PARADISE VALLEY COMMUNITY COLLEGE

16th Annual Science Symposium

Volume II

May 13th, 2010

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Foreword

The 16th Annual Science Symposium was held on May 13, 2010. 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.

William L. "Hank" Mancini, PhD
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Anabolic Steroids

By Matthew Mooneyham

April 21, 2010
This report will contain much information to do with anabolic steroids. The information will include the history, synthesis, biological mechanism, effects, use demographic, and the ways of administration. Also, other charts and structures will be included. The report will also contain a personal preference about anabolic steroids.

Anabolic steroids are medicinal supplements used primarily to gain strength. Anabolic steroids, also known as androgenic steroids are related to the build-up of muscles. “The word anabolic comes from the Greek word anabolein meaning “to build up”. (BBS-2009) “The word androgenic also has a Greek derivative of Andros meaning “to produce”. Anabolic steroids increase the rate at which protein synthesis occurs, especially within that of muscle cells. Anabolic steroids also have a close relation to the male sex hormone called testosterone.

The first isolated anabolic steroids were called gonadal steroids. Gonadal steroids were first isolated in 1931 by Adolf Butenandt, a chemist in Marburg. “This began when Adolf Butendandt purified 15 milligrams of the male hormone androstenone from tens of thousands of litres of urine.” (BBS-2009) This steroid was further synthesized in 1934 by Leopold Ruzicka, a chemist from Zurich. By the 1930’s they had determined that the testicles contained a much more powerful androgen than androstenone. In 1935, this hormone came to be named testosterone. Historically, testosterone was mainly associated with sexual characteristics. The word testosterone was derived from it being part of the testicles and belonging to the family of ketones. The hormone testosterone was at that time only known to increase muscle mass, and as indicated determined sexual characteristics. The muscle building properties were further pursued by the Soviet Union during the 1940’s. “Steroid programs were used to enhance the performance of Olympic and other amateur weight lifters”. In response to the success of the Russians, the U.S. began work on the design of an anabolic steroid with less androgenic effects. The work resulted in the production methandrostenolone. Methandrostenolone is known to promote protein synthesis at a greater rate within skeletal muscle cells. Pharmaceutically the drug was marketed as Diannabol. The first prescription uses of Diannabol were to the elderly and burn victims. Mostly body builders and weight lifters were the other users of Diannabol. This drug was placed on the banned list by the International Olympic Committee in 1974. (BBS-2009)

Methandrostenolone is the generic name given to the main chemical in Diannabol. The actual chemical name is referred to by IUPAC (International Union of Pure and Applied Chemistry) as (8S,9S,10S,13S,14S,17S)-17-hydroxy-10,13,17-trimethyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-3-one. Many anabolic steroids can be made starting with the simple base ingredient of testosterone. Testosterone by itself has many androgenic effects that are not wanted. Anabolic steroids are synthetic derivates of testosterone with far less androgenic effects. Today, many websites and others claim to sell legal anabolic steroids. These legal steroids are not made through testosterone as the base ingredient. Legal anabolic steroids are now made through the combination of many steroidal extracts to promote the further secretion of the human growth hormone. These steroidal extracts can be taken from plants and
other naturally occurring substances. (1-888# 03-16-10) Also, these steroidal extracts main function is to produce a higher amount of testosterone in the body.

Most anabolic steroids are similar in structure to that of testosterone. Below is a structure of testosterone and other anabolic steroids.

![Anabolic Steroids](image)

(Elmhurst-2005)

In analysis, every anabolic steroid has a very similar relation to that of testosterone. Some of these structures, such as 4-Androstene, are called prohormones. Prohormones are converted to testosterone within the human body. The synthesis of anabolic steroids from testosterone is an illegal process, but still readily done by many manufacturers. There are a multitude of different androgenic anabolic steroids produced from testosterone. The major factors in reducing androgenic effects presented were alkylation at 17 alpha position with a methyl or ethyl group. This allows for a slower degradation of the drug by the liver. Other ideas were also presented such as esterification at the 17 beta position. This would allow the substance to be administered parenterally and would increase the duration of effectiveness. Finally, modifications were done to the ring for oral and parenteral users wanting different ratio of anabolic to androgenic effects. (BBS-2009)

Anabolic steroids are membrane permeable substance unlike other peptide hormones and have direct action on the nucleus of a cell. After entry into the cell, the anabolic steroid diffuses into the cytoplasm where it meets up with an androgen receptor. Different anabolic
steroids have different chemical affinities for how they bind. Some such as Methandrostenolone bind very weakly to this receptor but still produce the same androgenic effects. Others will bind very tightly and effect the gene expression produced within the nucleus by the cells. (Fahey 1998) Anabolic steroids cause many changes within the muscle mass. The changes are first seen through an increased production of proteins by the skeletal muscle cells. "Secondly, anabolic steroids reduce the recovery time by blocking the effects of stress hormone cortisol on muscle tissue, so that catabolism of muscle is greatly reduced". (BBS-2009) Glucocorticoids are steroid hormones that promote the breakdown of muscles. In turn, one of the mechanisms of an anabolic steroid is to inhibit the action of these steroid hormones so that muscle recovery time is reduced. Anabolic steroids can also affect the number of cells that turn in to fat storage cells. Cellular differentiation is the process in which a cell goes from being a less specialized in to a more specialized type of cell. Anabolic steroids have an impact on cellular differentiation by allowing for an increase in muscle cells by decreasing the fat cells. Fat is consequently lost by an increase in the basal metabolic rate which is indicated through the increase in muscle cells. (AA-2006)

Testosterone by itself has been mainly known for its functionalities in the formation of sexual characteristics. The effects produced from testosterone are androgenic effects. When in excess in the human body, testosterone has been known to produce many not wanted effects. These effects are stabilized with the "anabolic" effects of an anabolic steroid. These effects are different between every anabolic steroid on the market. (BBS-2009)

The effects from the mechanism of the anabolic steroid are either going to be anabolic or androgenic. The anabolic effects are the ones that promote cell growth. The androgenic effects are the ones that affect the masculine characteristics. "Some of the anabolic effects are increased protein synthesis from amino acids, increased appetite, increased bone remodeling and growth, and stimulation of bone marrow". (BBS-2009) The stimulation of bone marrow increases the amount of red blood cells produced. Most of these anabolic effects lead to the most prevalent effect of increased skeletal muscle size. "The androgenic effects of anabolic steroids are numerous". (Kennard-2006) Some of the effects include increased sebaceous gland production, growth of the clitoris or penis in children, and sexuality. Some of the other effects have a direct impact on the hair in androgenic places such as the pubic and chest hair. The deepening of the voice has been noted in some patients due to the increased vocal cord size. Also, the suppression of natural sex hormones, and the production of sperm in impaired in some users. Many of these effects can be associated with the increased production of testosterone within the body.

The androgenic to anabolic effects of these steroids are important. Many of the compounds will have a higher amount of androgenic than anabolic effects. Hypogonadism is when the sex glands produce little or no hormones. Steroids with a higher androgenic effect
are needed in these patients. Those with higher androgenic effects are also known to have a closer relation to testosterone. The others, with higher anabolic effects are used more in patients following a surgery or immobilization. A chart of the anabolic to androgenic effects seen in some anabolic steroids is shown below.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>1:1</td>
</tr>
<tr>
<td>Methyltestosterone</td>
<td>1:1</td>
</tr>
<tr>
<td>Fluoxymesterone</td>
<td>1:2</td>
</tr>
<tr>
<td>Oxymetholone</td>
<td>1:3</td>
</tr>
<tr>
<td>Oxandrolone</td>
<td>1:3-1:13</td>
</tr>
<tr>
<td>Nandrolone decanoate</td>
<td>1:2.5-1:4</td>
</tr>
</tbody>
</table>

(Chrousos-2006)

Anabolic steroids are used in the treatment of many different things. When administered for anabolic purposes they are used to increase the appetite, protein synthesis, and help with wound healing. Also, anabolic steroids can be used in the treatment of many chronic diseases. Many patients with these diseases experience the symptom of cachexia. Cachexia is an imbalance between nutritional intake and resting energy expenditure. These symptoms a lot of times will occur because of a depletion of androgens in the body. This happens in many of the chronic diseases that we have seen such as AIDS, and pulmonary diseases where anabolic steroids can be used as a treatment.

Uses are also seen in patients with liver disease. Many of these patients have a hepatitis-related malnutrition. (Basaria, et al-2001) The anabolic steroid oxandrolone was then used along with a high calorie supplement to increase the appetite of the patient. "Significant improvement was seen in liver function and overall survival in these patients". (Basaria, et al-2001) Anabolic steroids have also been used in the treatment of wound healing. When applied to human dermal fibroblasts the anabolic steroid of stanozolol increased the synthesis of collagen. Collagen is used by the body to fill cuts and wounds within the body. Anabolic steroids have also been seen as an aid in healing of burn patients. Many of these patients will experience catabolic or breaking down effects. The use of an anabolic steroid higher in anabolic effects is needed to help them gain weight. "Burn patients administered with the anabolic steroid oxandrolone produced less weight loss, increase in nitrogen retention, and a decrease in healing time when compared with other methods". (Basaria, et al-2001)

During the cancer phase of chemotherapy, anabolic steroids can also be used. Anorexia and weight loss are symptoms that are commonly seen in cancer patients. Androgen therapy can be used in some of these cases to increase the appetite and decrease the amount of weight lost by the patient. As seen, anabolic steroids have many medical uses. Certain types of anemia can even
be treated with anabolic steroids. The swelling of the face, arms, and other sexual organs is another symptom that is treated through anabolic steroids. Anabolic steroids also have other ranges of treatment not included in the prescription. Treatment of clotting diseases, growth failure, and Turner's syndrome are some examples of the vast range of treatment from anabolic steroids. (Basaria, et al. 2001)

Body composition and strength improvements are the main effects of anabolic steroids on the human body. The formation of new muscle fibers has been seen in consistent steroid use. Due to an increased amount of androgen receptors in the axial region of the human skeleton growth in these areas seems to be more predominant. The differences in muscle fiber sizes were seen in type 1 muscle fibers. Type 1 muscle fibers are those known as fast twitch muscles and are used for quick bursts of strength. The largest difference noted between non-users and users is the buildup of type 1 muscle fibers in the vastus lateralis and the trapezius muscle. The most significant improvement of anabolic steroid use is in the area of bench press. (Marieb, Hoehn-2010)

Those using anabolic steroids for sports purposes to enhance performance are using it for ergogenic purposes. Ergogenic use is attributed to those using it for bodybuilding and sports purposes. These uses are considered to be cheating thus anabolic steroids being banned by every major professional sport. They were first banned by the Olympic committee in 1974. These uses of steroids have spiraled all the way into games such as baseball where quick strength is a necessity for many batters.

According to a league of their own study the majority of anabolic steroid users are not participating in professional sports. The main goal of these users is to build skeletal muscle mass, physical attractiveness and strength. According to the study, 74.1% of the users have past secondary degrees, 77.7% are fulltime employees, and the average income is 60-80,000 per year. These statistics represent that the population using these steroids are very middle class educated people using it for their own purposes. (Cohen, et al. 2007)

Many of the users who participate in steroids for strength purposes can exhibit some very serious side effects. One of the major side effects is considered aggression and hypomania. Many of these users can experience what is predominantly called the "roid rage". The "roid rage" is considered the increased rage of somebody due to steroid use. After habitual use of anabolic steroids this is not uncommon. According to CNS Drugs, "significant psychiatric symptoms including aggression and violence, mania, and less frequently psychosis and suicide have been associated with steroid abuse". (BBS-2009)

Use of anabolic steroids in adolescents can have some of the more serious side effects. One of the side effects is lengthening of the bones is halted. "Due to increased level of estrogen metabolites, the epiphyseal line will close earlier than usual". (BBS-2009) This results in the closing of the epiphyseal line, stunting the growth of the individual. Other side effects seen in
other users are increased thickening of the left ventricle of the heart. When one of the ventricles of the heart is thickened the contraction and relaxation are impacted. Many effects are known when these alterations occur. Some of the known effects are cardiac arrhythmias, congestive heart failure, heart attacks, and sudden cardiac death. Possibly the most abused bodily organ from anabolic steroid use is the kidneys. The increased working of the kidneys can produce a dark urine color. This represents the kidneys are working overtime to produce their goal. Possible complications with the kidneys can result in kidney failure. (BBS-2009)

Anabolic steroids have three main routes by which they can enter the human body. They can either be oral, injectable steroids, and skin patches. Orally is the best administration for them. When taken orally, the testosterone is rapidly absorbed, leaving some metabolites. Only about 1/6th of the testosterone is actually available in its active form. When taken by mouth the synthetic derivates have to be alkylated at the 17th carbon. These forms are anabolic steroids such as methyltestosterone and fluoxymesterone. When the anabolic steroid is alkylated at the 17th position it decreases the liver's ability to break it down before it reaches the circulatory system. Steroids in the injectable form generally have a prolonged absorption time. When injected, the free testosterone is released in the injection spot. Injection is most commonly seen in those using it for ergogenic purposes. "When administered by injection it has greater activity in the propionate, enanthate, undecanoate or cypionate ester form". (BBS-2009) The greater time in these forms allows for compound to be hydrolyzed, and for the free testosterone to be released.

