again, we find that the distance between the two points, already twice its initial size, doubles again. In this pattern, we find that the distance between the two points, \(T^n(X_0)\) and \(T^n(X_1)\), is \(2^n d\). After only ten iterations, the distance has grown to a whopping \(2^{10} d = 1024d\)” (library.thinkquest.org 14).

According to deterministic theory, Lorenz shouldn’t have run into any problems at all. The result he got should have been very close to the original, and any error should have been negligible. “A scientist considers himself lucky if he can get measurements
with accuracy to three decimal places. Surely the fourth and fifth, impossible to measure using reasonable methods, can't have a huge effect on the outcome of the experiment” (imho.com). The differences between small changes in the starting data were so big that they appeared to be random, or chaotic. Only in the short-run did the results bear any resemblance; the long-run could only be predicted with infinitely precise starting conditions. Like Poincare, Lorenz had stumbled upon a true chaotic system. Lorenz realized that long-term meteorology was doomed, since even the slightest errors would lead to huge inaccuracies. When he published his findings in an article titled “Predictability: Does the Flap of a Butterfly’s Wings in Brazil set off a Tornado in Texas?” Lorenz permanently tied the popular phrase “the Butterfly Effect” to chaos, and a new science was born.

The Lorenz Attractor

This picture, based on Lorenz’s water wheel experiment, “became an emblem for the early explorers of chaos. It revealed the fine structure hidden within a disorderly stream of data, that there was a certain pattern to chaos. At any instant in time, the three variables fix the location of a point in 3-D space... because the system never exactly repeats itself, the trajectory never intersects itself.”

(Image from Gleick, p. 29)

Since Lorenz’s discovery, many scientists have pursued the study certain dynamic (changing with time), deterministic systems that are highly sensitive to their initial conditions, alternatively known as deterministic chaos, or just chaos. Subsequently, chaos has found its way into many scientific (and non-scientific) disciplines, and changed the way people look at the world.
For example, in a recent article in the American Journal of Public Health, authors Kenneth Resnicow and Scott Page propose that changes in public health behavior are best understood “through the lens of chaos.” The two propose that health behavior change is better understood through the lens of chaos theory and complex adaptive systems. Behavior change (1) is often a quantum event; (2) can resemble a chaotic process that is sensitive to initial conditions, highly variable, and difficult to predict; and (3) occurs within a complex adaptive system with multiple components, where results are often greater than the sum of their parts” (Resnicow and Page).

Essentially, the two are proposing that human health behavior forms a complex system, with many variables impacting the overall result. “Health behavior change may mirror other complex systems found in nature that involve multiple component parts that interact in a nonlinear fashion. Factors such as knowledge, attitude, belief, and efficacy no doubt exert influence on health behavior change” (Rescinow and Page). The
complexity of the system built on the interaction of these variables can be compared to way chaotic deterministic systems are highly sensitive to initial conditions. “In addition to differences in starting points, there may be key vectors along the pathway that propel the individual into a dramatically different space. These events may be thought of as trigger points that lead to large changes in direction or location (i.e., an epiphany)” (Rescinow and Page).

Chaos has also been found to exist in the neural networks in the human brain. “For some well-known but complex stimuli, recognition is almost instantaneous. A person recognizes a familiar face, or the scent of a barbeque, or the taste of chocolate almost as soon as that stimulus is presented to her... Freeman found that there is constant activity in the olfactory cortex and that this activity is chaotic. He believes that it is likely that the rest of the brain behaves in a similar fashion” (Gross). Chaotic systems often exhibit large jumps in phase space, which could be represented on the Lorenz attractor as movement from one “wing” (so called because of the shape of the graph) to the other. “The way the brain uses chaos to ensure continual access to previously learned patterns is to develop these wings for different learned inputs. According to researchers, the background chaotic activity enables the system to jump rapidly into one of these wings when presented with the appropriate input” (Gross). Some scientists believe that this type of activity is necessary for the brain to learn. Chaotic systems are known to never repeat themselves, and the brain could act like a chaotic system, in that it “categorizes a novel input into a novel category rather than trying to fit it into an existent category” (Gross).

Chaos can also be found outside of the physical and biological sciences. There are numerous articles and books on Chaos in leadership. According to a chaos text for students at the U.S. service academies, “the universal properties of chaotic systems point to practical suggestions for applying chaos results to strategic thinking and decision making. The power of chaos comes from this universality: not just the vast number of chaotic systems, but the common types of behaviors and transitions that appear in completely unrelated systems. In particular, the results of chaos theory provide new information, new courses of action, and new expectations in the behavior of countless military systems. The practical applications of chaos in military technology and strategic thought are so extensive that every military decision maker needs to be familiar with chaos theory’s key results and insights” (Glenn). It is also present in the social sciences, pushing “researchers in many fields to analyze their well-worn data from a new perspective” (LeBaron).

Conclusion

Chaos theory has posed some interesting questions for science as a whole, and caused many people to revisit “old” topics for evidence of chaotic behavior. While it seems to me that much of the research and progress in chaos is still in its infancy, I
believe that it holds further surprises for us in the future in a larger variety of fields. Whether it be in neuroscience of economics, chaos is certain to become even more influential.
Bibliography


Rheumatoid Arthritis
Autoimmune Disease

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Organic Chemistry 236
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April 24, 2009
Abstract:

Rheumatoid Arthritis is an autoimmune disease that is presently the most predominate disease in America. It is receiving far fewer of our governments dedicated budget funds for research than other diseases we are currently allotting funds for. Many of those diseases are reflected less frequently among the population than those associated with arthritis. All indications are that our society should re-assess these issues in-order to best service its public.

What disease affects more than half of the entire U.S. population, but receives only 5% of national health budget? Why is the national health budget to study these conditions only 8% of the budget compared to the study of heart disease and cancer? Even now, this condition is more prevalent in women than breast cancer and heart disease combined. Why has the number of cases of the disease tripled in the last few decades? What is this disease? It is autoimmune disease and it is an epidemic (National Institute of Diabetes and Digestive and Kidney Diseases 2009). The medical community is frustrated because it comes in so many types and crosses so many medical boundaries. We tend to think of all these problems separately, when they really are just one disease with many different symptoms, depending on the age and affected genes. Currently there are hundreds of these autoimmune diseases affecting more people. Something confuses the immune system. Autoimmune disorder is an illness in which the body’s immune system mistakenly attacks and damages tissues of the body (Autoimmune 2009). The immune system is considered a defense against foreign antibodies. If, for some reason, the body’s own tissues become infected with something unknown it attaches itself to the proteins of the tissues and changes the arrangement of the proteins. The body becomes confused. An inflammatory process begins, and we are on the road to developing autoimmune disease.

“There are many types of autoimmune disorders, including Hashimoto’s thyroiditis, Scleroderma, Graves’ disease, Lupus, Multiple Sclerosis (MS), and Rheumatoid Arthritis. All these diseases are related because the autoimmune system is malfunctioning and attacks our own tissues as well as the bacteria and virus (Autoimmune 2009). For purposes of brevity, we will focus on rheumatoid arthritis for the remainder of this paper.

Almost 2.1 million adults in the United States have rheumatoid arthritis, making it the most common form of inflammatory arthritis. “The word “arthritis” comes from the Greek word arthro, meaning “joint” and “inflammation” (Bernarr 2009). Arthritis is a number of different disorders that can affect the joints at any stage of life, from the early days of childhood until the closing stages of old age. Thus, it would seem that arthritis is a group of conditions in which the joints are inflamed. “Rheumatoid arthritis is the most common form of inflammatory arthritis. It primarily affects the synovial, the membrane that lines and lubricates a joint” (Rheumatoid 2005). In the body, Synovial joints are movable and elastic, which forms the thin, smooth, moist inner lining of the joint capsule. It also stretches into bursae (sacs) close to the joint that proceeds as fluid-filled support among formations that or else would rub alongside each other, for instance, the muscles
or tendons. The synovial fluid acts as a vital role, in a healthy joint cartilage. The cartilage at the ends of the bones’ shielding has to be soft, spongy, and sturdy. The nutrients that the cartilage needs, is provided by a fluid, then the cartilage refreshes and cleans the waste as the outside coating are worn away. Joint movement persistently pushes and liberates the cartilage like a “sponge”, which lets the deep cover of cartilage to provide nourishment (Leon 1980). “With degeneration of the joint, the cartilage becomes rough and worn out, causing the joint halves to rub against each other, creating inflammation, pain, and the formation of bone spurs. The fluid lubricant may become thin and the joint lining swollen and inflamed” (Arthritis 2009).

In America, almost forty million people have arthritis or other rheumatic condition. Fifty-nine million is the predicted amount of people with arthritis by the year 2020. At the age of sixty-five and older, Rheumatic diseases are the cause of disability (The National Women’s Health Information Center, CDC) (National 2008).

The escalating quantity of arthritis in America is an incredibly high number and this leading disease will continue on in generations. Since arthritis is the most common cause of disability in America, analysts are trying to gain perspective on "the looming disease burden and its impact on our nation's health care and public health systems" by estimating disease prevalence (Arthritis 2008). Death and mortality is the risk of this disease (National 2008).