Over the years anabolic steroids have been associated with sports figures. In order to enhance their skill and performance these athletes will partake in anabolic steroid use. The adverse side effects can be strongly noted in these users. Even though, the bad reputation is given to anabolic steroids the medical uses are countless. In summary, anabolic steroids do not portray as bad of a name that has been given to them over the years.

Throughout my study of anabolic steroids, my thoughts have changed a lot from before. I am an athlete, I grew up during the steroid era of baseball and have seen the effects noted on many of these athletes. When posed with a question of whether or not steroid use should be allowed, before this research my answer would have been absolutely not, it has zero use for anything except making athletes stronger. Now, after much research the answer is much different. When in the wrong hands, drugs are bad for anybody. Anabolic steroid use is ok for those who actually need it to help them gain weight or recover from a surgery or any of the other medical uses I have listed. Illegal use of anabolic steroids for any sports purposes needs to absolutely remain banned. Steroid use in sports is not only cheating, but is slowly hurting the user with the many androgenic effects. As listed earlier, the majority of users are using it for non athletic purposes. This use needs to absolutely be watched more closely; many of these users have no idea of the harmful effects. So, for a final solution to the problem the production of anabolic steroids needs to be limited very much. Anabolic steroids need to be only given out if the complication is in absolute need for the individual because these illicit substances are ending in the hands of the wrong individuals and resulting in a cheated game.
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A Leader of Death: AIDS

Kinjalben Patel

CHM 236

Dr. Hank Mancini

Date: April 23, 2010
Abstract:
AIDS (Acquired Immune Deficiency Syndrome) is the final and most serious stage of HIV disease, which causes severe damage to the immune system in human body. AIDS is a fatal disease without a known cure as of today and a disease that responds to little treatment. This paper will discuss the nature of the AIDS virus, the transmission and the prevention of transmission, as well as the available treatments for people with this disease.

Definition:
Human immunodeficiency virus (HIV) caused the acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS). Mostly it is a sexually transmitted disease and a disease of the human immune system. This disease progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumors. CDC (Centers for Disease Control and Prevention) estimates that about 1.1 million people in the United States are living with HIV or AIDS. An estimated 21% of these people do not know that they are infected: not knowing puts them and others at risk.

Nature of HIV virus and transmission of virus:
HIV is a fragile virus. Scientists agree that HIV does not stay alive in the environment. So it cannot live for very long outside the body and the virus is not transmitted through day-to-day activities such as shaking hands, hugging, or a casual kiss. One cannot become infected from a toilet seat, drinking fountain, doorknob, dishes, drinking glasses, food, or pets. One also cannot get HIV from mosquitoes.

This virus is primarily found in the blood, semen, or vaginal fluid of an infected person. There are three main ways the HIV transfer from one body to other:
- Having sex (anal, vaginal, or oral) with someone infected with HIV
- Sharing needles and syringes with someone infected with HIV
- Being exposed (fetus or infant) to HIV before or during birth or through breastfeeding

Electron microscope image of HIV, seen as small spheres on the surface of white blood cells.

When any person infect by human immunodeficiency virus, that virus enters the body and lives primarily in the white blood cells. White blood cells are the immune cells that normally protect us from disease. This HIV infection causes the progressive loss of a specific type of immune cell called T-helper or CD4 cells. As the virus grows, it damages or kills infected cells and other cells. That cause weakening the immune system and leaving the individual vulnerable to various opportunistic infections and other illnesses, ranging from pneumonia to cancer. AIDS is the last stage of HIV infection, when a person’s immune system is severely damaged. When there was no medication available to this condition, people with HIV could progress to AIDS in
just a few years. The U.S. Centers for Disease Control and Prevention (CDC) defines, "someone as having a clinical diagnosis of AIDS if they have tested positive for HIV and meet one or both of these conditions:

- They have experienced one or more AIDS-related infections or illnesses.
- The number of CD4 cells has reached or fallen below 200 per cubic millimeter of blood (a measurement known as T-cell count). In healthy individuals, the CD4 count normally ranges from 450 to 1200".

Prevention of HIV transmission:

To prevent the spreading of AIDS avoid the behaviors that helps the HIV to transfer from one body to another body as example; exposure to infected body fluids, including unprotected sexual intercourse or sharing needles to inject drugs. Avoiding such behaviors is not possible, and then uses the latex condoms during vaginal, anal or oral intercourse that can also significantly reduce the risk of HIV transmission. HIV-positive pregnant women have more chances to transfer the HIV to her baby so take medications that reduce the risk of HIV transmission to her child. Injection drug users should not share needles or injection equipment to other patient or person. HIV infection is so dangerous because a person can have the virus for a long time without knowing it. That infected person can then spread the virus to others through high-risk behaviors.

Treatment of AIDS:

There were no effective treatments for AIDS, but people in the United States and other countries can use a number of drugs to treat HIV infection and AIDS. Some of these drugs are designed to treat the opportunistic infections and illnesses that affect people with HIV/AIDS. In addition, several types of drugs seek to prevent HIV from reproducing and destroying the body's immune system.

The groups of antiretroviral drugs:

There are five groups of antiretroviral drugs. Each of these groups attacks HIV in a different way (Table).

<table>
<thead>
<tr>
<th>Antiretroviral drug class</th>
<th>Abbreviations</th>
<th>First approved to treat HIV</th>
<th>How they attack HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside/Nucleotide Reverse Transcriptase Inhibitors</td>
<td>NRTIs, nucleoside analogues, nukes</td>
<td>1987</td>
<td>NRTIs interfere with the action of an HIV protein called reverse transcriptase, which the virus needs to make new copies of itself.</td>
</tr>
<tr>
<td>Non-Nucleoside Reverse Transcriptase Inhibitors</td>
<td>NNRTIs, non-nucleosides, non-nukes</td>
<td>1997</td>
<td>NNRTIs also stop HIV from replicating within cells by inhibiting the reverse transcriptase protein.</td>
</tr>
<tr>
<td>Protease Inhibitors</td>
<td>PIs</td>
<td>1995</td>
<td>PIs inhibit protease, which is another protein involved in the HIV replication process.</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----</td>
<td>------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Fusion or Entry Inhibitors</td>
<td></td>
<td>2003</td>
<td>Fusion or entry inhibitors prevent HIV from binding to or entering human immune cells.</td>
</tr>
</tbody>
</table>

1) Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs):
NNRTIs such as nevirapine (Viramune) and efavirenz (Sustiva). There are currently two drugs approved for use in this class. It works by targeting the structure of reverse transcriptase enzyme to inhibit enzyme activity. By inhibiting the enzymatic activity it stops the reverse transcription. So NNRTIs successfully interfere with one of the steps of the HIV life-cycle and prevent the virus from being able to reproduce. Although NNRTIs are very potent antiretroviral, a significant drawback is that resistance can develop quickly if the drugs are not taken exactly as prescribed, and once resistance develops to one drug in the class he or she will probably be resistant to all the drugs in that class. Many combination therapies include one NNRTI plus two or more drugs in another class.

Efavirenz (Sustiva)
IUPAC name: (4S)-6-chloro-4-(2-cyclopropylethynyl)-4-(trifluoromethyl)-2,4-dihydro-1H-3,1-benzoxazin-2-one.

\[
\text{Nevirapine (Viramune)}
\]
IUPAC name: (11-cyclopropyl-4-methyl-5,11-dihydro-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one).
2) Nucleoside Reverse Transcriptase Inhibitors (NRTIs):
In the drug combination therapy the NRTIs given with the NNRTIs, and also sometime combined with the "boosted" protease inhibitor. Examples of a common antiretroviral combination are:
1) Abacavir, Lamivudine, Zidovudine (Trizivir)
2) Lamivudine, Zidovudine (Combivir)
3) Stavudine (Zerit, d4T)
4) Tenofovir DF (Viread, TDF)
5) Zalcitabine (Hivid, ddC)
6) Atripla (tenofovir, emtricitabine, efavirenz)

Zidovudine (Retrovir, AZT, ZDV) \(^8\).
IUPAC name: 3'azido-3'-deoxythymidine.

Lamivudine
IUPAC name: (4-amino-1-\{[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one) \(^8\).
3) Protease Inhibitors (PIs):
PIs interrupt HIV replication at a later stage in its life cycle by interfering with an enzyme known as HIV protease. This causes HIV particles in body to become noninfectious. Among these drugs are:

1) Atazanavir (Reyataz, ATV)
2) Indinavir (Crixivan, IDV)
3) Lopinavir, Ritonavir (Kaletra, LPV/r)
4) Nelfinavir (Viracept, NFV)
5) Ritonavir (Norvir, RTV)
6) Saquinavir (Fortovase, SQV)
7) Tipranavir (Aptivus)

Protease inhibitors are usually prescribed with other medications, to help avoid drug resistance.

Nelfinavir
IUPAC name: (3S,4aS,8aS)-N-tert-butyl-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylphenyl)formamido]-4-(phenylsulfonyl)butyl]-decahydroisoquinoline-3-carboxamide.

Lopinavir
IUPAC name: (2S)-N-[(2S,4S,5S)-5-[(2-(2,6-dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl]-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanamide.
Saquinavir

IUPAC name: (2S)-N-[(2S,3R)-4-[(3S)-3-(tert-butylcarbamoyl)-decahydroisoquinolin-2-yl]-3-hydroxy-1-phenylbutan-2-yl]-2-(quinolin-2-ylformamido)butenediamide §.

4) Fusion Inhibitors:

One of the most alarming developments in the AIDS epidemic is the emergence of drug-resistant strains of HIV. A majority of people receiving treatment for HIV are resistant to at least one drug, and many don't respond to a typical three-drug combination 6. But a drug called Enfuvirtide (Fuzeon), a new class of drugs called fusion inhibitors, appears to suppress resistant strains of HIV. This type of drug stops the virus from replicating by preventing its membrane from fusing with the membrane surrounding healthy cells. It is used in combination with other HIV drugs for people who have advanced infection and who have developed resistance to other drugs. Enfuvirtide is the biomimetic peptide, and it was designed to mimic components of the HIV-1 fusion machinery and displace them, preventing normal fusion. Fusion inhibitors are which disrupt fusion of virus and target cell. HIV has viral protein gp120; gp41 which helps the virus to binds to the host cells receptor, a viral transmembrane protein, and then undergoes a conformational change that assists in the fusion of the viral membrane to the host cell membrane. This drug binds to gp41 preventing the creation of an entry pore for the capsid of the virus, keeping it out of the cell 6,7,8.
In conclusion, I think AIDS is one of the world's greatest leading causes of death. It is one of the world's most well known diseases and most feared. AIDS is not particularly occurring to the specific race, age, or gender. HIV is a retrovirus which easily transmits to one person to other person, and constantly attack human's immune system. Currently, there are different kinds of antiretroviral treatments available for patients who are tested to be HIV positive as well as patients with AIDS. But this virus can easily develop resistance to its treatment through mutation each generation, which leads to ineffectiveness in treatment. The only way to continue to fight off HIV is to change treatment that is still available. So, I think patients have to cooperate with experienced doctors by adhering to their professional recommendations, while doctors are responsible for closely monitoring the patient's conditions through test results and their body's response to treatment, as well as helping them to live healthily without serious damage to their immune system over a long period of time.
Works cited


Malaria:
We have the drugs to stop the fatalities and vaccines are on the way to eradicate the disease

Kira Peters
April 23, 2010
Abstract: Malaria is a leading cause of death for infectious diseases worldwide. The life cycle of the five Plasmodium malaria parasites infecting the human body, current drug treatments available, and research in finding a vaccine for malaria are discussed.

Malaria is one of the most important global public health issues. It is a disease that is preventable, treatable, and has the potential to be eradicated with purposeful and vigilant efforts by citizens, governments, and international organizations. However, the current reality is that malaria is killing almost a million people per year, and much more attention and effort into its prevention and treatment, continued research in overcoming the obstacle of drug resistance, and success in developing effective vaccines needs to take place. According to the Center for Disease Control, half of the world’s population, 3.3 billion people, live in areas where they are at risk of being infected with malaria and it is the 5th leading cause of death from infectious diseases worldwide. Most of these deaths are young children in sub-Saharan Africa. According to the World Health Organization, “In Africa one in every five childhood deaths is due to the effects of the disease. An African child has on average between 1.6 and 5.4 episodes of malaria fever each year. And every 30 seconds a child dies from malaria”. Malaria is a global problem but it is most detrimental to Africa. Ninety-eight percent of malaria deaths occur in 35 countries and 30 of them are in sub-Saharan Africa. Nigeria, the Democratic Republic of Congo, Ethiopia, Tanzania, and Kenya are most affected by the disease.

There are five species of the malaria parasite: Plasmodium Falciparum, Plasmodium Vivax, Plasmodium Malariae, Plasmodium Ovale, and Plasmodium Knowlesi. The most severe species that can be life-threatening is Plasmodium Falciparum. However, Plasmodium Knowlesi has recently been recognized as a strain that can also be fatal due to the parasite’s rapid replication in 24 hours. Organ failure due to prolonged untreated malaria is the cause of death for Falciparum and Knowlesi. The other species do not cause fatalities but rather a short term febrile illness. The symptoms of a mild malaria infection can resemble an influenza like illness with: fever, chills, sweats, nausea, vomiting, body aches, cough, headache, and diarrhea. Symptoms of Vivax malaria and Ovale malaria can reoccur in an infected patient because these species can lay dormant in a hypnozoite stage for months or years after the initial infection. The onset of symptoms may come much later than initial exposure with reoccurrences in times of immune deficiencies. Falciparum and Vivax malaria are the most common species with Falciparum being dominant in Africa and Vivax in Asia, the Middle East, and Central and South America. The Knowlesi species is currently isolated to Southeast Asia.

Severe malaria is characterized by the Center for Disease Control as a Plasmodium Falciparum infection that is complicated with serious organ failure. With a severe case of malaria, a patient may present with: severe anemia, hemoglobinuria, pulmonary edema, acute liver or kidney failure, hyperparasitemia (more than 5% of red blood cells infected), metabolic acidosis, hypoglycemia, or cerebral malaria resulting in seizures or coma. One could die from Plasmodium Falciparum because, if left untreated, all of these complications can be fatal.

Plasmodium, is a genus in the protist phylum, Apicomplexa (common name Sporozoan). The life cycle of malaria in the human body begins when a female Anopheles mosquito bites a person infected with malaria and ingests gametocytes. The male and female gametocytes (germ cells) produce zygotes in the mosquito’s stomach and eventually oocysts rupture to release sporozoites. The mosquito is then a vector for malaria when it bites another human for its next blood meal. The sporozoites in the mosquito’s saliva enter the human bloodstream to start the first phase of infection called the exo-erythrocytic stage. The sporozoites first move into the
liver cells (hepatocytes) within 30 minutes of infection. With *Vivax* and *Ovule*, hypnozoites can stay dormant in the hepatocytes for up to 3 years. In the other species, the sporozoites immediately multiply asexually via schizogony for 1-3 weeks. When the sporozoites mature into schizonts they undergo cytokinesis and divide into identical daughter cells called merozoites. The hepatocytes burst from overexpansion and the merozoites enter the bloodstream and infect red blood cells. This starts the erythrocytic stage (lasting 48 hours) and the pathogenesis of the malaria infection continues. In the red blood cells, the merozoites develop into ring forms, then trophozoites (feeding stage), and schizonts (sexual stage) and finally release more merozoites into the bloodstream. The release of new merozoites into the bloodstream causes the symptoms in the patient to spike. Some trophozoites however, develop into male and female gametocytes instead of trophozoites and allow for transmission of the infection to other humans to continue since mosquitoes pick up the gametocytes from the blood.

The immune system does not easily recognize the infection due to the parasites residing in the liver and red blood cells. Free floating infected red blood cells eventually enter the spleen and are destroyed. To prevent this fate, an infected red blood cell with the *Plasmodium Falciparum* parasite produces a protein, PfEMP1, that makes the red blood cells sticky so that they adhere (sequester) to tissues, organs, blood vessel walls, or uninfected red blood cells to make clumps of red blood cells called rosettes. Sequestering and rosetting are key factors in severe malaria.

The life cycle of malaria is shown below:

Image from: [http://www.cdc.gov/malaria/about/biology/](http://www.cdc.gov/malaria/about/biology/)
Where light microscopy is available, a blood smear can be used to diagnose the infection because some of the red blood cells will have the *Plasmodium* parasite present. Under the microscope, the parasite is noticeable because it stains dark purple and looks like a ring.

In poverty stricken countries where light microscopy is not readily accessible, rapid diagnostic testing to confirm the malaria parasite is another option for diagnosis. This test is done through a finger prick and gives a positive or negative result in 15 minutes. These tests are extremely useful because they can be performed inexpensively and in remote villages. They can also reduce the time from infection to diagnosis and treatment which can be critical in saving lives. Some patients may have to walk for days to travel to a large city for diagnosis and treatment. By the time their symptoms are severe enough to decide to make the trip, their parasitemia infection rate may be dangerously high and upon arrival, the symptoms may have been exacerbated enough that the patient presents with severe organ failure.

Treating malaria is becoming more complicated as the parasites are becoming tolerant of the current drugs and drug resistance is on the rise. The most important factors to consider when a doctor is deciding how to treat a malaria infection are: where the malaria was contracted and the drug resistances in that area, the age of the patient, and the severity of symptoms when diagnosed.

Chloroquine was the most prevalent anti-malarial drug used to treat *Falciparum* malaria starting in the 1950’s. It was highly effective with only a couple doses and the cost was only about ten cents per dose. However, the *Falciparum* parasite has become resistant to the drug in many parts of the world due to “mutations in *PfCRT*, a gene in the parasite that encodes a putative transporter”.

Artemisinin-based combination therapy is now the most prevalent form of malaria treatment. Artemisinin is derived from the Chinese Qinghao plant and has been used since the 4th century. The World Health Organization’s 2010 “Guidelines for the Treatment of Malaria” recommends Artemisinin-based combination therapy to treat uncomplicated *Falciparum* malaria. Artemisinin-based combination therapy is defined by the WHO as “the simultaneous use of two or more blood schizontocidal medicines with independent modes of action and, thus, different biochemical targets in the parasite”. Combination therapy is used to prevent further resistance because if the parasite is resistant to one of the drugs administered, the other one should still be effective in killing the parasite.

Artemisinin-based combination therapy drugs are the fastest acting drugs available (acting within 12 hours). They work by “inhibiting a *Pfalciparum*-encoded sarcoplasmic-endoplasmic reticulum calcium ATPase”. Growth of the trophozoites is inhibited and in *Falciparum*, the free floating parasites are killed before they can sequester. Gametocytogenesis is also reduced which prevents the transmission of the parasite. Artemisinin-based drugs can reduce parasite numbers 100-1000 fold in one asexual cycle. A three day treatment can reduce parasitemia by 90%. The five combination therapies recommended by the WHO are:
Artemether plus Lumefantrine, Artesunate plus Amodiaquine, Artesunate plus Mefloquine, Artesunate plus Sulfadoxine-pyrimethamine, and Dihydroartemisinin plus Piperaquine. The most effective forms of the drugs are fixed dosage tablets because they ensure the correct dosage which can minimize drug resistance. The recommended dosages for these drugs are:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Times per day</th>
<th>Number of Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemether plus Lumefantrine</td>
<td>20 mg Artemether/120 mg Lumefantrine (5–14 kg: 1 tablet; 15–24 kg: 2 tablets; 25–34 kg: 3 tablets; and &gt; 34 kg: 4 tablets)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Artesunate plus Amodiaquine</td>
<td>25/67.5 mg, 50/135 mg or 100/270 tablets (Artesunate 4mg/kg and Amodiaquine 10mg base/kg)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Artesunate plus Mefloquine</td>
<td>Artesunate (4 mg/kg once daily) for 3 days + Mefloquine (25mg base/kg) as a split dose of 15 mg/kg on Day 2 and 10 mg/kg on Day 3 (Alternatively 8 mg/kg Mefloquine daily for three days)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Artesunate plus Sulfadoxine-pyrimethamine</td>
<td>Artesunate 4 mg/kg once daily for 3 days and SP single dose of 25 mg/kg and 1.25 mg/kg respectively</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Dihydroartemisinin plus Piperaquine</td>
<td>4 mg/kg/day Dihydroartemisinin and 18 mg/kg/day Piperaquine</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

The structures for the Artemisinin-based combination therapy drugs are shown below.

Artemether

![Artemether](image)

Lumefantrine

![Lumefantrine](image)

Artesunate

![Artesunate](image)
There are various other drugs that are widely administered for prevention and treatment of malaria, especially where Artemisinin-based combination therapy is too expensive or not available. The most commonly used antimalarials that are not Artemisinin-based are: Chloroquine (where not resistant), Quinine Sulfate, Mefloquine, Sulfadoxine and Pyrimethamine, Atovaquone and Proguanil, Doxycycline, and Clindamycin.\textsuperscript{20}
**Non Artemisinin-based Treatment for Malaria**

<table>
<thead>
<tr>
<th>Species</th>
<th>Drug</th>
</tr>
</thead>
</table>
| Uncomplicated *Falciparum*                   | - Chloroquine phosphate (Aralen) or  
                                        | - Hydroxychloroquine (Plaquenil)                                     |
| Uncomplicated *Falciparum* with Chloroquine Resistance | - Atovaquone-Proguanil (Malarone) or  
                                        | - Quinine sulfate plus: Doxycycline, Tetracycline, or  
                                        | - Clindamycin,  
                                        | - Mefloquine (Lariam)                                |
| Uncomplicated *Vivax* or *Ovule*             | - Chloroquine phosphate plus Primaquine phosphate or  
                                        | - Hydroxychloroquine plus Primaquine phosphate                      |
| Uncomplicated *Vivax* with Chloroquine resistance | - Quinine sulfate plus either Doxycycline or Tetracycline  
                                        | - plus Primaquine phosphate or  
                                        | - Atovaquone-proguanil plus Primaquine phosphate or  
                                        | - Mefloquine plus Primaquine phosphate             |
| Uncomplicated *Malariae* or *Knowlesi*       | - Chloroquine phosphate or  
                                        | - Hydroxychloroquine                                                 |
| Severe *Falciparum*                          | - Quinidine gluconate plus one of the following:  
                                        | - Doxycycline, Tetracycline, or Clindamycin                          |
| Pregnant Women with Uncomplicated malaria    | - Chloroquine phosphate or  
                                        | - Hydroxychloroquine or  
                                        | - Quinine sulfate plus Clindamycin (Chloroquine resistant *Falciparum*) or  
                                        | - Quinine sulfate (Chloroquine resistant *Vivax*) |

The structures of these drugs are:

**Chloroquine**

![Chloroquine structure](image1)

**Quinine Sulfate**

![Quinine Sulfate structure](image2)
Malaria drugs have various ways of being effective in the body based on which part of the parasite's life cycle they attack. Blood schizonticides, tissue schizonticides, gametocytocides, and sporontocides are the mechanisms of treating malaria. Blood schizonticides such as Chlorquine, Quinine, and Mefloquine destroy parasites in the blood and are the most important drugs to treat malaria. Tissue schizonticides, such as Primaquine, kill parasites in the liver so that the erythrocyte stage of the life cycle is prevented. However, the symptoms of malaria are not present until the merozites infect and rupture red blood cells, so this form of treatment is most practical to kill Plasmodium Vivax and Plasmodium Ovale when their hypnozoites are in the liver. Blood gametocytocides kill the male and female germ cells that are involved in transmission of malaria since they are what the mosquito takes in to start the cycle. Chloroquine and Quinine have this ability against Vivax and Malarias but not Falciparum. Sporontocides, such as Primaquine, prevent the oocysts in the mosquito from developing and prevent transmission.

There are more than a dozen vaccines in development for malaria currently, but only one is in Phase III of clinical testing in Africa. The results to whether or not this vaccination by GlaxoSmithKline is approved should be released in 2011 and it could be on the market by 2012. To start Phase III, the RTS,S vaccine was administered to 5 infants in Tanzania on May 26, 2009, and 16,000 more children under the age of 2 are expected to receive the vaccine at 11 different sites in Africa to finish the trials. The vaccine is expected to prevent at least half of the children from contracting malaria and should last for several years. The new drug is a combination vaccine which "fuses fragments of a protein from the malaria parasite with a surface antigen from the hepatitis B virus."
The Malaria Vaccine Initiative, which is the main public-private partnership for developing vaccines stated in Nov 2009 that they will be focusing on the development of vaccines that not only prevent infection of the individual but also aim towards eradicating the disease by preventing transmission. The "transmission-blocking vaccines" will prevent the spread of malaria because when a mosquito bites a person who has been vaccinated, they take in antibodies that destroy the parasites as they replicate, and this lowers the number of infected mosquitoes that can act as vectors. By 2025, the MVI is aiming to have a vaccine that is 80% effective and can prevent against infection for 4 years. Since the RTS,S vaccine targets just the beginning phase of the infection, combining it with other drugs that target other parts of the lifecycle could be more effective.28

Fatalities from malaria are an unnecessary all too common occurrence worldwide. If the poorest of the poor had ready access to the drug treatments many of our world's young children could be saved. Malaria is a pressing global health issue that requires more attention and research so that it can be eradicated as a disease that kills. It is a disease that, with prompt attention, is curable and can be treated to prevent fatalities.