Arthritis is an autoimmune disease, but the factors that confuse the immune system are unknown and there are many hypotheses about the causes (Rheumatoid 2000). Some doctors and researchers believe people who have rheumatoid arthritis have bad bacteria in their intestinal tract that causes irritation in the lining. When the tract becomes irritated with bad bacteria, the cells become damaged, broken, and sometimes the barrier between intestinal track and the blood becomes a passage allowing bacteria to infiltrate the blood stream. (Rispoli 2009). Some other researchers believe that environmental toxins are responsible for a large majority of autoimmune diseases. Recent government surveys found an average of one hundred forty environmental chemicals in the body and those are the only ones that they tested so far. Others believe there is number of other causes besides environmental toxins including heat stroke, processed foods, (refined and enriched) stress, and interaction with certain genes can cause disease (Autoimmune 2003). Some important risk factors that doctors believe contribute are genetics, age, and gender. Other factors include heavy smoking, obesity, and a history of blood transfusions. In women, a shorter fertile period associated with low levels of reproductive hormones has been linked to the disease. Drinking coffee and trauma may also be predisposing risk factors, although the evidence is inconclusive. Some other doctors believe a gene called HLA-B27 plays a role in the condition. Rheumatoid Arthritis is dependant upon the presence of a protein on the surface of white blood cells called HLA-DR4. The table below indicates research that links HLA to autoimmune diseases (Human 2009).
### HLA and autoimmune diseases

<table>
<thead>
<tr>
<th>HLA allele</th>
<th>Diseases with increased risk</th>
<th>Relative risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B27</td>
<td>Ankylosing spondylitis</td>
<td>90-100</td>
</tr>
<tr>
<td></td>
<td>Postgonococcal arthritis</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Acute anterior uveitis</td>
<td>15</td>
</tr>
<tr>
<td>HLA-DR3</td>
<td>Autoimmune hepatitis</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Primary Sjögren syndrome</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus type 1</td>
<td>5</td>
</tr>
<tr>
<td>HLA-DR4</td>
<td>Rheumatoid arthritis</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus type 1</td>
<td>6</td>
</tr>
<tr>
<td>HLA-DR3 and DR4 combined</td>
<td>Diabetes mellitus type 1</td>
<td>15</td>
</tr>
<tr>
<td>HLA-B47</td>
<td>21-hydroxylase deficiency</td>
<td>15</td>
</tr>
</tbody>
</table>

Age has a significant effect on the risks of developing the disease, but alarmingly it can start at any age. Gender is a dominant risk factor, with up to three quarters of people with rheumatoid arthritis being women. In 100,000 adults there will be about thirty-six new cases of rheumatoid arthritis in women and fourteen in men each year. Mostly men develop the disease when they grow older (Autoimmune 2003). There are many symptoms to rheumatoid arthritis disease that develop slowly over weeks, months or years. Symptoms include having fatigue and stiffness, being the most common. A low-grade fever and weight loss may also come about. The hands, wrists, elbows, feet, ankles, knees, or neck joints are typically affected. Morning stiffness, aching, bloating, tender, stiff joints are some of the contributing symptoms of rheumatoid arthritis. Joint stiffness may develop after long periods of sleep or sitting and could last at least sixty minutes and often up to several hours. The stiffness of joints may grow rheumatoid nodules, ranging in size from a pea to a mothball developing in nearly one-third of people who have rheumatoid arthritis. Nodules usually form over pressure points in the body, such as the elbows, knuckles, spine, and lower leg bones. It usually affects both sides of the body at the same time, and more than three sets of joints are affected at one time. (Symptoms 2009).

Diagnosis is the first step on the road to proper treatment and control of rheumatoid arthritis. The list of diagnostic tests mentioned in various sources used in the diagnosis of rheumatoid arthritis includes: Physical exam including skin exam, pelvic examination, digital rectal exam, rheumatoid factor blood test - and antibody test. The rheumatoid factor blood test determines the presence of an antibody that binds to immunoglobulin G in the blood; this forms an immune complex that can lead to painful inflammation. Erythrocyte sedimentation rate (ESR), is a measure of inflammation. The hour-long test calculates how fast red blood cells (erythrocytes) fall to the bottom of a glass tube filled with blood. The more rapid the rate of fall indicates a higher presence of the disease. Another test used in diagnosis is CBC complete blood count, which is an elevated level of C-reactive protein that is a substance in the body that indicates the presence of
inflammation. A complete blood count is a test that measures the levels of different blood cells in the blood. Antinuclear antibody (ANA) test is another test for abnormal antibodies in the body. ANA detects auto antibody (proteins that attack certain tissues or organs) that combines with the nuclei of cells which is useful for particular JRA Joint x-rays. Many people with rheumatoid arthritis have distinctive antibodies in their blood such as rheumatoid factor. The higher the level of rheumatoid factor in the blood, the more severe the rheumatoid arthritis and the poorer the prognosis. Usually the number of hemoglobin and red blood cells are low in those with rheumatoid arthritis (Diagnostic 2008).

The main categories of drugs used to treat rheumatoid arthritis are the non-steroidal anti-inflammatory drugs (NSAIDs) slow-acting drugs, corticosteroids, and methotrexate or other immunosuppressive drugs, including the tumor necrosis factor (TNF) inhibitors. A newer biologic therapy, involving the use of interleukin-1 receptor antagonists, is available. Generally, the stronger drugs have important side effects that must be evaluated during treatment. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely used drugs to treat the symptoms of rheumatoid arthritis. They can reduce the swelling in affected joints and relieve pain. However, they can upset the stomach and cannot be taken by anyone who has ulcers. Aspirin is one of NSAIDs drugs and it has been the traditional cornerstone of treatment for rheumatoid arthritis for many years. Other NSAIDs, including ibuprofen, naproxen, and diclofenac, are more often prescribed than aspirin. Slow-acting drugs, such as gold compounds, penicillamine, hydroxychloroquine, and sulfasalazine, sometimes can improve the course of rheumatoid arthritis, although improvement may take several months. Conventional approaches to autoimmune disease is to shut down the immune response with powerful medication including anti-inflammatory steroids; prednisone, anti-cancer drugs; methotrexated and other new drugs such as ambien and ranicat. These drugs slow down our immune system so powerfully that they increase the risk of cancer and they all have serious side effects. These drugs may be effective for pain in the short-term, but for the long-term do nothing to deal with the causes.

methotrexate

“Methotrexate abbreviated MTX and formerly known as amethopterin, is an antimetabolite and antifolate drug used in treatment of cancer and autoimmune diseases. It acts by inhibiting the metabolism of folic acid. Methotrexate replaced the more powerful and toxic antifolate aminopterin, and the two should not be confused with each other. In Bangladesh there is only one manufacturer of methotrexate with the brand name Methotrax. They only manufacture it in oral solid dosage form (2.5 mg and 10 mg tablet). They promote the drug only in rheumatoid arthritis, ankylosing spondylitis and psoriasis” (methotrexate 2009).
“Penicillamine is a pharmaceutical of the chelator class. It is sold under the trade names of Cuprimine and Depen. The pharmaceutical form is D-penicillamine, as L-penicillamine is toxic (it inhibits the action of pyridoxine). It is a metabolite of penicillin, although it has no antibiotic properties. It can cause an antibody-mediated myasthenic syndrome which may persist even after its withdrawal” (Penicillamine 2009).

“Hydroxychloroquine is an antimalarial drug, sold under the trade name Plaquenil, also used to reduce inflammation in the treatment of Rheumatoid arthritis” (hydroxychloroquine 2009).

“Sulfasalazine (brand name Azulfidine in the U.S., Salazopyrin in Europe) is a sulfa drug, a derivative of Mesalazine (5-aminosalicylic acid abbreviated as 5-ASA), used primarily as an anti-inflammatory agent in the treatment of inflammatory bowel disease as well as for rheumatoid arthritis. It may be abbreviated SSZ. It is not a pain killer” (Sulfasalazine 2009).

“Cyclophosphamide (the generic name for Endoxan, Cytoxan, Neosar, Procytox, Revimmune), also known as cytophosphane, is a nitrogen mustard alkylating agent, from the oxazophorines group. It is used to treat various types of cancer and some autoimmune disorders. It is a "prodrug"; it is converted in the liver to active forms that have chemotherapeutic activity” (cyclophosphamide 2009).
Corticosteroids, such as prednisone, are the most dramatically effective drugs for reducing inflammation anywhere in the body. Although corticosteroids are effective for short-term use, they tend to become less effective over time, and rheumatoid arthritis is usually active for years. The long-term use of corticosteroids almost invariably leads to side effects, involving almost every organ in the body. Although corticosteroids suppress the immune system, other drugs do so even more potently and are referred to as immunosuppressive drugs. Each of these drugs can slow the progression of disease and decrease the damage to bones adjacent to joints. Such drugs include methotrexate, leflunomide, azathioprine, cyclophosphamide, cyclosporine, and tumor necrosis factor inhibitors. Along with drugs to reduce joint inflammation, a treatment plan for rheumatoid arthritis should include non-drug therapies, such as exercise, physical or occupational therapy, and sometimes surgery. Inflamed joints should be exercised gently so they do not freeze in one position. As the inflammation subsides, regular active exercises can help. Exercise in water is more helpful. The buoyancy of the body while in the water allows movement to relieve and exercise the joints and muscular system. If drugs have not helped, surgery may be needed. Surgically replacing knee or hip joints is the most effective way to restore mobility and function when the joint disease is advanced. In this disease there is no single treatment that works for all people; each person experiences his or her own symptoms and disease course. In addition, different people may experience different responses to some of the drugs frequently used. One person may find a medication to be useful, while a second person may receive no benefit at all. A third might even have adverse effects from the drug and have to stop taking it (Rheumatoid 2005).

A regular, healthy diet is generally appropriate. A diet rich in fish (omega-3 fatty acids) and plant oils but low in red meat can have small beneficial effects on the inflammation. Some people have flare-ups after eating certain foods, so these foods should be avoided (Drugs 2008).

With regards to herbal medication, few herbs have been tested for their effect on the symptoms of arthritis but evidence suggests that some may help relieve inflammation and pain. The plants such as Cats claw, Devil claw, Ginger, Bromelain (extracted from the pineapple plant), Thhrmeric, Vakerua, and green tea are all types of plants that are remedies for inflammation and have been used for boosting Immunity (Drugs 2008).

The estimation of the life-shortening outcome of rheumatoid arthritis varies. The majority of bases cite a duration decrease of five to ten years. Extensive disease periods, the concurrent existence of further health problems, and distinctiveness of rigorous rheumatoid arthritis – for instance lacking functional capability or general health condition, plenty of joint destruction on x-rays, the requirement for hospitalization or participation of organs excluding the joints – have been shown to associate with advanced mortality. Optimistic responses to medication may possibly designate an advanced prognosis (Accommodation 1991). In 2005, a study distinguished that rheumatoid arthritis victims go through a dual threat of heart disease, independent of further risk factors for example diabetes, alcohol mistreatment, and elevated cholesterol, and blood pressure. The mechanism by which rheumatoid arthritis causes this increased
risk remains unidentified; the existence of chronic inflammation has been proposed as a contributing factor (Clinical 2001).

Research has shown that many risk factors for joint disease have to do with daily lifestyle decisions and habits. People who maintain proper body weight and keep their muscles strong are less likely to experience joint problems than those who are overweight or allow their muscles to become weak. People who exercise regularly have less functional decline and less joint pain than people who do not exercise regularly. Swimming is a best exercise for these diseases. More than a quarter of all American adults are physically inactive and sixty-five percent are overweight. That can be changed. There are steps we can take toward healthier lifestyles and there are things governments can do to battle this epidemic. Educating and convincing Americans, young and old alike, about the importance of changing their behavior and life style so they eat right and become physically active should be the heart of government (Water 1997).

Health commissions, national institutes of health, the U.S. Food and Drug Administration (FDA), the centers for disease control and prevention (CDC), the department of veteran’s affairs (VA) and private organizations should supply a meeting for managing research labors in the subject of autoimmunity and autoimmune diseases to assemble a variety of individuals that are interested in autoimmune disease research. These groups which assist the research program should include a wide-ranging, crucial scientific events referring to several diverse diseases and aspects. Private organizations must stand for the wellbeing of patients and should be required to take part in a unique role in the research endeavor. They need to bring colossal strength and provide the biomedical study and training programs. We need to cut down the cause of disability. The budget for studying autoimmune disease should be highly increased so that more scientific discoveries are made. Setting up priorities, organizing research money and infrastructure should approach the tactic of the research arrangement. Such an approach will reduce repeating activities, taking benefit of the economies of balance, and speedily distributing new scientific discoveries. This would allow successful and professional supervision of research activities that include numerous controls and duration of the tasks of many government agencies. The coordinating committee should emphasize the requirement for research in numerous thematic parts, concentrating on all advantages expected to contain the maximum effect on accelerating discoveries and medical developments required to prevent or treat autoimmune diseases (Autoimmune 2008).
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Understanding Interstitial Lung Disease (Interstitial Pulmonary Fibrosis)

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CHM 236-0002

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Abstract

Interstitial lung disease can be a general term given to different, but somehow related diseases of the lungs. Interstitial lung disease is an insidious disease because its symptomology can be quite subtle. Most believe their symptoms are remnants of upper respiratory track infections. Once diagnostic tests are conducted and diagnosis is confirmed it becomes clear that those “lingering symptoms” are more indicative of a serious disease. After diagnosis if a specific cause for interstitial lung disease can be determined, treatment of that cause can begin. If no specific cause can be found the label idiopathic is added. At this point no specific treatment is available to treat idiopathic interstitial lung disease.
Interstitial lung disease (ILD) is an umbrella term that encompasses many different types of lung diseases. These types of lung disorders are “characterized predominantly by diffuse and usually chronic involvement of the pulmonary connective tissue principally the most peripheral and delicate interstitium in the alveolar walls. The interstitium consists of the basement membrane of the endothelial and epithelial cells, collagen fibers, elastic tissue, proteoglycans, fibroblasts, a few mast cells, and occasionally lymphocytes and monocytes” (Abbas, Fausto, Kumar, 2005, p. 728). The interstitium of the lungs is a tissue that lines the alveoli. Normally the interstitium is highly elastic to expand and contract as air enters and leaves the lungs. There are two different ways to classify the different types of ILD; into categories of chronic interstitial lung diseases†, or by the differential diagnosis of interstitial lung diseases‡

Each type of ILD is unique in its primary cause and severity, however they all share similar signs and symptoms. Common symptoms of ILD include: feelings of breathlessness (dyspnea), especially during or after physical activities, a dry cough, and wheezing. These symptoms being not severe are often ignored until they are persistent enough to where one feels it is necessary to consult a physician. At this point in time the disease is often in advance stages where irreversible and extensive damage to the lungs has occurred. Other less common signs or symptoms are chest pain, and clubbing of the fingers. Clubbing of the fingers or digits is a thickening of the flesh under the nail bed, where the nail curves downward in a similar shape to that of the round part of an upside-down spoon (Schriber, Medline Plus, 2007). Because

† See Table I in Appendix I
‡ See Table II in Appendix I
clubbing can be caused by many other diseases, other diagnostic tests are needed to determine
the etiology, or cause of the clubbing.

"The term “interstitial” is misleading since the pathologic process usually begins with
injury to the alveolar epithelial or capillary endothelial cells. Persistent alveolitis may lead to the
obliteration of alveolar capillaries...accompanied by irreversible fibrosis" (McPhee, Papadakis,
Tierney 2008 p. 244). This is also the common link between all forms of ILD, they all start with
inflammation. When inflammation becomes out of control, which then causes the scarring of the
interstitium is when a person can be at risk for ILD. Inflammation can effect different parts of
the lungs, this difference could account for the different types of ILD. Generally the pulmonary
function of one who is diagnosed with ILD is restricted rather than obstructed as in other
pulmonary diseases. The restriction comes from the repeated inflammation and scarring of the
interstitium. Scar tissue is not as flexible as the natural lining of the alveoli therefor it restricts
the natural expanding and contracting of the lungs during normal breathing. Due to this
restriction, secondary symptoms can emerge. One of the secondary symptoms are a decreased
absorption of oxygen. This causes a lower carbon monoxide diffusion capacity which leads to
more problems. If carbon monoxide cannot diffuse out of the body, tachypnea (heavy breathing
to help aid in gas diffusion) will occur. Tachypnea is often accompanied by hypoxemia, or low
blood oxygen levels. The lack of fresh oxygen can cause central cyanosis, which is when the
skin and mucous membranes turn blue because there is less than 5g/dl of deoxygenated
hemoglobin in the blood vessels near the surface of the skin. Another secondary symptom is
inspiratory crackles at the lungs base. This is marked by a noticeable cracking sound when a
person inhales and exhales; the sound of velcro being pulled apart. Additional complications that arise from ILD are pulmonary hypertension, cor pulmonale, and respiratory failure.

There are many factors that can cause ILD to occur. Some factors are related to environmental or occupational hazards. Chronic or extensive exposure to silica dust, asbestos, chemical fumes, or the dust from bird or animal droppings, even constantly being around moldy hay can lead to inflammation of the lung tissue. For example the condition silicosis occurs when a person routinely inhales silica dust. Asbestosis is caused by the constant inhalation of asbestos. Moldy hay and the dust from animal dropping can trigger hypersensitivity pneumonitis.

Depending on the etiology of hypersensitivity pneumonitis it falls into many common names: farmers lung, and bird-breeders lung to name a few. Other factors than can lead to ILD are certain types of medical conditions. These conditions “do not directly attack the lung tissue, rather they involve systemic processes that affect tissue throughout the body” (MayoClinic.com, 2009). Conditions such as connective tissue disorders can lead to ILD. Due to the composition of the interstitium which contains connective tissue it seems only plausible that disorders of connective tissue would affect the lungs as well. Rheumatoid arthritis, RA, is another condition that can lead to ILD. RA can lead to ILD not just through the specifics of the disease itself but also due to the treatment with medications such as methotrexate or leflunomide. This brings to light another causation of ILD, certain medications can inadvertently cause ILD. While there are many known causes of ILD there is still one classification of ILD so named idiopathic pulmonary fibrosis.

*Table II, Appendix I*
Diagnostics

There are several diagnostic tests a patient can undergo to eliminate any other possible disease and to determine the correct diagnosis of ILD. Some of these tests include: a chest examination, a pulmonary function test, a chest radiograph, and a conventional and/or high-resolution CT imaging. Currently there are three diagnostic techniques that are commonly used: bronchoalveolar lavage, transbronchial biopsy, and surgical lung biopsy. Bronchoalveolar lavage (BAL) is a test that requires the extraction and examination of cells from the lower respiratory tract. The extracted cells are examined for signs of infection or for the presence of malignant cells. BAL may be able to provide the doctor and patient with a specific diagnosis in cases of infection, “particularly with P. jiroveci, or mycobacteria infections” (McPhee et. al 2008 p.245). If malignant cells are discovered this could suggest a possible diagnosis of eosinophilic pneumonia, Langerhans cell histiocytosis, and alveolar proteinosis. A transbronchial biopsy is slightly more invasive than a bronchoalveolar labage, however it is easily preformed in most patients through a bronchoscope. With a transbronchial biopsy there is a low risk of pneumothorax and/or hemorrhaging. This test however allows for “a definitive diagnosis of sarcoidosis, lymphangitic spread of carcinoma, pulmonary alveolar proteinosis, miliary tuberculosis, and Langerhans cell histiocytosis” (McPhee, et. al. 2008, p245). Even though a transbronchial biopsy can offer a precise diagnosis, sampling error is common. Due to the small size of the tissue being removed for study, it can be easily crushed which may complicate the diagnosis. The third and most invasive diagnostic technique is a surgical lung biopsy. A lung
biopsy is a standard procedure for a diagnosis of ILD. Two or three biopsies are taken from multiple sites on the same lung. These biopsies include tissue that has a normal as well as abnormal appearances. Not only can a lung biopsy offer a specific diagnosis it allows the physician to see the extent of fibrosis versus active inflammation.