23. Atovaquone Image. [Internet]. Available from: http://upload.wikimedia.org/wikipedia/commons/thumb/0/0e/Atovaquone_structure.svg/800px-Atovaquone_structure.svg.png


The Past, Present & Future of Dilated Cardiomyopathy

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April 20th, 2010
Abstract
Every year there are 726,000 annual deaths from heart failure, making up 30.3% of all deaths in the United States. Among the numerous forms of heart failure, dilated cardiomyopathy, although relatively infrequent in annual diagnosis, maintains an extremely grim prognosis. Dilated cardiomyopathy has been relevant for decades, however, minute knowledge in the disease remains. This report centers on the history of dilated cardiomyopathy along with an in-depth understanding to the known biochemistry as well as future prospects of the disease in terms of treatment.

History
Of the countless diseases that affect the heart in our modern day, from arrhythmia to coronary artery disease, the numerous breakthroughs in medicine have yet to lend complete understanding in terms of contracting and curing the majority of illnesses at hand. Diseases that affect the muscles of the heart have been known since the mid-19th century. However, due to a lack of knowledge in the subject, it was not until 1957 that the term cardiomyopathy was coined. Cardiomyopathy means ‘heart muscle disease’ which is considerably appropriate given the effects such an illness exerts on the muscles of the heart. When an individual contracts the disease, the myocardium’s function deteriorates. This deterioration can lead to many abnormalities, from the enlargement of the heart to the cease of function of the ventricular walls. Due to the evolving knowledge of cardiomyopathy as well as the greater understanding of molecular genetics, the disease itself has been divided into three classifications; Dilated, Hypertrophy and Restrictive. Though all three classes of cardiomyopathy are just as relevant and important as the next, the focus of this report centers on dilated cardiomyopathy.

Dilated cardiomyopathy is the number one cause for heart transplants in the United States and affects more than 4 million Americans. What happens to the heart when one contracts dilated cardiomyopathy is that sections of the heart, such as the left ventricle for example, begin to shut down quite rapidly, generally speaking. There are numerous effects the heart undergoes, leading to all four chambers of the heart dilating, expanding outwards as if it were an inflating balloon. Due to the enlargement of the heart's muscles, the entirety of the heart becomes thick and rigid. This causes the heart to weaken, thus, not allowing blood to be pumped efficiently as well as causing a restriction of blood to refill after a contraction. Due to the lack of sufficient circulation along with the back up of fluid, the congestion one undergoes causes damage to many body systems and organs.

Signs & Symptoms
For the most part, those who have dilated cardiomyopathy do not even know it. It is commonly seen that in the early stages of cardiomyopathy, there are no signs or symptoms until the disease has already progressed. At this point in time, the heart has severely weakened causing symptoms to finally take notice. In saying so, one typically experiences fatigue, trouble breathing and shortness of breath.

Perhaps one of the best indicators that the heart is experiencing difficulties functioning is
during physical activity. Usually after moderate to intense physical activity one with dilated cardiomyopathy will encounter chest pain, dizziness and/or fainting. There are also signs of cardiomyopathy that can be visible such as swelling of the abdomen, legs and the veins of the neck. 

Diagnosis
In order to diagnosis dilated cardiomyopathy, a physician will primarily begin by conducting a physical examination. In doing so, the physician will be focusing his attention on signs of heart failure as well as cardiac volume overload. Vitals signs will be taken and scrutinized, such as ones blood pressure to test for hypertension. The physician will also pay close attention to ones medical history. Surprisingly, many of those who have contracted cardiomyopathy have reported to have lived a healthy life, free of medical problems and pre-existing conditions. This is the sole factor that has puzzled many researchers and physicians to date.

Of the many tests that will be conducted in order to finalize a diagnosis are the following; Chest X-Ray, EKG, stress test, blood tests, etc. With the results collected from the tests, cardiomyopathy can then be diagnosed. Forever has it been known that one must diagnose before treating. Instinctively, for the most part, it is extremely beneficial for physicians who are treating patients to know how a particular illness was contracted. Unfortunately, cardiomyopathy is a disease that carries with it a mystery in terms of it’s past.

Contracting
Perhaps one of the most puzzling cases to cardiologists to date lies with the question as to how one contracts cardiomyopathy. As previously stated, diagnosis typically occurs after the disease has progressed. Due to this, the biochemistry of cardiomyopathy is unclear leaving physicians uncertain as to what exactly caused the illness.

Although in most cases a physician cannot pinpoint the exact cause, there is a diverse range of possible primary and secondary causes. The range is broad from the use of drugs such as cocaine, to pre-existing medical conditions such as breast cancer. For this report, the focus will center on two causes that have a more in-depth understanding of the biochemistry in terms of contraction.

Acute Alcohol Consumption
Studies show that many of those diagnosed with dilated cardiomyopathy have shown to have had a history with excessive alcohol consumption. This leads physicians to question the mechanism as to how alcohol plays a role in contracting the disease. Although the mechanism is unclear as well, researchers can estimate numerous possibilities leading to cardiomyopathy.

Ethanol, commonly known to many as simply drinking alcohol is the main catalyst for one to fall ill. Being a very volatile, flammable liquid with a molecular formula of C2H5O, research has noted that ethanol exerts massive effects to the ventricular walls of the heart.
What is occurring is that with an acute consumption of ethanol, the ventricular contractility of the heart is depressed. Much research indicates that this is due to acetyldehyde impairment of mitochondrial phosphorylation. Acetyldehyde is oxidized from ethanol by alcohol dehydrogenase, an enzyme produced by the liver. It is believed that when the myocyte mitochondria is exposed to acetyldehyde, the function of the mitochondria is impaired. This ultimately leads to damaging effects of the entire cell.

**Viral Infections**

Dilated Cardiomyopathy can also be brought on by a viral infection, having evolved from myocarditis in most cases. The viruses that can cause such damage have a broad range, from HIV to Coxsackie B virus. For the most part, when one contract’s a virus, their immune response limits viral replication, thus, ridding the virus from the host. In these cases, the host may not even know that they had a virus to begin with. On the other hand, the same virus that may have had no effect on person A could have detrimental effects on person B, thus, progressing to dilated cardiomyopathy.

In many cases, one’s own immune response can lead to damage of the myocardium, increasing the extent of cardiac cell loss leading to cardiomyopathy. What is occurring is that the T lymphocytes, which play a role in viral clearance, begin to react with the host antigen which in turn causes myocyte damage in the myocardium. This is due to the similarities between the viral proteins and the myocardial antigens. Thus, the T cells cannot distinguish the difference between one’s own host antigen to that of a viral protein, ultimately leading to the destruction of the host’s cells.

**Cardiomyocytes**

A recurring theme is seen in all dilated cardiomyopathy and that is cardiomyocyte injury or loss. The destruction of the cardiac cells begins with the dissociation of a proteins composition. The human body produces thousands of new proteins every second that allow our body to function properly. Under normal and healthy conditions, proteins in the human body are associated in pairs or in subunits. This association protects the proteins given that the aggregation-prone region is covered by its paired counterpart.

When these proteins undergo genetic mutations, be it from alcohol consumption, a viral infection, etc., the composition of the protein is altered. This mutation causes a dissociation of the proteins, thus, causing the aggregation-prone region to go uncovered and unprotected. This dissociation ultimately leaves the proteins vulnerable to the formation of toxic macromolecular aggregates. When this occurs, the entire protein will eventually become toxic, thus, preventing them from carrying out the functions assigned by the genetic coding of the human body. In the final analysis, the death of the cell takes place causing the heart to progressively shut down until all of the cells have died.
Treatment
Dilated Cardiomyopathy, like all forms of cardiomyopathy is incurable without a heart transplant. In fact, within five years of diagnosis, 50% of patients die without the surgery. Much of this is due to the limited understanding of the underlying disorder in the early stages of cardiomyopathy. Although years of research have been invested for a cure, there has not been much therapeutic nor scientific progress for decades. Thus, the symptoms of cardiomyopathy can only be treated, not cured.

Those who do not undergo heart transplants are required to take numerous medications as well as undergo drastic lifestyle changes. Among the medications prescribed, diuretics are unquestionably essential. Spironolactone, known to many by its trade name Aldactone, is a potassium-sparing diuretic hormone that works by competing for the intracellular aldosterone receptors. By interfering with these receptors, aldosterone is unable to regulate the salt and water balance in one's body. Therefore, the medication will prevent excess salt and water reabsorption while at the same time decreasing the secretion of potassium.

\[
\text{Spironolactone.11}
\]

Alpha and beta blockers also play a crucial role in the cure for dilated cardiomyopathy. One of the more recognized forms of treatment is the prescription drug Carvedilol, trade name Coreg. First approved by the FDA in 1995 with a molecular formula consisting of \( \text{C}_{24}\text{H}_{26}\text{N}_{2}\text{O}_{4} \) and molecular weight of 406.47 g/mol, Coreg acts as both a beta blocker and an alpha blocker.

\[
\text{Carvedilol.2}
\]

The adrenergic nervous system of the human body releases norepinephrine which binds to the beta receptors of the heart. In doing so, the heart is stimulated, thus, causing the heart to beat more forcefully and rapidly. Apart from the beta receptors, norepinephrine also binds to the alpha adrenergic receptors on the blood vessels of the heart. Because of
this, the binding of the norepinephrine causes the blood vessels to constrict, thus, raising blood pressure.2

Carvedilol’s reaction in the human body blocks the binding of both beta and alpha receptors of the heart. Therefore, the heart rate is dramatically reduced as well as the force of the heart’s contraction due to the blockage of the beta receptors.2 The blockage of the alpha receptors reduces the constriction of the blood vessels of the heart, thus, lowering blood pressure. In general, the use of Carvedilol reduces the workload of the heart while allowing the arteries to relax. The reduction of stress the heart would otherwise be experiencing, drastically prolongs the life of one living with cardiomyopathy.4

**Stem Cell Therapy**

Stem cell therapy, although relatively new, is one of the more promising forms of treatment for dilated cardiomyopathy to date. Stem cells, known as the “Master Cells” of the human body, work by regenerating heart tissue as well as repairing damage to treat dilated cardiomyopathy.12 There are no restrictions for stem cell therapy placed by the government due to the fact that the stem cells used are not taken from a fetus. Instead, the stem cells originate from one’s own body (autologous transplant) and/or from another human being (allergenic transplant). Although allergenic transplants are common, autologous transplants are more frequent due to the fact that one’s own stem cells will not be rejected by the human body.5

Research conducted by the Mayo Clinic in Rochester, Minnesota support the new and invasive form of stem cell therapy, thus, furthering support for personalized regenerative medicine. The research conducted entailed genetically altered mice whose hearts resembled prominent features of dilated cardiomyopathy. The team focused their attention on a KATP channel, a critical heart protective protein causing ventricular dilation as well as interference with heart contractions.1

The wall of the left ventricle of each mouse was injected with 200,000 stem cells. Following a month after treatment, cell cycle activity of the heart was regenerated along with the formation of new cardiac tissue. More importantly, the deterioration of the mouse’s heart had ceased while at the same time increasing the stamina of the mice. Although further testing is needed, researchers at the Mayo Clinic strongly believe that their findings demonstrate that stem cell therapy for dilated cardiomyopathy holds the key to functional repair.

Unfortunately, such a form of treatment is limited in terms of candidacy for patients. With this said, a potential candidates overall health and age will be detrimental in terms of determining the placement.12 Also, if an individual has had cancer previously, that individual must be cancer free for a particular amount of time, typically five years post cancer treatments. Specialized equipment along with specially trained physicians and nurses are required, thus, further limiting hospitals able to perform such procedures. More often than not, patients seeking therapy may have to travel to a particular hospital or practice which specializes in stem cell therapy.5
Conclusion
Throughout time, cardiomyopathy has drastically altered the lives of many, bringing heartbreak and unanswered questions to the families left behind. Although enormous research has been invested in dilated cardiomyopathy, there are several factors which limit further knowledge. To begin, researchers must gain a strong understanding in the underlying disorder. Without this knowledge, researchers do not have a true foundation in terms of the onset of the disease. Thus, a physician can only treat the symptoms one is experiencing, if of course the symptoms are treatable at the time of diagnosis. The understanding of the biochemistry in the beginning stages of the disease can allow scientists an insight as to how to intervene before the illness has progressed.

What also needs to be seen is an improvement of the current therapy for heart failure. This can be done by permitting more rapid testing of new medications along with an increase in funding. However, it is important to keep in mind that one must take responsibility for their own physical examinations. Remember, cardiomyopathy is often a silent killer due to the feint symptoms and rapid progression. By spreading knowledge of this disease will make people aware of the symptoms that are typically overlooked.

Personally speaking, my mother was diagnosed with dilated cardiomyopathy in the Spring of 2006. Before that diagnosis, my mothers disease was repeatedly overlooked by countless physicians trying to determine her illness. Those physicians error was due to the fact that they did not associate heart disease in a middle-aged woman who physically appeared to be healthy. My mothers story is one of thousands where individuals such as herself fall ill to a disease they could have never foreseen. With adequate knowledge in cardiomyopathy and all heart disease for that matter will stress the importance of self awareness, thus, potentially saving ones life.