Treatment

Once a diagnosis is obtained treatment of ILD can begin. There is no way to reverse the damage that has occurred in the lung, however if any on the tests reveals a definitive diagnosis of ILD, then the underlying cause is treated; and hopefully slow or stop the progression of the fibrosing. If an infection was found to be the cause then treatment would include a regiment of antibiotics or antiinfectives to help fight off the infection. If carcinoma is found to be the underlaying cause of the ILD then treatment options would include chemotherapy. As with most everything in medicine sometimes and underlying cause can not be diagnosed. When this occurs it becomes a specific diagnosis of ILD, idiopathic fibrosing intersitial pneumonia. Idiopathic fibrosing intersstitial pneumonia is the most common diagnosis among patients with ILD. As stated in Table II, there are five different types of idiopathic fibrosing intersstitial pneumonia. Each one has a unique clinical presentation, histopathology, radiographic pattern, response to therapy and prognosis. Treating idiopathic fibrosing intersstitial pneumonia is somewhat of a challenge. “No randomized stud has demonstrated that any treatment improves survival or quality of life compared to no treatment at all” (McPhee, et al., 2008 p. 246). It is suggested that patients who are diagnosed with respiratory bronchiolitis-associated with interstitial lung disease (RB-ILD) or nonspecific interstitial pneumonia are given a course of corticosteroids. Typically prednisone in a dose of 1-2 mg/kg/d for a minimum of two months. Clinical trials have shown
those types of idiopathic fibrosing interstitial pneumonia to be responsive to corticosteroid treatment.
Reference List


Cyanosis. (n.d.). Retrieved April 21, 2009, from Wikipedia:

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Table I

Major Categories of Chronic Interstitial Lung Disease*

Fibrosing

Usual interstitial pneumonia (idiopathic pulmonary fibrosis)
Nonspecific interstitial pneumonia
Cryptogenic organizing pneumonia
Associated with collagen vascular diseases
Pneumoconiosis
Drug reactions
Radiation pneumonitis

Granulomatous

Sarcoidosis
Hypersensitivity pneumonitis

Eosinophilic

Smoking-Related

Desquamative interstitial pneumonia
Respiratory bronchiolitis-associated interstitial lung disease

Other

Pulmonary alveolar proteinosis

* (Abbas. et al., 2005, p. 729)
Table II
Differential diagnosis of interstitial lung disease. *

**Drug-related**
- Antiarrhythmic agents (amiodarone)
- Antibacterial agents (nitrofurantoin, sulfonamides)
- Antineoplastic agents (bleomycin, cyclophosphamide, methotrexate, nitrosoureas)
- Antirheumatic agents (gold salts, penicillamine)
- Phenytoin

**Environmental and occupational (inhalation exposures)**
- Dust, inorganic (asbestos, silica, hard metals, beryllium)
- Dust, organic (thermophilic actinomycetes, avian antigens, *Aspergillus* species)
- Gases, fumes, and vapors (chlorine, isocyanates, paraquat, sulfur dioxide)
- Ionizing radiation
- Talc (injection drug users)

**Infections**
- Fungus, disseminated (*Coccidioides immitis, Blastomyces dermatitidis, Histoplasma capsulatum*)
- Mycobacteria, disseminated
- *Pneumocystis jiroveci*
- Viruses

**Primary pulmonary disorders**
- Cryptogenic organizing pneumonia (COP)
- Idiopathic fibrosing interstitial pneumonia: Acute interstitial pneumonitis, desquamative interstitial pneumonitis, nonspecific interstitial pneumonitis, usual interstitial pneumonitis, respiratory bronchiolitis-associated interstitial lung disease
- Pulmonary alveolar proteinosis

**Systemic disorders**
- Acute respiratory distress syndrome
- Amyloidosis
- Ankylosing spondylitis
- Autoimmune disease: Dermatomyositis, polymyositis, rheumatoid arthritis, systemic sclerosis (scleroderma), systemic lupus erythematosus
- Chronic eosinophilic pneumonia
- Goodpasture's syndrome
- Idiopathic pulmonary hemosiderosis
- Inflammatory bowel disease
- Langerhans cell histiocytosis (eosinophilic granuloma)
- Lymphangitic spread of cancer (lymphangitic carcinomatosis)
- Lymphangioleiomyomatosis
- Pulmonary edema
- Pulmonary venous hypertension, chronic
- Sarcoidosis
- Wegener's granulomatosis

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* McPhee et al., 2008 p245
Mahtab Taghipour

Organic Chemistry 236

Dr. Mancini

General Anxiety Disorder
This paper will discuss the mental disorder categorized as General Anxiety. The areas covered will include: introduction, definition, symptoms, causes, physical and psychological effect, treatment options, and medications. Also discussed will be the structure of medication and the prevention of this disorder.

Anxiety disorders cause people to feel excessively frightened, distressed, and uneasy during situations in which most others would not experience these symptoms. If left untreated, these disorders can dramatically reduce productivity, and significantly diminish an individual’s quality of life. Anxiety disorders in children can lead to poor school attendance, low self-esteem, deficient interpersonal skills, alcohol abuse, and adjustment difficulty.

Anxiety disorders are the most common mental illnesses in America; they affect as many as one in 10 people. Unfortunately, these disorders are often difficult to recognize, and many who suffer from them are either too ashamed to seek help or they fail to realize that these disorders can be treated effectively. Chronic, exaggerated worry about every day, routine life events and activities that lasts at least six months is indicative of generalized anxiety disorder. Children and adolescents with this disorder usually anticipate the worst and often complain of fatigue, tension, headaches, and nausea (“Canadian Mental Health Association,” 2009).

Anxiety disorder is a blanket term covering several different forms of abnormal, pathological anxiety, fears, and phobias. It describes nervous system disorders such as irrational or illogical worry concerning possible conflicts. Physiological researchers suspect a chemical imbalance in the brain may be involved in the development of an anxiety disorder. However, it’s still uncertain whether this imbalance is the cause or result of the disorder (“Encyclopedia,” 2009).

Symptoms of this disorder anywhere range from muscle pain, trembling and weakness, to heart symptoms, balance disturbances, strange and disturbed thoughts, panic attacks, lethargy, and insomnia. The main symptom of GAD is an exaggerated or unfounded state of worry and anxiety, often concerning such matters as health, money, family, or work (“Answers.com”).

The exact cause of GAD is not yet fully known. However a number of factors including genetics, brain chemistry and environmental stresses appear to contribute to its development.

- Genetics: Some research suggests that family history plays a part in increasing the likelihood that a person will develop GAD. This means that the tendency to develop GAD may be passed on in certain families.
- Brain chemistry: GAD has been associated with abnormal levels of certain neurotransmitters in the brain. Neurotransmitters are special chemical messengers that help move information from nerve cell to nerve cell. If the neurotransmitters are out of balance, messages cannot get through the brain properly. This can alter the way the brain reacts in certain situations, this may lead to anxiety.
- Environmental factors: Trauma and stressful events, such as abuse, the death of a loved one, divorce, changing jobs or schools, may lead to GAD. GAD also may worsen during periods of stress. The use of and withdrawal from addictive
substances, including alcohol, caffeine and nicotine, can also worsen anxiety (“Anxiety Causes,” 2009).

Physical and psychological effects of anxiety disorders include:

- **Nervous Effect**: When an individual feels some sort of danger, the brain sends messages to the autonomic nervous system that has two sub-sections; sympathetic nervous system and parasympathetic nervous system. The sympathetic nervous system is also called the fight/flight system. The system releases energy and prepares the body for action. The parasympathetic nervous system is a restoring system, which brings the body to the normal state.

- **Cardiovascular Effect of Anxiety**: The action in sympathetic nervous system results in increased heart beat rate, high blood pressure, heavy delivery of oxygen, and removal of waste product from the tissues. The blood flows to the larger muscles such as muscles of thighs and biceps. This prepares the body for action.

- **Respiratory Effects of Anxiety**: Since the fight response is linked with increased and deep breathing, the tissues require more oxygen to ready for action. The individual can feel breathlessness, a choking or smothering feeling, or tightness in the chest. The symptoms also include giddiness, blurred vision, confusion, unreality and hot flushes. However, these effects are not dangerous at all.

- **Sweat Gland Affects of Anxiety**: The fight/flight response results in increased sweating. Heavy sweating makes the organism skin slippery so that it becomes hard to grip.

- **Other Physical Effects of Anxiety**: Anxiety leads to a decrease in salivation and hence a dry mouth. Digestive systems do not function properly. This results in nausea, heavy stomach and constipation. Some anxiety is also accompanied by trembling and shaking.

- **Behavioral System**: The fight/flight response system prepares the body to either wrestle or escape, but when an individual cannot do either for any reason, the urges are often shown as tension, guilty, shivering, improper speaking, foot tapping, pacing or snapping at people. Overall, a person develops the feelings of being trapped and needs to escape.

- **Mental System**: The one principal effect of Anxiety Disorders on the mental system is the immediate and automatic attention of the individual to search the vicinity. When a person is clutched by anxiety attacks, he/she become unable to perform/concentrate on regular tasks, even those which do not require much attention (“Ochello,” 2003)

Specific treatment for generalized anxiety disorder will be determined by an adolescent's physician based on:

- adolescent's age, overall health, and medical history
- extent of your adolescent's symptoms
- adolescent's tolerance for specific medications or therapies
• expectations for the course of the condition

Anxiety disorders can be effectively treated. Treatment should always be based on a comprehensive evaluation of the individual adolescent and family. Treatment recommendations may include cognitive behavioral therapy for the adolescent, with the focus being to help the child or adolescent learn skills to manage his/her anxiety and to help him/her master the situations that contribute to the anxiety. Some adolescents may also benefit from treatment with antidepressant or anti-anxiety medication to help them feel calmer. Parents play a vital, supportive role in any treatment process. Family therapy and consultation with the adolescent's school may also be recommended ("Anxiety Disorder Treatment," 2009).

In general, anxiety disorders are treated with medication, specific types of psychotherapy, or both. Treatment choices depend on the problem and the person's preference. Before treatment begins, a doctor must conduct a careful diagnostic evaluation to determine whether a person's symptoms are caused by an anxiety disorder or a physical problem. If an anxiety disorder is diagnosed, the type of disorder or the combination of disorders that are present must be identified, as well as any coexisting conditions, such as depression or substance abuse. Sometimes alcoholism, depression, or other coexisting conditions can have such a strong effect on the individual that treating the anxiety disorder must wait until the coexisting conditions are brought under control ("Canadian Mental Health Association," 2009).

Often people believe that they have "failed" at treatment or that the treatment didn't work for them when, in fact, it was not given for an adequate length of time or was administered incorrectly. Sometimes people must try several different treatments or combinations of treatment before they find the one that works for them. Effective treatments for anxiety disorders include medication, specific forms of psychotherapy (known as behavioral therapy and cognitive-behavioral therapy), family therapy, or a combination of these. Cognitive behavioral treatment involves the young person's learning to deal with his or her fears by modifying the way he or she thinks and behaves by practicing new behaviors. Ultimately, parents and caregivers should learn to be understanding and patient when dealing with children with anxiety disorders. Specific plans of care can often be developed, and the child or adolescent should be involved in the decision-making process whenever possible.

There are types of medication prescribed for generalized anxiety disorder:

• Buspirone – This anti-anxiety drug, known by the brand name Buspar, is generally considered to be the safest drug for generalized anxiety disorder. Unlike the benzodiazepines, buspirone isn't sedating or addictive. Although buspirone will take the edge off, it will not entirely eliminate anxiety. Buspirone (Buspar), an azapirone, is a newer anti-anxiety medication used to treat GAD. Possible side effects include dizziness, headaches, and nausea. Unlike benzodiazepines, buspirone must be taken consistently for at least 2 weeks to achieve an anti-anxiety effect. A Buspirone hydrochloride tablet, USP is an antianxiety agent that is not chemically or pharmacologically related to the benzodiazepines, barbiturates, or other sedative/anxiolytic drugs. Buspirone hydrochloride is a white crystalline, water soluble compound with a molecular weight of 422.0. Chemically, buspirone hydrochloride is 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]...
butyl]-8-aza-spiro [4.5] decane-7, 9-dione monohydrochloride ("Smith and Segal," 2009). The empirical formula \( C_{21}H_{31}N_5O_2 \cdot HCl \) is represented by the following structural formula:

![Buspirone Hydrochloride](image)

BuSpar is supplied as tablets for oral administration containing 5 mg, 10 mg, 15 mg, or 30 mg of buspirone hydrochloride, USP (equivalent to 4.6 mg, 9.1 mg, 13.7 mg, and 27.4 mg of buspirone free base, respectively). The 5-mg and 10-mg tablets are scored so they can be bisected. Thus, the 5-mg tablet can also provide a 2.5-mg dose, and the 10-mg tablet can provide a 5-mg dose ("Web MD," 2009).

- Fluoxetine (Prozac) which has a monograph number: 04185 and CAS Registry number: 54910-89-3 and CAS Name: \( N \)-Methyl-\( \gamma \)-[4-(trifluoromethyl) phenoxy] benzenepropanamine other additional names are: (\( \pm \))-\( N \)-methyl-3-phenyl-3-[(\( \alpha \), \( \alpha \), \( \alpha \)-trifluoro \( p \) tolyl) oxy] propylamine; \( d,l \)-\( N \)-methyl-3-(\( p \)-trifluoromethylphenoxy)-3-phenylpropylamine. The molecular formula for fluoxetine is: \( C_{18}H_{21}F_{12}NO\) the molecular weight of fluoxetine is: 309.33 and the percent composition of fluoxetine is: C 66.01%, H 5.87%, F 18.43%, and N 4.53%, O 5.17% ("Web MD," 2009). The structure of fluoxetine is shown below:

![Fluoxetine (Prozac)](image)

- Benzodiazepines – These anti-anxiety drugs act very quickly (usually within 30 minutes to an hour). The rapid relief the benzodiazepines provide is a major benefit, but there are serious drawbacks as well. Physical and psychological dependence are common after more than a few weeks of use. They are generally recommended only for severe, paralyzing episodes of anxiety. Diazepam rectal gel rectal delivery system is a non-sterile
diazepam gel provided in a prefilled, unit-dose, rectal delivery system. Diazepam rectal gel contains 5 mg/ml diazepam, propylene glycol, ethyl alcohol (10%), hydroxypropyl methylcellulose, sodium benzoate, benzyl alcohol (1.5%), benzoic acid and water. Diazepam rectal gel is clear to slightly yellow and has a pH between 6.5 - 7.2.

Diazepam, the active ingredient of diazepam rectal gel, is a benzodiazepine anticonvulsant with the chemical name 7-chloro-1, 3-dihydro-1 -methyl-5-phenyl-2H-1, 4-benzodiazepin-2-one ("Web MD," 2009). The structural formula is as follows:

- Tricyclics include imipramine (Tofranil), which is prescribed for panic disorder and GAD, and clomipramine (Anafranil), which is the only tricyclic antidepressant useful for treating OCD. Tofranil, imipramine hydrochloride USP, the original tricyclic antidepressant, is a member of the dibenzazepine group of compounds. It is designated 5-3-(Dimethylamino) propy1-10, 11-dihydro-5H-dibenz[b,f]-azepine monohydrochloride. Imipramine hydrochloride USP is a white to off-white, odorless, or practically odorless crystalline powder. It is freely soluble in water and in alcohol, soluble in acetone, and insoluble in ether and in benzene. Inactive ingredients: Calcium phosphate, cellulose compounds, docusate sodium, iron oxides, magnesium stearate, polyethylene glycol, povidone, sodium starch glycol ate, sucrose, talc, and titanium dioxide ("Web MD," 2009). The structural formula is:

- Antidepressants – A number of antidepressants are used in the treatment of generalized anxiety disorder (GAD). However, the relief antidepressants provide for anxiety is not immediate, and the full effect isn’t felt for up to six weeks. Some antidepressants can also exacerbate sleep problems and cause nausea ("University of Maryland Medical Center," 2009).
Medications will not cure anxiety disorders, but they can keep the symptoms under control when the person receives psychotherapy. Medication must be prescribed by physicians, usually psychiatrists, who can either offer psychotherapy themselves or work as a team with psychologists, social workers, or counselors who provide psychotherapy. Cognitive-Behavioral Therapy (CBT) is very useful in treating anxiety disorders. The cognitive part helps people change the thinking patterns that support their fears, and the behavioral part helps people change the way they react to anxiety-provoking situations. CBT can help people with panic disorder learn that their panic attacks are not really heart attacks and help people with social phobia learn how to overcome the belief that others are always watching and judging them. When people are ready to confront their fears, they are shown how to use exposure techniques to desensitize themselves to situations that trigger their anxieties. Exposure-based behavioral therapy has been used for many years to treat specific phobias. The person gradually encounters the object or situations that are the causes of fear, perhaps at first only through pictures or tapes, then later face-to-face. Often the therapist will accompany the person to a feared situation to provide support and guidance. CBT is undertaken when people decide they are ready for it and with their permission and cooperation. To be effective, the therapy must be directed at the individual’s specific anxieties and must be tailored to his or her needs. There are no side effects other than the discomfort of temporarily increased (“Anxiety Guide to Treat,” 2009)

CBT or behavioral therapy often lasts about 12 weeks. It may be conducted individually or with a group of people who have similar problems. Group therapy is particularly effective for social phobia. There is some evidence that the benefits of CBT last longer than those of medication for people with panic disorder, and the same may be true for Obsessive Compulsive Disorder, Post Traumatized Stress Disorder, and social phobia. If a disorder recurs at a later date, the same therapy can be used to treat it successfully a second time. Medication can be combined with psychotherapy for specific anxiety disorders, and this is the best treatment approach for many people (“University of Maryland Medical Center,” 2009)

Anxiety disorders cannot be prevented, but known triggers can be avoided and they can be managed effectively with medication and psychotherapy. However, even after medication and psychotherapy, some people will continue to experience higher than normal levels of anxiety throughout their lives. This may get worse during particularly stressful times.

Interventions that can help prevent the development of an anxiety disorder are:

- taking regular exercise
- practicing relaxation or yoga and attending meditation classes, which will help regulate breathing
- resting when necessary
- simplifying everyday tasks and prioritizing them
- taking deep breaths if feel a panic attack coming on
- Joining a support group ("Prevention of Anxiety Disorder," 2009)
In conclusion, regular aerobic exercise may reduce general anxiety levels. Habitual exercisers often state that they feel better as a result of engaging in vigorous activity. This may be because exercise stimulates the brain to secrete endorphins, natural chemicals which have characteristics similar to morphine. Relaxation exercises may also reduce anxiety. Also walking, hiking, and thinking positive, spending time with friends or family can reduce anxiety (“Teens Health,” 2007). Talking to God about your problems, reading devotion material, taking a self-help class, going on a short trip to a quiet place for relaxation is also effective anxiety reducing activities.
Bibliography


Peds_adolescent/gad.cfm


SOLAR AND WIND POWERED HOMES
PAUL WAWERU
4/24/2009
Abstract

In today's world we are faced with multiple challenges on how to replace the expensive and rare fossil fuel sources that we have available. We however have overlooked the energy we can obtain from the sun. Our sun produces billions of photons carrying light and heat energy which we can use to our benefits by converting it to a useful source of energy for millions of homes, businesses, schools, and industries. In this essay we will explore the many ways we can exploit this resources.