Unfortunately, through my cynical yet realistic point of view, I see no progression for future understanding of cardiomyopathies underlying disorder’s. I believe there will be advances in medications for heart failure, including cardiomyopathy, though no cure will come about for quite sometime. I base this on the knowledge that when a heart undergoes such extravagant damage causing the majority of the heart to die, the revitalization of the cardiac cells is unquestionably impossible by any form of medication to date.

However, I strongly feel that the cure to dilated cardiomyopathy lies with stem cell therapy. Unlike the countless medications which only treat the symptoms, stem cell therapy can actually cure the damaged regions of the heart by inhabiting new and healthy cells. The heart is revitalized as if it were reborn, without a heart transplant or a lifelong prescription to endless medications. It is crucial that research in stem cell therapy progresses, given its potential in terms of healing.

Years of research have passed and countless more are bound to follow. Unfortunately, as time slips away, those diagnosed along with their loved ones struggle for more to hold on to. But we must always keep our sights on the sunrise of hope in the distant horizon. In life I have come to learn that nothing lasts, for the better or worse and with this
knowledge, along with resiliency and perseverance, nothing is beyond attainment. As Ernest Hemingway once wrote, "He should always try for something that has never been done or that others have tried and failed. Then sometimes, with great luck, he will succeed."
Cited References


Vitamin Deficiency

Lacey Reed
4-23-10
Abstract:

This paper will address key issues concerning vitamin D, the effects of vitamin D deficiency, and ways to avoid becoming deficient. Over the years vitamin D deficiency has been on the rise. This rise is contributed to changes in lifestyles over the years. This paper will discuss those changes and how they effect our vitamin D levels today. Vitamin D is not a prevention of disease, but a lack of vitamin D could cause serious problems (1). This is why there are certain levels of vitamin D that should be found in adults, children, and babies. These levels are carefully calculated and ways to obtain those safe levels are provided. It is important to understand the chemistry of vitamin D and how it works in the body before learning about these key concerns and solutions to the problem.

Introduction:

Vitamin D deficiency was scientifically discovered in the seventeenth century by Dr. Daniel Whistler and Professor Francis Glisson. They came about this discovery through the research of rickets disease. Rickets disease is a lack of vitamin D causing weakening and softening of the bones which leads to fractures and deformities (2,3). In the 1930s Professor A. Windaus was able to determine chemical structures for the two main forms of vitamin D. Vitamin D2 was determined in 1932 and vitamin D3 in 1936. Through these chemical structures, it was discovered that vitamin D is a secosteroid (3). Steroids typically have four rings but with a secosteroid, two of the B-ring carbons C9 and 10 are not joined (4). In the following images, the red in Vitamin D2 indicates the differences chemically in the two.

Vitamin D3 (image 1)  
Vitamin D2 (image 2)

Images found at (www.natuurlijkkerwijs.com/english/vitamines.htm)
Vitamin D and its Chemistry:

Vitamin D (calcitriol) is a fat soluble vitamin that aids in absorbing and metabolizing calcium and phosphorous (2,5,6,7). There are two main ways of absorbing vitamin D: endogenous and exogenous. Endogenous means that it is created in the skin due to sunlight and it includes Cholecalciferol (vitamin D3). Exogenous means that it is taken in through supplements and foods and includes ergocaliferol (vitamin D2) (8). D2 and D3 are both beneficial. Food alone does not contain the vitamin D necessary to prevent deficiencies so it is important to also get enough sunlight and take vitamin D supplements or foods that are supplemented with vitamin D (7). Images one and two show that vitamin D3 and D2 are very similar in structure. The only difference is the methyl group in red and the double bond in red that are on the vitamin D2.

As stated earlier vitamin D is a tool in the body to control levels of calcium and phosphorus. As research continues, it shows that there are more uses for vitamin D in the body. Vitamin D3 and vitamin D2 are not active until hydroxylated (7). There are two steps to make this happen. The first step happens in the liver and is when the cholecalciferal (D3) is hydroxylated to make 25-hydroxycholecalciferol (25-hydroxy vitamin D). This is done with the enzyme 25-hydroxylase (7). The next step happens in the kidney and is when the 25-hydroxy vitamin D becomes a substrate from 1-alpha-hydroxylase and gives 1,25-dihydroxy vitamin D. The 1,25-dihydroxy vitamin D is the active form of vitamin D in the body (7). The 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D are the two forms of vitamin D that can be measured in the blood for deficiency (8).

Vitamin D is hydrophobic which means it is resistant to water. Vitamin D is transported in the blood with the help of carrier proteins. In this case these carrier proteins are called vitamin D-binding protein (7). There is a difference in half life numbers of the vitamin D forms in the liver and the kidney. The 25-hydroxy vitamin D's half life is weeks and 1,25-dihydroxy vitamin D's half life is just hours (7). The 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D are the forms of vitamin D that can be measured in the blood for deficiency (8). The 25-hydroxy vitamin D, although not the active form, is the one that is usually measured since its half life is longer than that of the active form. When measured it helps assess vitamin D levels in individuals.
These tests are conducted if there is suspicion of vitamin D deficiency like low calcium or bone weakness. It could also be ordered if there are signs there is too much vitamin D in the system like high calcium levels or other diseases found that could raise vitamin D levels in an individual. The test is done by taking a blood sample from a person’s arm (8).

**The Effects of Vitamin D Deficiency:**

Being deficient in vitamin D can lead to more problems which include but are not limited to cancers, heart risks, osteoporosis, and bone fractures. The main reason that vitamin D deficiency can lead to so many other problems is that most cells and tissues in the body have, receptors for vitamin D (9). This leads to vitamin D being needed in many areas for a person’s health. Everyone needs the correct level of vitamin D, but the correct levels are different for everyone. The following describes levels of vitamin D and the effects at each level.

**Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health**

<table>
<thead>
<tr>
<th>ng/mL**</th>
<th>nmol/L**</th>
<th>Health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10-11</td>
<td>&lt;25-27.5</td>
<td>Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults [4,13]</td>
</tr>
<tr>
<td>&lt;10-15</td>
<td>&lt;25-37.5</td>
<td>Generally considered inadequate for bone and overall health in healthy individuals [4,13]</td>
</tr>
<tr>
<td>≥15</td>
<td>≥37.5</td>
<td>Generally considered adequate for bone and overall health in healthy individuals [4]</td>
</tr>
<tr>
<td>Consistently &gt;200</td>
<td>Consistently &gt;500</td>
<td>Considered potentially toxic, leading to hypercalcemia and hyperphosphatemia, although human data are limited. In an animal model, concentrations ≤400 ng/mL (≤1,000 nmol/L) demonstrated no toxicity [11,14].</td>
</tr>
</tbody>
</table>

* Serum concentrations of 25(OH)D are reported in both nanograms per milliliter (ng/mL) and nanomoles per liter (nmol/L).

** 1 ng/mL = 2.5 nmol/L

One of these health concerns is the risk of osteoporosis (5). Osteoporosis deals with fragile bones and usually is from low levels of calcium but as stated earlier, vitamin D controls levels of calcium so they go hand in hand. This happens because when there is not vitamin D to absorb new calcium from foods and other sources, the body takes the calcium from the bone causing the fragile bones (5,10). So there is a benefit to the correct amount of vitamin D when it comes to osteoporosis. This problem with fragile bones is one effect of low levels of vitamin D that goes unnoticed until it is too late. This is why it is important to absorb normal levels from a young age to avoid the problems that could arise.

Another benefit of vitamin D is the new evidence that links it to helping with cardiovascular health. One situation with cardiovascular health to consider is blood pressure. Usually there is an increase in blood pressure as a person becomes older, but this new evidence shows that when people have adequate amounts of vitamin D, it reduces the elevation of blood pressure as we age (11). When 1.739 Framingham Heart Study participants were studied, research showed that the participants that had low vitamin D levels (below 15 ng/ml) had two times the risk of heart problems than those with higher level. Those heart problems include heart attack, heart failure or stroke (12). When another study was done for high cholesterol, diabetes and high blood pressure, the results were the same. Those with low levels of vitamin D were at a great risk than those with higher levels (12).

Even fetuses are at risk of being born with low levels of vitamin D based on what their mothers do. A vitamin D study was conducted by Lisa M. Bodnar from the University of Pittsburgh School of Public Health. In this study blood was collected from 400 first time mothers at the beginning and end of their pregnancy to test for vitamin D levels. This study included half white women and half black woman. They had 90% of women take vitamin D supplements during their pregnancy and half of them also took vitamin D supplements before they were pregnant. This study found that 4 percent of the black women had vitamin D blood concentrations that were at a healthy level and 37 percent of white women had their vitamin D blood concentrations that were at a healthy level. Then when the babies umbilical cords were tested, it showed that 17 percent of the black babies had good health levels of vitamin D and half of the white babies had good levels of vitamin D. They concluded that the cause for the differences between races was that the African Americans have more pigmented skin and that would absorb less sun than the whites. The whites were better but not perfect and the conclusion was that although whites absorb more sunlight in the winter time there is less sun to absorb (13). Although the vitamin D levels in their blood are low, it is shown that most African Americans suffer from less fractures and osteoporosis. This could be due to the advantage of bone density from childhood (5). Although their bones may be stronger than Caucasians, their blood levels are worse which could lead to heart problems and more over time.

There are also beliefs that the reason for more colds and flu in the winter than the summer is due to continued deficiency of vitamin D. The biggest difference in the summer and winter months is the sun exposure. In the winter the sun exposure is less because people stay inside more to avoid the snow or cold, and because the rays are weaker from being further from the sun. In the
summer, however, the earth is closer to the sun with stronger rays and with the better weather people are outside getting more sun exposure and less sickness (10). The sun exposure and seasons contributing to more sickness as a result of less sun exposure is just a theory but should be taken seriously.

**Where Can We Get Vitamin D?**

There are many sources of vitamin D. One of these sources is found in foods. Although most natural foods do not contain enough vitamin D, the most efficient ones include flesh of fish and fish oils. There are also small amounts in beef liver, cheese, and egg yolks (5). Since natural foods alone do not provide the levels of vitamin D needed today there are foods that are fortified with vitamin D to help a person absorb the recommended amount of vitamin D. These fortified foods include milk, cereals, some orange juice, yogurt, and margarine (5). It is important to understand what foods contain vitamin D and try to implement them into everyday life. For example, when buying orange juice instead of buying the original buy one that is fortified with vitamin D.

Another effective way to absorb vitamin D is sun exposure. Adequate amounts of sun exposure will give the body vitamin D3. This does not work as well in winter months. Severe cloud coverage blocking the UV energy will reduce exposure by half and standing in the shade reduces sun exposure by 60% (5). Using sunscreen will also reduce the sun exposure needed for proper levels of vitamin D in the body. UV rays are also found to be a carcinogen, it is important to limit sun exposure to just what is needed for vitamin D levels and protect your skin after that amount (5). “It has been suggested by some vitamin D researchers, for example, that approximately 5-30 minutes of sun exposure between 10 AM and 3 PM at least twice a week to the face, arms, legs, or back without sunscreen usually lead to sufficient vitamin D synthesis and that the moderate use of commercial tanning beds that emit 2%-6% UVB radiation is also effective (5).

There are also dietary supplements that aid in giving the correct amount of vitamin D intake to a person’s diet. This is done with vitamin D2 or vitamin D3. “Vitamin D2 is manufactured through UV irradiation of ergosterol in yeast, and vitamin D3 is manufactured from the irradiation of 7-dehydrocholesterol from lanolin and a chemical conversion of cholesterol” (5). It has been said that both vitamin D2 and vitamin D3 give the same benefits. Recent research has shown that vitamin D3 may be more beneficial than vitamin D2. Although this is not yet proven and is still being research some supplements are being switch so that they are completely vitamin D3.

**Regulations, Recommendations and Who Needs to be Concerned:**

There are certain levels of vitamin D for different ages, sexes, and pregnant individuals. These numbers are carefully calculated by the Food and Nutrition Board (FNB) so that everyone can receive adequate levels in their body (5). Research has found that 4 percent of men and 1 percent
of women over the age of 51 meet the recommendations from food for their vitamin D (14). Even some people that take vitamins are still coming up with a deficiency of vitamin D. This suggests that vitamin D amounts may be too low and these numbers are continually being tested to increase or decrease as needed (10). The current correct levels of vitamin D for different types of people are displayed in table two.