Solar and Wind powered homes

The Sun is the source of all forms of energy on our planet. It generates it's energy by nuclear fusion which is the combination of light nuclei to produce a heavier nucleus. Huge amounts of energy are released when this processes occur. "Spectroscopic evidence indicates that the sun is tremendous fusion reactor consisting of 73 % H 26% He, and 1 % other elements its major fusion reactions is thought to involve the combination of deuteron,$^2$H, and a triton, under tremendously high temperatures to form a helium nucleus and neutron with the release of a huge amount of energy" (Whitten., 962). "The sun radiates energy at the rate of 3.9 X 10$^{26}$ W (watts) and has been doing so for several billion years"(thinkquest.org)

\[
\begin{align*}
1^H + 1^H & \rightarrow 2^H + e^+ + \nu \\
\nu^+ + \nu^- & \rightarrow \gamma + \gamma
\end{align*}
\]

\[
\begin{align*}
2^H + 1^H & \rightarrow 3^He + \gamma \\
2^H + 1^H & \rightarrow 3^He + \gamma
\end{align*}
\]

\[
3^He + 3^He \rightarrow 4^He + 1^H + 1^H
\]

Overall reaction

\[4^H + 2e^- \rightarrow 4^He + 2\nu + 6\gamma\]

Energy released in the reaction:(thinkquest.org)

\[
\Delta E = [(4)(1.007825u) - 4.002603u][931 MeV]\]

\[= 26.7 \text{ MeV}\]
The major challenges that face scientists today is how to harness this energy into electricity that can be used to fuel billions of homes, commercial buildings, industries, schools and other applications for electricity. Consumption of Energy worldwide has grown exponentially with industrialization of developing countries and the fast growing developed countries. Due to the high consumptions of fossil fuels, concerns have risen for our environment. Scientists believe that huge pollution caused by release of carbon dioxide and methane reacts with the Ozone in the atmosphere depleting the environmental blanket that protects us from high temperatures from the sun. This concerns of a future with raised temperatures and threatened land and aquatic life has resulted in a worldwide campaign to “go green” and provide better renewable resources for our energy needs.

The USA is a big contributor in consumption of fossil fuels. “According to the Department of Energy, it uses more oil and natural gas and is a larger net importer of energy than any other country in the world. For the most part, the energy sources from which electricity is generated and by which cars are powered in the U.S. belong to the category of fossil fuels—oil, coal and natural gas. Fossil fuels are considered to be finite, nonrenewable resources because of the vast amounts of time the Earth needs to produce them; an energy source is only considered renewable if it can be replenished in a brief period of time. Around 85% of energy used in the U.S. comes from fossil fuels, and a closer look at the individual category of transportation fuels, the percentage is much higher.” (National High School Debate Topic: Alternative Energy Incentives)

The use of these fossil fuels though more readily combusted into electricity has gained unpopularity due to the negative byproducts and huge short and long term costs. Although the talk about solar energy may be very exciting, the challenges that face the technology are still a milestone. Solar energy is harnessed into electricity in two ways. First there’s thermal solar conductors that have huge coiled tubes filled with water and trapped between two glasses that have a black material with high photon absorption rates. The radiation of the sun carrying high energy photons is then used to heat the water in the coils producing steam which rotates turbines producing electricity. This process is inefficient and since water has a boiling point of 100 degrees Celsius and requires a high latent heat of evaporation, it takes a lot of energy to convert the sun’s radiation into electricity. This form of a solar panel has been used for the longest time since ancient Greek and Rome. There are two kinds of solar thermal systems. The first is called a passive or batch collector system and its really simple in that the water circulates without aid from pumps. This system is used in areas where temperatures do not go beyond freezing points. In comparison, an active thermal system utilize pumps to circulate the water or antifreeze through heat absorbing thermal collectors. Solar thermal conductors are used mainly to heat water in buildings and swimming pools.
The other kind of solar panels is photovoltaic cells. "The first photovoltaic module was built by Bell Laboratories in 1954. It was billed as a solar battery and was mostly just a curiosity as it was too expensive to gain widespread use. In the 1960s, the space industry began to make the first serious use of the technology to provide power aboard spacecraft. Through the space programs, the technology advanced, its reliability was established, and the cost began to decline. During the energy crisis in the 1970s, photovoltaic technology gained recognition as a source of power for non-space applications" (Gil). This actually utilize the chemistry of a semiconductor. In General chemistry, oxidation-reduction reactions occur by exchange of a pair of electrons. In photovoltaic cells, a thin layer of a semiconductor like silicon absorbs the photons of light energy and undergoes oxidation releasing a pair of electrons. This electrons bounce back and forth generating electricity. According to Gil, "a thin semiconductor wafer is specially treated to form an electric field, positive on one side and negative on the other. When light energy strikes the solar cell, electrons are knocked loose from the atoms in the semiconductor material. If electrical conductors are attached to the positive and negative sides, forming an electrical circuit, the electrons can be captured in the form of an electric current" (Gil). This photovoltaic cells are more efficient due to the fact that electric current is generated
right away. It's found that "An amorphous silicon film only one micron thick can absorb 90% of the usable solar energy falling on it. Other thin-film materials include cadmium telluride and copper indium diselenide. Substantial cost savings are possible with this technology because thin films require relatively little semiconductor materials." (solar energy systems)

Si oxidized to give Si₂⁺ plus 2 electrons

The photovoltaic cells are collected in what's called modules that are arranged to form a bigger supply of voltage. This modules are designed to supply electricity at a certain voltage, such as a common 12 volts system. "The current produced is directly dependent on how much light strikes the
module.” (Gil). The modules are then arranged and interconnected in a grid called an array. A big surface area will basically generate more electricity. With the availability of this panels, the sky is the limit in terms of what we can achieve energy wise. To start, we can incorporate this solar panels in commercial buildings that occupy huge surface areas. The architectural designs of our buildings should be geared towards achieving self powered buildings. Sky scrapers should be built with alternating solar panels for windows and calculations should made on the direction the they face and the maximum solar exposure. In America today, millions of homes are powered by conventional non renewable energy. If a little percentage of the sun’s energy was tapped into this homes, individuals will have saved thousands of dollars and kept the environmental concerns at a minimum. While the cost of buying solar panels is still high for most American families, there have been individuals who have taken a step in creating sustainable energy for their consumption. In a story featured on the science channel, A former chemist has put up solar panels on his roof. He used thermal solar panels which are cheaper but are inefficient and the energy has to be stored elsewhere for use during times when sunlight is absent. He has derived a way to store up the solar energy by using that energy to electrolysis water by running electricity through the water breaking its components and collecting the hydrogen gas in huge tanks. He has actually build several big tanks that he stores up the hydrogen gas. Moreover, he has readjusted his Honda civics’ transmission to use hydrogen gas instead of gasoline. He has a tank in the trunk that he refills right from home. The independence of this individual in providing for his own energy needs is quite striking and should emulated nationwide. The government should give incentives to individuals and businesses that invest in solar energy.

Another way that we can harness the energy of the sun is by using convex lenses. The sun sends out its energy in photons of light. This travel in parallel lines radiating from the sun to all sides. In physics, study of convex lenses has shown that it’s possible to converge those parallel rays into one ray. In so doing all light energy is focused onto one spot causing a huge buildup of energy that can be used to boil water. In very sunny parts of the world especially sunny deserts, this technology can be used to boil millions of gallons of water and that steam can be used to rotate turbines for electricity production. “If energy is collected from a large area and concentrated into a smaller area, very high temperatures can be achieved. As well as being able to produce steam (to run steam turbines) it is possible to get temperatures high enough to melt iron and other metals. Converging lenses (like a magnifying glass) and concave mirrors can collect the radiation (light & heat) coming from the sun and concentrate them in a small area. As the energy collected from a large area is concentrated into a smaller area the temperature in the concentration zone can become very high. It is possible to boil water, even to melt iron with a big enough collector, at the focus of a concentrating collector.”( concentration ratios)
In further exploitation of our available resources, a look at wind energy gives promising results. Wind energy has been used for many years as a source of energy and for mechanical advantages. In the beginning of the 19th century, wind mills propelled by long blades were used as a mechanical pump for wells and dams and to grind grain. "Machines that converted wind to electricity were developed in the 1920s. Researchers turned to wind energy in the 1970s when the U.S. faced oil shortages. Wind turbines--modern windmills that generate electricity--were developed, and groups of thousands of turbines, called wind farms, began selling electricity." (wind energy)

In a more detailed look, "The 1980s saw an explosion of wind technology in California, where about 95% of the installed wind capacity in the U.S. is located. The most recent wind installations have been in Texas and Minnesota. In 1995, wind energy generated 3.2 million kilowatts of power in the U.S., comprising 0.04% of all electricity consumed" (wind energy). Wind energy has a zero impact on the environment. Many governments and leaders worldwide are beginning to focus on funding projects that encourage creation of this industry. "Growing numbers of countries and U.S. states are incorporating wind power into their energy infrastructures. Through the use of large wind turbines towering between 200 feet and 330 feet above the surrounding landscape, the force of atmospheric winds is harnessed and converted into electricity." (What Is Energy Independence). Wind energy can be harnessed on buildings too using smaller blades in making a centrifugal wind mill. This operates on the same principle as ordinary wind mills but will also capture the centrifugal force generated by the blades, this kinetic energy is easily be converted to mechanical energy for rotating turbines. Models of this wind technology can been used on commercial buildings, homes, apartment complexes, industries and schools.

In a document by Dotson, "The United States government issued a report forecasting what it would take to get 20 percent of U.S. energy from wind power. Oklahoma's Department of Commerce heard that call and is ready to be a part of the answer, relying on CfireerTech to get the state there. Commerce department officials estimate that Oklahoma will be the nation's second-largest generator of wind power by 2030, generating 9 percent of electricity in the United States." (Dotson). The magnitude of such investment in wind energy would see a rise in job creations and a more recognized awareness of wind energy. In a time when the US economy is hard hit by the recession, it would be a key element of
success to exploit this resources while steering away from the dependence on fossil fuels and creating a much needed domestic job market while promoting this technologies.

Although this resources are very efficient if fully exploited, many countries are still willing to remain persistent on using fossil fuels. The market for crude oil highly influences the progress of this revenues. “After 3 years of rapid growth, solar thermal collector shipments reported to EIA declined substantially in 2007 “(Energy Information Administration). The reason for the unexpected numbers in 2007 was due the high cost in gasoline.

The world now is facing climatic changes that haven't been observed before. Increasing numbers of hurricanes like hurricane Katrina, Tsunami, earthquakes, and rising temperatures are major concerns for scientists and environmentalist. This year in Arizona we are already experiencing triple digits of temperature three weeks before schedule, glaciations of north and south pole indicates further rises in temperatures; We need to make a quick transition to safer energy sources. The faster we invest and focus in this fields the sooner we will have the energy crisis under control.
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X-ray Emission and Characteristics

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Abstract
The X-ray is an electromagnetic wave that has the same characteristics of light (2). X-rays, like all electromagnetic waves, are no more than little packets of energy called photons produced when electrons release energy (1). Out of all the electromagnetic waves known to man, X-rays posses the second highest amount of energy after gamma rays (8). X-rays have the ability to pass through matter and react with atoms delivering enough energy to completely knock orbiting electrons free into space. When passing through a human body, an X-rays energy can rip cells apart causing bodily damage (1).

Have you ever thought to yourself, "Wow I wish I could see what is going on beyond those doors", wondered how interesting it would be to have the ability to see through anything? Those thoughts were ludicrous until the year 1895 when the X-ray was first discovered (7). An electromagnetic wave with enough energy to pass right through most matter and present the ability to see right through objects as the image shows up on fluorescent film (7). The X-ray is utilized every day from uses in the medical field finding cracked or broken bones by seeing right through the very flesh of the human body, to security purposes in an airport granting the ability to look right through peoples luggage without ever having opened it (1). But how far can X-rays travel, can they really penetrate through anything, and is anything really there? As you know if you have ever had an X-ray, when the rays pass through our bodies we don’t notice or feel a single thing. It is as if nothing went through your body, but in reality the rays are altering the atoms and molecules that they come into contact with. Too much exposure can be harmful to the human body because X-rays are a type of radiation (7). The X-rays we use today are a type of electromagnetic radiation that is generated in an X-ray tube in the scientific field of radiology (2). The use of X-rays is now just a part of modern society but very few actually understand the science of what it really is, how they are generated, and the effects of using them.

A German Professor named Wilhelm Conrad Roentgen discovered the X-ray in 1895 at Wuerzburg University (7). While Roentgen was experimenting in his laboratory with electron beams in a gas discharge chamber called a cathode ray tube (5), he noticed a fluorescent glow of crystals on his desk right next to the tube (2). This puzzled Roentgen and led him to further experiment with this by shielding the cathode tube with a heavy piece of black paper. He turned on the tube and again he saw a green colored fluorescent light but this time generated on a barium platinocyanide screen just a few feet away from the tube (2). Roentgen concluded that a new type of ray that no one before had discovered was being emitted. The ray was exiting the fluorescent materials in the room as it passed through the heavy black paper (7). He finally realized after his tests that this newly discovered ray had the ability to pass through most substances including human tissue, however could not pass through more dense objects like metal and human bones (7). One of his first experiments performed was on his wife Bertha in 1895, when a film of his wife’s hand was taken showing all of the bones in her hand including a ring that she had been wearing at the time (5).

What Roentgen had discovered was an explosion in the news and had become a huge interest to both the average media and scientists alike. The type of cathode ray tube that Roentgen had used was also being used by many other scientists during this time, this made it simple for them to perform experiments of there own (7). The discovery of the X-ray interested
scientists so much that many of them put a halt to their own research and began studying X-rays in the field of radiology (7). Most everyone was intrigued by the new invisible ray that combined with a photographic plate could look right inside the human body and see human skeletal bones (7). However most scientists were more intrigued by the discovery of a new electromagnetic wave that was smaller than visible light waves with a wavelength just \(1*10^6\text{cm-10^8-10cm}\) in length (5). Lots of talk was going around about the potential uses of the X-Ray in medicine and in surgery and almost immediately after the discovery many radiographs were being made throughout the United States and Europe helping doctors in all areas of medicine. Only 6 months after this huge discovery doctors were using X-ray technology to locate bullets in shot soldiers (7). It seemed as though all this was impossible to your average person and even in today’s society most people do not understand the science and physics behind this mysterious phenomenon.

To understand what X-rays are then it is essential to understand the basics of electromagnetic radiation. Now we all know that atoms have positively charged particles called protons and negatively charged particles called electrons. The electrons orbit the nucleus of an atom and the magnetic attraction between the opposite charges keep the electrons from spinning off of the atom. Think of the attraction between the two particles as a straight line, when one of the particles is disrupted the attraction between them is altered creating a wave like motion as they are shifted (1).

In the 19th century, physicists finally discovered this phenomenon and realized the disruption or wiggling of the electrons around the nucleus gave off light (1). What they did not know was what was causing the orbiting electrons to wigggle and why every atom would give off different spectra of light. Physicists would heat up different elements till they would glow, then the light would be shined through a prism producing different lines of color coming out of the other side of the prism (1). When they heated up hydrogen the whole rainbow was not present as it is with sunlight, instead certain colors would appear. It was the same for every atom that was put to the test. This made them wonder why the electrons in different atoms were giving off different types of light.

The question was answered when Niels Bohr a Danish physicist came up with a new model of the atom (1). He proposed a model that did not just have the electrons in an atom orbiting around the nucleus, as did the Rutherford model, but he had them in designated orbitals or specific orbits around the nucleus. The electrons circle the nucleus billions of times per second as they spin in their designated energy levels (4). When heat or energy is given to an atom the electrons around it have the ability to jump between energy levels or orbitals (2). When an electron gets exited or gains energy it will jump to a higher energy level and eventually fall back to its original energy level or another electron from a higher energy level takes its place (3). In order for this to occur the electron in both cases has to release its excess energy so that it can orbit in the lower energy level. When the electrons of an atom release energy they release little packets of it called photons, and in this case the photons are in the form of visible light (3). Every photon released has a certain wavelength or frequency that is directly proportional to the distance the electron had to fall back to its original orbital (3). The frequency is how many times a wave passes through a point in a specific time period and each frequency

![How atoms emit light (2)]
gives of its own colors or spectra of light. (1). The photons being produced are radiation and take on the characteristics of a wave. These light waves are produced by the disruption of the electric and magnetic field characteristics of the atom when energy is released (6). James Clerk Maxwell discovered this by deriving a wave equation from electric and magnetic equations, giving the name electromagnetic waves (6).

X-rays are waves in the same nature as light waves. They are part of what is called the electromagnetic spectrum (2). X-rays, gamma rays, radio waves, light waves are all part of the electromagnetic spectrum. What differs them from each other is the amount of energy in a particular photon or in other words the wavelength of the ray (2). The electromagnetic spectrum classifies all waves by wavelength and the shorter the wavelength the higher the frequency and this results in higher energy. X-rays of all the electromagnetic waves known to man possess the second most energy next to that of gamma rays (4). Visible light has a wavelength of around (400-700 nanometers) while x-rays have a wavelength of (1*10^6 cm-1*10^-10 cm)(5). X-rays and visible light are both created with electrons releasing energy called photons. When a photon hits another atom the energy of the photon can be absorbed boosting an electron to higher energy level if the energy difference between the two electron positions is the same as the photons energy (2). Light photons fit very well with almost any matter and can easily be absorbed. X-rays on the other hand have an extremely high amount of energy eliminating the possibility of it being absorbed by some forms of matter, like human tissue, and instead pass right through it (2). The creation of a photon with that kind of energy is a lot more complex and takes a higher amount of energy that to produce light waves.

An X-ray is produced when free electrons come into contact with the orbiting electrons or the nucleus of another atom. The interaction of the free electron forces a decrease in energy, which produces a form of electromagnetic radiation that is the X-ray (5). There are two processes that force certain atoms to generate X- radiation. One of them is called Bremsstrahlung and the other is called K- shell emission (7). Both of these will create electromagnetic radiation but on slightly different wavelengths, the process for both starting with the firing of electrons at very high speeds (5). Bremsstrahlung is a German term for breaking radiation. This happens when the high velocity of an electron suddenly decreases (5). This happens when negatively charged electrons slow down as they approach another atoms positively charged nucleus. Electrons are accelerated to several hundred kilometers per hour and shot into material dense enough so that the X-ray will interact with it rather than pass right through (7). When the electrons get close to the nuclease of the reacting material the positive charge pulls the negatively charged electron. This causes the electron to loss a high amount of energy as it slows down dramatically causing the electron to emit a photon, which is X-radiation (8). However some electrons not only drop in acceleration but their entire direction can be altered as the electron curves around the nucleus because of the high attraction. This results in elastic scattering of electrons, which ultimately fails to emit enough energy to produce an X-ray (7).