Table 2: Adequate Intakes (AIs) for Vitamin D [4]

<table>
<thead>
<tr>
<th>Age</th>
<th>Children</th>
<th>Men</th>
<th>Women</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 13 years</td>
<td>5 mcg (200 IU)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>14-18 years</td>
<td>N/A</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
</tr>
<tr>
<td>19-50 years</td>
<td>N/A</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
<td>5 mcg (200 IU)</td>
</tr>
<tr>
<td>51-70 years</td>
<td>N/A</td>
<td>10 mcg (400 IU)</td>
<td>10 mcg (400 IU)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>71+ years</td>
<td>N/A</td>
<td>15 mcg (600 IU)</td>
<td>15 mcg (600 IU)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>


Lifestyle changes are a big reason vitamin D intake is becoming worse. One change is that more people are staying inside to watch TV, play video games, or just to avoid the heat of the summer. As stated earlier sunlight is one of the main sources of vitamin D. If a person stays inside too long they will not take in adequate amounts of sunlight and increase their chances of becoming deficient in vitamin D (15). Another reason for the increase in vitamin D deficiency is the change in diet over the years. More people are eating processed foods and junk that does not contain any vitamin intake including vitamin D. With this decrease of healthy eating, vitamin D deficiency is on the rise. There are also genetic effects and diseases that cause vitamin D deficiency. Diseases that effect vitamin D levels are liver or kidney disease which can hinder the production of the active form of vitamin D. Genetic effects include a defect in the vitamin D receptor. That defect of the receptors cause those individuals to become vitamin D deficient (7).

There are problems resulting from too much vitamin D, so it is important to not go too far under or too far over the recommended amount for your gender or age group. Symptoms of too much vitamin D are nausea, vomiting, loss of appetite, constipation, weakness, and weight loss. The
most serious effect is the rise in blood levels of calcium. Most of the toxic levels are obtained through supplements since the skin will get too hot before having the dose become toxic (5).

Everyone should be aware of their vitamin D intake and manage it accordingly, but there are groups with a higher risk of becoming deficient. These groups include breastfed infants since vitamin D is obtained through milk that is fortified with vitamin D and human milk will not yield the required amounts. There are vitamins available for breastfed infants to help them maintain healthy levels while still getting the added benefit of breast milk. Another group is the elderly since their skin does not function as well as young people in synthesizing vitamin D. Aged individuals also have more problems with their kidneys. This becomes a problem since the biologically active form of vitamin D is formed in the kidney. Kidney problems in younger people would give the same effect as the elderly (7).

Sun is an effective way to absorb vitamin D so people with limited sun exposure are also at risk. This includes people that stay indoors most of the time, people whose clothes cover a good portion of the body, and people who wear sun block whenever exposed to the sun. Demographics is also a factor in less vitamin D absorbed from the sun. This becomes a problem when a person lives in an area with less sunshine, cold weather that keeps them inside, or hot weather that keeps them in the shade. As stated early people with darker skin like African Americans do not produce vitamin D from the sun as well in their skin leading to negative effects.

People suffering from obesity do not release vitamin D as well due to blockages in the blood and therefore can become deficient. People who have had gastric bypass surgery for their obesity are also at risk of being deficient in vitamin D, as well as people with other conditions that interfere with fat absorption. This problem arises because “vitamin D is a fat soluble vitamin and is absorbed from the intestine like a fat.” (8)

**Conclusion:**

As the paper states, vitamin D is an important vitamin for everyone. Its importance lies in the fact that with a deficiency, serious problems have occurred, but adequate amounts have proven to yield healthier individuals. Vitamin D is important for developing strong bones, normal growth of teeth, absorption and metabolism of calcium and phosphorous, boosting the immune system, helping the brain function properly throughout life, among aiding with other important functions of the body (16). Adequate levels of vitamin D are different for everyone, so it is important to be aware of the proper amounts since too little is harmful and as stated in the paper, too much can also be harmful. There are many sources of vitamin D including food, supplements, and sunlight. Once a person’s vitamin D levels are evaluated, the amounts of the sources needed can be determined as well. These numbers are important to know so that the person can avoid a deficiency of vitamin D. Although vitamin D is not a cure for problems that could arise, a deficiency of vitamin D can be serious.
References:


Aspirin and Cancer

by

Gary A. Rosenberg

April 23, 2010
Abstract

Aspirin, or acetylsalicylic acid, has been used by mankind for many years in various different forms. There have been many discoveries for the use of aspirin besides its analgesic effect. It has been shown to possess anti-inflammatory, and anti-pyretic properties. Recently the drug has been studied for other beneficial health effects such as the prevention and treatment of cancer.

Aspirin

Introduction

Aspirin, or acetylsalicylic acid, has been used by mankind for many years as a pain reliever and a wonder drug. It has a distinctive history of origin and use by many cultures. Since the advent of aspirin, there have been many other pain relievers and anti-inflammatory drugs that have hit the market. Many of these new drugs have been prescribed more by doctors for aches and pains than aspirin. Recently, aspirin has been researched more for its properties and other beneficial health effects. Some of these beneficial effects have included cardiomyopathy and cerebral vascular accident prophylaxis. Other uses for aspirin include arteriosclerosis prevention. While these benefits are becoming better known and aspirin is being prescribed daily by medical professionals, there may also be other benefits that are not as well known. One of these unknown benefits is aspirin’s ability to prevent and reduce reoccurrences of cancer. To think that taking one small pill a day could not only relieve aches, prevent strokes, heart attacks, but also prevent some types of cancer. Truly, this is a wonder drug.

History

To understand aspirin better, the origins of how this drug was discovered must be discussed. The first reported use of a derivative of acetylsalicylic acid was in ancient Greece and Rome.\(^1\) This derivative, Salicin, was found in the bark of willow and poplar trees. It was also found in the plant called meadow sweet. A form of Salicin had been used for many centuries for medicinal use but was not fully synthesized to acetylsalicylic acid until the mid 19th century. In 1853, Charles Frederic Gerhardt, prepared the first sample of acetylsalicylic acid. He was studying the properties of various acid anhydrides and mixed acetyl chloride with sodium salicylate. He called the compound salicylic-acetic anhydride. This was documented in his paper of anhydrides, but he did no further work toward the preparation of aspirin.\(^2\)

This structure created by Gerhardt was studied further by Von Gilm in 1859. He combined salicylic acid and acetyl chloride to make acetylsalicylic acid. The experiments done by Von Gilm and Gerhardt were repeated in 1869 by Schroeder, Prinzhom, and Kraut. They found that both experiments gave the same product as acetylsalicylic acid. They were the first to
discover the correct chemical structure of aspirin with the acetyl group attached to the oxygen of the hydroxyl substituent of salicylic acid.\textsuperscript{2}

In the mean time, salicylic acid and sodium salicylate were widely used analgesics in the nineteenth century. Unfortunately, they both had undesirable side effects. Salicylic acid irritated the mucous membranes of the mouth and the stomach. Sodium salicylate was said to be too sweet for most patients.\textsuperscript{3} The structure was also being studied by Felix Hoffman, who was a German chemist for Friedrich Bayer, a German dye company. He discovered that the corrosive nature of aspirin was altered when the acetyl group was attached to salicylic acid. He developed a feasible and pure commercial synthesis of aspirin. The Bayer Company obtained a patent on the drug and called it "Aspirin". The first aspirin was sold in 1899.\textsuperscript{2}

Hoffman's work was also motivated for personal reasons. His father suffered from rheumatoid arthritis and was unable to tolerate the sweet taste of sodium salicylate. By discovering how to synthesize a pure product of aspirin, he was able to help his father.\textsuperscript{3}

Aspirin was named by the Bayer Company because of its chemical structure. The A- in aspirin represents the acetyl group used in the compound. The -spir was derived from the Latin name spirea for the meadow sweet plant where salicylic acid is located. The -in was placed at the end as a typical drug name ending to make it easier to pronounce.\textsuperscript{2,3}

The Bayer Company sales of aspirin were very prosperous until World War I and in between the world wars. The rights to aspirin in America were sold after World War I to an American drug company named Sterling Drug. This company was bought and sold many times over the next few decades. In 1997, Smith-Kline Beecham sold the American rights to the Bayer name and trademark back to Bayer A.G. for $1 billion.\textsuperscript{1}

There was much competition throughout the world for the synthesis and distribution of generic aspirin. This medicine was being used in England, Europe, the Americas, all the way to Australia. The Bayer Company tried to enforce the patents that they had in various countries, and also to stay at the top of the market where there were no patents available.

Originally aspirin was used for its pain relief for various maladies. But it was soon discovered that it could be used for other problems as well. In 1899, it was discovered that aspirin has anti-pyretic properties and was marketed to physicians.\textsuperscript{4} This property became especially important after the Spanish Flu pandemic and the influenza of the 1920s. The effectiveness of aspirin for treating the flu created even more competition for the marketing of this drug.

In 1950, Lawrence Craven, MD, published a report that aspirin may reduce the risk of myocardial infarction. He first discovered how some of his patients who had tonsillectomies, were chewing a gum called Aspergum that was laced with aspirin. The patients that used this gum frequently had increased bleeding and had to be hospitalized. He studied over 8,000 patients but his report was not taken seriously secondary to not having a placebo controlled study.\textsuperscript{2}

Aspirin had been the main drug of choice for many years. The competition was fierce over the marketing and selling of this drug in many countries and the Bayer Company had
difficulty competing. Because of this competition, Bayer looked into a new drug that was discovered at Yale University in 1946 that was determined to be acetaminophen. They marketed this drug as Panadol in 1956 but had difficulty getting companies to sell this drug since aspirin was doing so well.\textsuperscript{2} Other companies did market this drug in 1955 as Tylenol and was made available without a prescription in 1967. This new drug did not cause gastric irritation and became popular enough to displace aspirin sales.

Another drug came to the market in 1962 that also provided aspirin with some competition. This drug was ibuprofen. This was also an analgesic and anti-inflammatory drug. Ibuprofen became available without a prescription that in 1980s which undermined even more sales of aspirin.\textsuperscript{2}

Aspirin also declined in use and sales when it was linked to Reyes syndrome. Reyes syndrome is characterized by acute encephalopathy and a fatty liver which can lead to death. A link was found between persons under 18 who took aspirin for a fever, or other illnesses or infections. Warnings labels were put on bottles of aspirin by 1986, warning of this possible side effect which even further decreased sales.\textsuperscript{3}

In 1972, John Vane published his study on “The effect of Aspirin”. He discovered that aspirin has anti-pyretic properties, anti-inflammatory properties, and was an analgesic. He found that aspirin inhibits prostaglandin activity which causes inflammation. He later received the Nobel Prize for his discoveries concerning aspirin.\textsuperscript{4}

There has been other research about aspirin’s effectiveness as a heart drug. Beside Lawrence Craven, Harvey Weiss discovered in the 1960s that aspirin had an anti adhesive effect on blood platelets. Other studies were done later in the 1970s and 1980s that showed the effectiveness of aspirin for preventing heart attacks and it gained US FDA approval. As a result, aspirin became one of the top selling drugs analogesics in the United States.\textsuperscript{2}

**Chemical structure and Reaction**

The chemical formula of aspirin is C\textsubscript{9}H\textsubscript{8}O\textsubscript{4}. This means that there are nine carbon atoms, eight hydrogen atoms and four oxygen atoms. See Table 1 for physical data.

![Chemical structure of aspirin](image)

**Table 1**

<table>
<thead>
<tr>
<th>Product</th>
<th>Molecular weight</th>
<th>MP deg celsius</th>
<th>BP deg celsius</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>180.15</td>
<td>128-137</td>
<td>140</td>
</tr>
</tbody>
</table>
The complete reaction of the synthesis of salicylic acid is show below. In the first reaction phenol reacts with sodium hydroxide to make sodium phenate and water. The sodium phenate reacts with carbon dioxide in the second reaction to make sodium salicylate. This in turn reacts with sulfuric acid to make salicylic acid and the sodium is displaced as a cation. Salicylic acid is reacted with acetic anhydride with phosphoric acid as a catalyst to make acetylsalicylic acid and acetic acid as the final products. See Table 2 for physical data.

![Chemical reactions](image)

Table 2

<table>
<thead>
<tr>
<th>Reagent</th>
<th>MW g/mol</th>
<th>MP deg Celsius</th>
<th>BP deg Celsius</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>94.11</td>
<td>40.5</td>
<td>181.7</td>
</tr>
<tr>
<td>Sodium Hydroxide</td>
<td>39.99</td>
<td>318</td>
<td>1388</td>
</tr>
<tr>
<td>Sodium Phenate</td>
<td>116.10</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>44.01</td>
<td>-78</td>
<td>-57</td>
</tr>
<tr>
<td>Sodium Salicylate</td>
<td>160.11</td>
<td>200</td>
<td>N/A</td>
</tr>
<tr>
<td>Sulfuric Acid</td>
<td>98.08</td>
<td>10</td>
<td>337</td>
</tr>
<tr>
<td>Salicylic Acid</td>
<td>138.12</td>
<td>159</td>
<td>211</td>
</tr>
<tr>
<td>Acetic anhydride</td>
<td>102.09</td>
<td>-73.10</td>
<td>139.8</td>
</tr>
</tbody>
</table>
Aspirin as Prevention

Aspirin has had a history of many uses during its discovery. It started as a simple analgesic but was found to have other properties such as an antipyretic, anti-inflammatory, and a prophylactic for myocardial infarction and cerebral vascular accidents. Aspirin was also tested for other possible uses.

Aspirin has been studied for its affect on cancer. Cancer is defined as a class of diseases that is characterized by the formation of abnormal cells that grow uncontrollably, invade other cells, and cause destruction. Cancer may also travel to other parts of the body. Most types of cancers form a tumor in the body, but others do not as in the case of leukemia. The focus on cancer has been mostly on treatment but there are several factors that have been cited to reduce the risk of developing this deadly disease. Some of these prevention factors include: stop smoking, avoid excessive sun exposure, eat a healthy diet, exercise for 30 minutes a day, maintain a healthy weight, schedule screening exams, and ask about immunizations.

Yet despite the advances in health care treatments and knowledge of prevention, many people still contract the disease and succumb to it. Cancer currently is the second leading cause of death in the United States. Because of the high mortality rate of cancer there is a need to find other treatments and prevention of this disease. Aspirin has been studied for both the prevention and for the treatment of cancer.

There have been several studies done to evaluate aspirin as a preventative measure for cancer. One of these studies was led by professor John Burn of Newcastle University. He followed 1071 people with Lynch Syndrome, which is an inherited form of cancer of the digestive tract. Over a time period of 4 years, half of the study’s participants received 600 mg doses of aspirin that were taken daily. The other half of the participants received a placebo. The participants that were given aspirin, had less than half as many colon cancers as compared to the placebo group.

The risks and benefits of using aspirin and other nonsteroidal anti-inflammatory drugs have been discussed by Takeo Iwama in the journal of gastroenterology. Aspirin has an inhibitory effect on prostaglandins, which are a 20 carbon fatty acid with a five membered ring, that are responsible for pain, inflammation, and other functions. Prostaglandins are unique because they are not stored in cells. They are made from arachidonic acid. Aspirin blocks the COX enzyme that converts arachidonic acid to prostaglandins. Control of cell growth is one of the functions of the prostaglandins which are involved in the rapid production and spread of cancerous cells. So by inhibiting the production of prostaglandins, the cancerous cells can be inhibited.

The study done by T. Iwama concluded that a high dose of COX-2 inhibitor suppresses adenomas through the toxic effects on the gastrointestinal epithelial cells. But a moderate dose of COX-2 inhibitors wasn’t effective for preventing adenomas. The drawback of using high doses of COX-2 inhibitors is the increase in death from cardiovascular events.

Another study done by Baron et al found that low doses of aspirin had a moderate chemo preventative effect on adenomas in the colon but high dose aspirin did not show a preventive effect for cancer.

Although there have been many studies to evaluate the chemo preventative nature of aspirin, there is still some disagreement whether aspirin is an effective drug. More research will need to be done to solidify the many experiments that have shown that aspirin is an effective treatment for the prevention of cancer.
Aspirin has also been studied for its use with people that have already been diagnosed with cancer. A study done by Chan et al.\textsuperscript{12} studied the use of aspirin after having been diagnosed with colorectal cancer. The authors studied the association between aspirin use and survival among 1,279 men and women with non metastatic (stage I, II, and III) colorectal cancer who were participating in two large cohort studies that were started in 1980 and 1986 before cancer was diagnosed. These people were followed through June of 2008.

The authors of the study found within the two different groups that regular aspirin use was associated with a decreased risk of developing primary colorectal cancer especially with tumors of “COX-2 overexpression”. The participants were also studied for the effects that aspirin had on the people in the group after they were diagnosed with colorectal cancer.

The median time for the follow up of the participants in the study was 11.8 years. There were 549 participants who used aspirin regularly. Of those participants, there were 193 total deaths (35%) and 81 colorectal specific deaths (15%). Of the 793 participants who did not use aspirin, there were 287 total deaths (39%) and 141 colorectal cancer-specific deaths (19%).

The five year survival period of the entire group was 88% for the participants who used aspirin as compared to those participants who did not use aspirin was 83%. The ten year survival rate was 74% for the aspirin group and 69% for the non aspirin users group.

This study found that regular use of aspirin is associated with a reduced incidence of colorectal death by 29% and 21% for overall mortality. The researchers of the study also analyzed the influence of aspirin of colorectal cancer among those with stage II and stage III cancer since those two groups tend to have a lower mortality rate than stage I.

They found among the 719 participants who did not use aspirin, there was a 47% reduction in colorectal deaths after initiating a regular aspirin regimen when diagnosed with colorectal cancer. They also found a 32% lower risk of overall mortality.

The researchers also studied how aspirin affected the type of cancerous tumor. They found that aspirin had a significant effect on COX-2 positive tumors. Regular use of aspirin after being diagnosed with this type of tumor resulted in a 61% lower risk of colorectal cancer mortality and a 31 % lower risk of overall mortality.

This significant data shows how an age old drug such as aspirin can be involved in reducing the mortality rate secondary to cancer and also the overall mortality rate. In addition, there is very significant data that shows that an aspirin regimen started after being diagnosed with a Cox-2 tumor, has a significant effect on mortality rates. This is positive news for people who have been diagnosed with colorectal cancer.

Ethics

Ethical considerations must also be taken into account with the use of aspirin. Gareth Morgan\textsuperscript{13} discusses some of the risks and benefits in his paper. As with any drug there are risks and benefits of its use. Mr. Morgan discusses how an increase in the use of aspirin may contribute to the increase in gastric bleeding. This risk must be balanced against the benefit for reducing the chance of having vascular events and for reducing the incidence of colon cancer.
There is a need for more research to define which populations are appropriate to take aspirin and the appropriate dose level in order to avoid risks of the side effects of aspirin.\textsuperscript{13}

Conclusion

The history of the use of aspirin and its derivative dates back through the centuries of time. The drug has been refined over the last century to reduce side effects and to prepare it for commercial use. New health benefits from this drug have been discovered recently to prevent myocardial infarctions and other vascular diseases. It also has been shown to prevent and reduce some types of cancer. More research will need to be done in the future to confirm how aspirin is effective with fighting cancer and how it can be beneficial for other health problems.
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Nuclear Power: The Meltdown at Chernobyl

Angela Rynearson

4-23-2010
Abstract

Nuclear power at the Chernobyl power plant was produced in an RBMK type plant. A safety experiment was conducted in 1986 which led to an explosion of one of the reactors at the power plant. Radioactive materials were released during the explosion which resulted in immediate and long term effects on the environment and people in surrounding cities.

Nuclear power is used as the primary source of energy for most communities around the world. Strict safety guidelines are implemented by government agencies which promote safe and effective operation of power plants. The meltdown at the nuclear power plant in Chernobyl in 1986 was the result of an experiment by engineers and plant operators who underestimated the power of nuclear reactions and disregarded safety regulations. The disastrous event exposed hundreds of thousands to high levels of radiation and led to long-term consequences for the environment.

The RBMK design (Reactor Bolshoi Moschnosti Kanalyni “Channelized Large Power Reactor”) was the reactor type of the nuclear accident in Chernobyl. This type of reactor produces fast and unstable nuclear chain reactions and undergoes a power increase when cooling water is lost. This is known as a positive void coefficient which contrasts the negative void coefficient reactors used in the U.S. that immediately cease nuclear chain reactions when coolant water is lost. The RBMK also lacked the steel or concrete structure that contains radioactive material in the event of an explosion; however, it is thought that the magnitude of the Chernobyl explosion was too great to be contained by such a structure.

Image obtained from Globalsecurity.org

The RBMK design is a thermal reactor that uses pellets of $^{235}$U as nuclear fuel to create energy. Naturally occurring uranium only contains about 0.7% of $^{235}$U and has to be
enriched to about 2% $^{235}$U-235 to be used in an RBMK reactor. The process of producing energy by nuclear fission from $^{235}$U involves splitting a $^{235}$U atom with a neutron. Once the atom is split, it releases more neutrons, lighter radioactive elements, and energy as heat. The neutrons released during the split go on to split more $^{235}$U atoms; this is known as a chain reaction. The energy produced from this reaction heats water to produce steam which powers a turbine that drives a generator to produce electricity.

During Nuclear fission of $^{235}$U, the atom is split into unstable fragments of a lighter weight; different combinations of fragments occur. Fragment pairs are produced as shown in the following example of fission chain reactions$^2$.

The Nuclear Fuel Cycle

Fission chain reaction

1st Generation

2nd Generation

3rd Generation

4th Generation

- Neutron  
- Uranium-235 atom  
- Fission fragment e.g. $\text{Kr}, \text{Cs}, \text{Rb}, \text{Ba}, \text{Xe}$ or $\text{Sr}$

Image obtained from Fraser, James$^2$

Nuclear fission takes place inside the core of the reactor. Graphite thermal moderators in the core slow neutrons during the fission process in order to maintain a constant rate of chain reactions. Also inside the reactor are boron carbide control rods which allow the rate of fission to be controlled. Boron carbide is an extremely hard substance with a reported melting point of up to 3000° C; it is used to absorb neutrons and maintain an even distribution of power. Control rods can be added to the core if there is an increase in power; they can also be removed if not enough power is being produced$^3$.

In 1986, a group of engineers with limited knowledge of the fundamental properties of nuclear power made the decision to experiment with the safety measures of reactor number 4 at the nuclear power plant in Chernobyl. Their goal was to analyze whether the turbine generator would produce enough energy to run the water cooling system in the event that the reactor stopped providing power to the turbine. Once the experiment was
started, it was quickly understood that the power level was decreased too rapidly which led to a build-up of neutron absorbing by-products in the reactor core. Control rods were removed in an attempt to regain a higher power level, which was against the plants' guidelines. The low level of power resulted in a high level of instability for the reactor; the sudden drop in power resulted in unfavorable cooling of the reactor core.

The engineers chose to continue with their experiment by bypassing and disabling safety mechanisms and generators, including the emergency core-cooling system. By doing so, they were unable to control the boiling water in the cooling channels of the graphite-uranium reactor core. The coolant water and control rods in the graphite reactor work to absorb neutrons and in turn the chain reactions are kept under control. Without cooling water and the correct amount of control rods, the available neutrons were free to react with the nuclear fuel and a great surge of power resulted. They were unable to gain control of the catastrophic situation that followed.

The Number 4 unit of the Chernobyl nuclear power plant exploded and sent radioactive chunks of graphite into the surrounding area and about 50 tons of nuclear fuel and radioisotopes into the atmosphere.

Image obtained from Environmental New Service

The blast resulted in the immediate death of 2 plant workers; another 28 who were involved in the post-explosion rescue died within a few weeks due to acute radiation
poisoning. An estimated 600,000 clean-up workers, termed "liquidators", were exposed to different levels radiation in the following months. For 9 days following the explosion, firefighters and military personnel attempted to extinguish the fire in the reactor and absorb radiation by dropping 2400 tons of lead and 1800 tons of sand from helicopters. By covering the reactor, more heat was trapped inside; the higher temperatures resulted in the emission of more radiation. They were finally able to get the temperature under control with nitrogen on May 6th. Of the initial 600 firefighters and other crew member who worked at the site, 134 received severe doses of radiation poisoning.

According to Greenpeace, between 600,000 and 800,000 men worked to clean up the Chernobyl accident and roughly half of them received doses of radiation 500 times what is considered safe for the public. There is some controversy surrounding death tolls related to the disaster; official government figures appear to be far less than those provided by workers associations.

A crew of 400 coal miners worked day and night for nearly 2 months to create an underground tunnel leading to the reactor site; a cooling slab was built underneath the reactor to prevent a second explosion from occurring. If the concrete slab underneath the reactor would have cracked, the 165 remaining tons of nuclear fuel could have obliterated half of Europe, making it uninhabitable for 500,000 years. Many of these workers had little or no protection against radiation and therefore many suffered from radiation poisoning and a variety of other exposure related illnesses. In the following months, a sarcophagus containment structure was built around the reactor to prevent the further release of radioactive elements into the environment. Before the structure could be built around the reactor, the area needed to be cleaned up. Chunks of graphite and highly radio-active debris would need to be removed from the roof of Reactor 4 prior to beginning construction. Remote operated machines were brought to the roof in an attempt to scrape the materials off the roof where they could be gathered.
and buried. The high level of radioactivity interrupted the functionality of the machines; they were unable to perform under such conditions.

The only alternative was to send teams of workers onto the roof to scrape off the rubble. The workers were uniformed with heavy steel suits and worked in 45 second shifts because the radiation levels were so high. The roof liquidators are said to have been exposed to the highest levels of radiation. The actual death toll related to this accident is impossible to determine for many reasons. People who lived in the surrounding cities were evacuated which makes it difficult to monitor their health over time. It is also unknown exactly what levels of radiation people were exposed to, making it difficult to link disease to the accident. The increase in the number of cases of cancer is thought by many to be a direct result of exposure to radioactive elements. The number of birth defects has also risen in areas that were heavily contaminated with radiation and genetic mutations will continue to be passed through generations.