The second process for producing X-rays is the k-shell emission (7). In any given atom there are electrons spinning around the atoms nucleus and as stated previously these electrons are in designated energy levels (2). The term K-Shell refers to the lowest energy level an electron can orbit around an atom. When a high velocity electron comes into contact with a k-shell electron and gives it enough energy, that particular electron is completely knocked off of the atom (2). The k-shell electron that gets knocked off is then replaced with another electron in the atom from a higher energy level. Just like in visible light in order for an electron from a higher energy level to fall down to a lower energy level that electron has to lose its excess energy (3).
The energy that is emitted in order for it to fall into the k-shell of an atom is in the form of an X-ray photon. This process is also known as an ionization process because it creates what is known as an ion (4). An ion is a particle with a positive or negative charge because of its imbalance of protons and electrons. When the K-Shell electron is kicked off the atom and an x-ray is produced, the atom becomes electrically incomplete possessing a positive charge because it now has 1 more proton than its electrons (4). The loss of the electron gives it a +1 charge until it reacts with something else. The k-shell emission produces electromagnetic waves with a slightly higher frequency than that of the bremsstrahlung process (7).

Once an X-ray is produced it reacts with matter whether it is through solid matter or through plain air (4). It does not seem like it but even the air around us is made up of matter. The higher the energy of the ray the further it will travel. X-rays can travel through air but like all radiation even the high energy of the X-ray will eventually be absorbed (4). When an X-ray is produced it travels through solid matter the same as it would with plain air reacting with the atoms it comes into contact with eventually losing all of its energy and dying. However the more subatomic particles in an atom the more likely the x-ray photon is to react with and lose some energy (4). More dense and heavy materials like steel have bigger atoms that are closely packed together with the potential of every atom absorbing its energy (4). The higher the atomic number of an element the better chance it has to absorb the X-ray and the shorter the ray will travel. Physicists use lead shielding when using X-rays to keep the radiation in a concealed area because of the hindered ability of the x-ray to pass through the dense lead.

To create an X-ray by either of the two processes require three essential components. First a source of free electrons is needed; second a way to speed up the electrons to an extremely high velocity, and lastly a target material is needed to take the collisions of the electrons for the reaction (4). To begin the process electrons must be separated from their orbit around an atom and in order to break electrons free there must be a tremendous amount of energy applied (4). This is done by passing a current through a conductive wire known as the cathode, which heats the wire due to its resistance. The extreme heat excites the atoms of the wire forcing the electrons to break free from their nucleus in order to release all of the gained energy (4). Once all of the excess energy from the exited electron is release it returns back to the wire and this serves as the source of electrons. The second necessity needed to produce an X-ray is the acceleration of those free electrons to extremely high velocities (2). The propulsion of electrons to high speeds is important because the velocity is directly proportional to the energy the electron has, and the energy must be great enough to reach the amount of energy needed to ultimately create the X-ray (2). The acceleration of the electrons is not altogether very complex. Since the electrons posses a negative charge and positive and negative charges attract, a metal known as the anode is placed a short distance away, which possesses a positive charge. Once a high voltage is passed through the anode, it gains an extremely high positive charge that highly attracts electrons and the free electrons from the conductive wire are pulled toward the anode creating a very high electron velocity.
that is controlled by the voltage applied to the positive anode (4).

The last requirement needed to make the system work is a material that the electrons can interact with, normally called the target material. The material is placed in between the anode and the cathode so that the accelerated electrons will slam into it and react (4). Normally the anode that is attracting the electrons has the target material embedded into it, which is almost always tungsten (2). When the high speed electrons come into contact with the tungsten either the electron slows as it gets close to the atoms nucleus releasing energy creating the bremsstrahlung X-ray, or the electron knocks another electron out of its energy level forcing another one to take its place creating k-shell emission (8). Tungsten is a great target material because of its high number of electrons. When an electron has a strong acceleration and its straight-line path gets disrupted it produces radiation as in the bremsstrahlung effect (8). The amount of energy given up to radiation increases with the increasing electron energy and it will release the largest amount when it is absorbed into materials with high numbers of electrons like tungsten with 74 (8). Another reason tungsten is used is because of the immense difference between its low and high energy levels found in the atom. When a k-shell electron is knocked off in k-shell emission there is a tremendous amount of energy that has to be released for another to take its place creating an X-ray as the electron makes the jump (8).

The modern day x-ray tubes are normally a metal ceramic tube known as an envelope style, and are high vacuum tubes rather than the early gas filled tubes used by early scientists like Roentgen (2). Modern tubes consist of cathode heated filament that sputters off electrons throwing them into a rotating tungsten disk. The disk rotates at high speeds keeping the tungsten cool so that it does not melt from the extreme heat of the beam of electrons (2). A thick lead shield surrounds the tube keeping the x-radiation from escaping in all directions. The X-rays that are utilized escape through a narrow window creating an X-ray beam, which is used for photographing (2).

Once the X-rays are produced creating a photograph requires a special recording mechanism (4). The photograph of an object is called a radiograph which is a photographic picture produced by the passage of radiation through a subject producing an image of the target (4). When a technician proceeds to take an X-ray image the film is placed directly behind the subject. When a dentist takes an X-ray of your teeth they put the actual film in your mouth and shoot the X-rays through your mouth and onto the film. A doctor does the same, when taking a radiograph of a broken foot for example; a photographic plate is placed under your foot as the radiation is passed through from the opposite side. The photographic film that is used is comprised of three layers (4). The first layer is simply a flexible plastic serving as a base that the other two layers sit on. The second layer is called the emulsion layer comprised of softer layers of gelatin. When the gelatin is made silver bromide a material sensitive to radiation is added, once the layers of gelatin harden the silver bromide crystals are held suspended at different depths (4). When the silver bromide is exposed to radiation, in this case X-rays, the crystals become ionized forming a latent image on the radiograph (4). Every radiograph is made of billions of silver crystals all individually exposed to radiation but all together creating an image. The last layer of the film is a thin gelatin layer, which protects the middle layer from damages like scratches and wetness (4).

When the X-rays are shot through the subject the radiation is able to pass through paper, soft material and flesh, but is unable to pass through the dense material like bones and metals. The radiation gets absorbed and cannot get through those areas to ionize the silver bromide crystals. In other areas the radiation is able to pass through allow the crystals to be exposed to the
X-rays. When the crystals absorb the radiation and ionize they form a grain of black metallic silver on the radiograph. In areas where the radiation does not pass through, a light fluorescent picture appears inside the dark ionized area around the subject. The less material the X-ray must pass through the more energy the photon will have giving it the ability to pass deeper into the emulsion layer and react with more silver bromide at different depths making that area darker than others. This allows for different shades of darkness rather than just black and white, giving the radiograph a sense of depth. When a doctor is looking for a crack in a patient’s bone more radiation is able to pass through the crack than the solid bone around it. This leaves a dark line where the crack is located allowing the doctor to make an easy conclusion that a cracked bone may be present.

Although X-rays are greatly useful, just like most things there is also a downside. Even though you cannot see or feel what X-rays are doing when they pass through your body, they are actually causing damage. When X-rays get absorbed inside the body the tremendous energy is transferred to an electron knocking it free ionizing other atoms in the cell. The free electrons rip through the cell tearing electrons off of the molecules it comes in contact with. In the human body there are three main body systems that X-rays can effect with over exposure. The first is the genatalia, if effected can cause negative effects on the progeny which is the direct offspring of the parent. Another system is the skin of the subject, which can begin to form a rash where the skin is exposed. Human blood can also be negatively affected causing anemia. This is a condition where there is a lower number of red blood cells than normal in the body or the red blood cells do not carry enough hemoglobin which is an iron rich protein that helps blood cells to carry oxygen. This makes it difficult for the body to receive enough oxygen rich red blood. White blood cells can also be affected causing them to attack the immune system leaving the body more susceptible to disease. The most serious hazard is the X-ray affecting the DNA in cells. The DNA holds the blueprint of a cell and tells the cell how to reproduce; when it gets damaged the cell produces copies of its damaged self, which can ultimately lead to cancer. In the early 19th century scientists had no idea of this and the widespread unrestrained use of X-rays was beginning to cause harm to scientists, such as skin burns and eye irritations. Today radiation is one of the most investigated causes of disease. There is more knowledge about the mechanism of radiation damage on the molecular and cellular level than there is known for more health stressing factors. Researchers have collected and documented information on the exposure of X-ray radiation on the human body and it has helped scientists understand how it reacts with living tissue. Sadly, much of the information was collected at the expense of many people. However, the levels of radiation received from a doctor or a dentist are low enough that the body can repair almost all of the cellular damage. Only with extreme over exposure to X-ray radiation can anything harmful happen to the body.

The accidental creation of the X-ray turned into a wonderful discovery that will permanently be used in the technological world of science. The X-ray is used more and more each year since its original discovery in 1895. However, even with today’s technology purchasing an X-ray tube is extremely expensive and not all corporations or medical facilities have the funding to buy one for their own uses. I think as time goes on with how drastically technology is moving forward, low cost X-ray tubes will be on the market, available and cheap enough that any average walk in medical clinic will have one at there disposal. I believe it is possible that one day the average person will be buying X-ray devices, assuming the government does not restrict it. It is important to realize that more X-ray use means more exposure and could possibly increase health problems. As said previously, X-rays can damage and alter the cells in
the human body, but an average person is only exposed to X-rays 1-2 times a year. This is not enough to cause any severe damage, but with frequent use could escalate the radiation related health problems (7). Although X-rays are electromagnetic radiation of the same nature as visible light, the energy is astronomically greater and people should be more aware about what they are subjecting themselves to.
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