More than 40 different radionuclides were discharged into the atmosphere in the days following the explosion. Iodine ($^{131}$I), cesium ($^{137}$Cs), strontium ($^{90}$Sr), and plutonium ($^{239}$Pu) are considered to be among those that have had and will continue to have the most significant impact to the environment. In the week following the accident, nearly every area that was tested for contamination had greatly increased levels of iodine. $^{131}$I has been directly linked to thyroid disease and is believed to be responsible for the large increase in the number of thyroid cancer, especially in children. Gomel, which is about 100 miles to the north of Chernobyl, recorded the greatest increase in thyroid cancer. In 1990, the number of cases of thyroid cancer in children and adolescents had risen to thirty times the reported cases prior to the accident. It is estimated by the World Health Organization that one-third of Gomel’s children who were under the age of four during the time of the explosion will develop thyroid cancer at some point in their life; an estimate of approximately 50,000 cases.
A common, highly unstable, and dangerous fragment combination is cesium-137 and strontium-90. The intermediate half-life of $^{90}\text{Sr}$ is approximately 30 years, which means that particles will linger for about 100 years. $^{90}\text{Sr}$ is thought to be extremely harmful because its properties resemble those of calcium. Once the radioactive element is absorbed by the bones, it can damage the bone marrow cells or possibly cause bone cancer (leukemia), or cancer of the tissue surrounding the bone$^3$.

$^{137}\text{Cs}$ also has an intermediate half-life of about 30 years and is considered to have long term effects on the environment. The radioisotope is passed through the food chain because it’s properties mimic those of potassium and are absorbed by plants, then animals, and people$^3$. $^{137}\text{Cs}$ has also been linked to the alteration of chromosomes; in most cases the body is able to repair the damage to cells. High levels of exposure can result in the body’s inability to overcome the gamma radiation, which can lead to cancer of the lymph nodes or bone marrow$^3$.

The $^{131}\text{I}$ fragment has a half-life of only 8 days and is directly linked to thyroid cancer. When large amounts of $^{131}\text{I}$ were released into the environment during the explosion, people were exposed to high levels of radioactive iodine. After exposure, the thyroid soaks up and retains the element which creates major health problems, especially with children who were directly exposed$^3$. Another source of radioactive iodine exposure was from drinking milk produced by cows who grazed in pastures that were contaminated with $^{131}\text{I}$ following the explosion. Thyroid nodules and cancer can result from high levels of $^{131}\text{I}$ exposure but are generally not fatal if treated properly. Many who were exposed will endure a lifetime of treatment for the effects of the radioactive iodine$^{12}$.

Beyond the physical effects from the radiation, psychological disorders resulting from the accident continue to affect many. Hundreds of thousands of citizens were relocated following the accident which led to an overall lack of economic and personal stability. Many wonder what the future will hold; will loved ones become ill as a result of the accident? More than 20 years later, mental health continues to be one of the most astounding effects on the population$^{12}$.

In an excerpt from ‘Voices from Chernobyl’ a woman tells her tragic story about the two weeks following the explosion. Her husband had been assigned to clean up the roof of Reactor 4 and suffered from acute radiation poisoning. As she stayed with him in a radiation treatment hospital, she describes his body as one big wound. She tells of his horrible condition during the last 2 days of his life “Pieces of his lung, of his liver, were coming out of his mouth. He was choking on his internal organs$^{13}$.” His body was so badly deteriorated and swollen that they had to cut his suit and wrap it around his body when preparing him for burial. To ensure that his body did not further contaminate the soil after he was buried, he was wrapped in a plastic bag and placed in a wood coffin. The
wooden coffin was wrapped in plastic, placed in a zinc casket, sealed, and then buried under cement tiles\textsuperscript{13}.

After reading countless articles and watching many videos on the Chernobyl disaster, I am left wondering why the magnitude of the incident continues to be minimized. On one hand I can't help but wonder how the government could justify sending thousands of uninformed laborers into a highly contaminated area to clean up chunks of graphite and other radioactive rubble. On the other hand it appears that they had no choice but to clean up the mess with the only resources they had available. There was really no way to prepare their community for the disastrous nuclear explosion.

The nuclear explosion in Chernobyl was a tragic accident that affected millions in one way or another. Many people have suffered as a result of the combination of RBMK design flaws and disregard for safety guidelines. From this disaster came a new understanding of how to effectively design a power plant, how to monitor its safety, and train plant operators. Global concerns have forced government agencies to work together to provide the safest methods to produce nuclear energy.

The Chernobyl accident led to a greater global awareness of nuclear power; this situation was addressed by engineers from all over the world. From this incident, government agencies have learned a valuable lesson and have implemented very strict guidelines for nuclear power plants.

Since the Chernobyl accident, all of Russia’s RBMK’s have been modified. After reading about the improvements, among the most important seem to be that the emergency response systems are no longer able to be bypassed\textsuperscript{8}. Overall it appears that great measures have been taken to avoid this type of accident in the future.

The U.S. had a similar incident in 1979 on Three Mile Island but on a much smaller scale. The estimated exposure, per person, to the minimal radiation released from the core meltdown was less than one-sixth of that received during an x-ray. Although no one was killed or reported harmed in this accident, it led to public concerns regarding the safety of nuclear power plants\textsuperscript{14}. The U.S. Nuclear Regulatory Commission takes nuclear safety very seriously and has made many changes to ensure the safety of nuclear power plants and the surrounding communities. Changes in plant design, improved operator training and surveillance, regular safety drills, and public reports of operator performance are all changes that have been made in order to improve safety and avoid accidents\textsuperscript{14}.

I am confident that nuclear power plants in the United States are safe because they must follow strict regulations and are routinely monitored by The Institute of Nuclear Power Operations. Detailed analysis of plant operations by the NRC is ongoing and plants across the United States are closely monitored. The NRC and the INPO also work
internationally with other government agencies to gain knowledge about current nuclear power advancements that are made\textsuperscript{14}.

Nuclear power plants have a promising future because they are efficient at providing a great deal of power. However, as technology advances, the methods for producing power for our growing population will also advance. In my opinion, nuclear power plants will continue to provide the majority of our nation's power because our current alternatives are often not as efficient and are very costly to research, build, and maintain. Wind, solar, and even wave generated energy are all options that could potentially produce enough power in the future to supplement the power we currently produce from nuclear power plants.
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Saccharin: Society and chemical substitutes

Andrea Schneider

April 23, 2010
Abstract:

Today's modern science has given us many food substitutes and supplements that have been criticized for their potentially harmful side effects in lab studies, but have not been shown to be true in human studies. With that, embracing modern scientific findings and products can hold the key to reducing obesity around the world and providing the next generation of people with a healthier lifestyle and healthier alternatives to common everyday products.

Introduction:

According to the American Heart Association 70.9 million Americans were diagnosed as being overweight and 74.1 million as being obese in 2009\(^1\). Reasons for obesity include an intake of too many calories, but not a high enough expenditure, having a sedentary lifestyle, and types of food that are eaten\(^2\). To prevent this health problem many have turned to diet supplements, exercise, food substitutes and food additives. One example is Saccharin also known as Sweet N Low. Saccharin was accidentally discovered by Constantine Fahlberg\(^3\) in 1879 while he was eating dinner. Earlier that day while he was in his lab he spilled material on his hand and while he was eating he noticed a sweet taste and traced it back to the chemicals in his lab\(^3\). Sugar companies at this time succeeded in obtaining bans on saccharin because it was reducing their revenues, but a shortage of sugar during World War I led to the reintroduction of saccharin as a sweetening agent in food. Another sugar shortage during World War II saw a new boom in saccharin production. This time, the compound's popularity continued after the war ended\(^4\). Sweet N Low was invented by Benjamin Eisenstadt using saccharin, dextrose and cream of tartar. Since then Sweet' N Low has become one of the most popular substitutes for sugar because it is 300 times sweeter than sugar\(^5\), it is inexpensive and has no calories\(^6\). Saccharin is the basis for many low-calorie and sugar-free products around the world. It is used in table top sweeteners, baked goods, jams, chewing gum, canned fruit, candy, dessert toppings and salad dressings. Although this modern food substitute has been proven to reduce caloric intake and add taste to many of our food choices, some critics have suggested it has long-lasting and potentially deadly side effects.
Background:

Saccharin or benzoic sulfimide, chemical formula C₇H₅NO₃S, contains an aromatic benzene ring with two of its carbons being part of a five-member heterocyclic ring. The molecular weight of saccharin is 183.19 g/mol and has a melting point of 228°C. Saccharin makes a good baking ingredient because it has a high resistance to heat. Saccharin is an acidic sulfonamide. Saccharin is not very soluble in water, and so it is most commonly used in the form of its sodium or calcium salt. The reason why it tastes sweet is still unclear, but its shape must be correct to fit into specific receptors in the taste buds. Evidence for this comes from the fact that if the shape is modified slightly, say by changing the H on the nitrogen to a methyl, the new molecule no longer tastes sweet. The hydrogen connected to the nitrogen is the sweet tasting part of the molecule. When a substitution reaction is performed in the number two or three position of the benzene ring with electron withdrawing nitro groups a bitter tasting product is produced, but when an electron donating group is used a sweet taste results.
Area (AH+) has hydrogen’s available to hydrogen bond to oxygen that is part of the sulfur group. Area (B-) has partially negative oxygen available to hydrogen bond to the partially positive hydrogen of the amine group. Area (X) is more or less perpendicular to the other two areas interacts through hydrophobic or non-polar properties to the non-polar the benzene on the saccharin molecule

The five sided ring in the structure is flat, which is unusual because it is normally puckered. Saccharin is absorbed rapidly in animals and men and exists in acidic media predominantly in the unionized form; pKa of 2.2. Saccharin can be produced in various ways. Originally Remsen & Fahlberg's started with toluene which is then treated with sulfur dioxide and ammonia to obtain saccharin, but the yield from this starting point are small. In 1950, an improved synthesis was developed at the Maumee Chemical Company of Toledo, Ohio. In this synthesis, anthranilic acid successively reacts with nitrous acid, sulfur dioxide and chlorine, and then ammonia to yield saccharin. Another route begins with o-chlorotoluene. Sulfonamides are absorbed well from the gut and eliminated in the urine without undergoing detectable metabolism. Saccharin appears in the urine of humans within a half hour of dosing and completely eliminated unchanged in 16-18 hours when administered orally and some 90% being excreted in the urine within 24 hours.

The interesting thing about anything in today’s world is that everything and everything is subjected to criticism and scrutiny. Regardless of the truth behind some of the allegations that are brought forth, today’s multi-media society can be long-lasting to great products. It seems very suspicious that everything has some sort of an issue and is linked to Cancer or obesity or
any number of health issues. My parents ate certain types of foods, their parents ate certain types of food and drank certain types of beverages and are still here today. Are there side effects or issues with food and beverage in this world, sure, but are they as serious as they are made out to be sometimes? I am not sure that they are. Tim Tebow, one of the most celebrated collegiate athletes of all time was scrutinized for having a long delivery and was considered a potential 4th round draft pick. Is that because the guy was not a first round talent or did not have first round credentials? No, it was because some pundit, some general manager, someone somewhere starting saying his delivery was too long and would not work in the National Football League. That could have potentially cost him millions of dollars. Tim Tebow ended up being drafted in the first round and will end up making good money, but the unfounded criticism spread like wildfire and could have pushed a first round talent into the 3rd or the 4th round. This is very similar to the Sweet N Low dilemma. Many of the statements about Sweet N Low causing Cancer are unfounded. It does cause serious side effects in lab rats, but has yet to show any significant issues in human beings and yet many people think that the product is a cancer causing supplement and refuse to use it.

Sweet N Low can give an individual a lot of the benefits of lower calories, while still providing the sweetening that many food need in order to taste “authentic” or old fashion. Sugar can be turned to fat within the body and is shown to do so in many scientific studies and yet some critics would argue that natural sugar is better because it only causes fat, where Sweet N Low could possibly cause cancer, but this has never been shown to be a fact in the scientific world, at least not in humans. I am of the belief that our society has become way too critical of everything. I think that we sometimes bypass the benefits of the scientific breakthroughs because someone is looking to break a big story or stir up the hornets’ nest. This has been a hot topic for several years now and has caused the rise of Truvia and other products that are considered more “natural” or healthy. How do we know that something within those products is not going to cause health problems down the road, 15 or 20 years from now? We really do not know yet and yet those products are not as scrutinized as of yet. It just does not make a lot of sense to me to be so critical of everything.

We, as a nation, a society or the world can look at anything and find fault in it. In fact, now celebrities are being blamed for creating image issues for teens and young adults and fashion designers are causing women and men to try and obtain unrealistic goals. People tend to not to want to take simple responsibility for their actions and for their thoughts and ultimate decisions. This can be the same for products such as Sweet N Low. It has the feel of a product that is out to get you. Let’s look at some of the new health insurance laws. We are going to be forced into having all health facts on every menu in the country and this is supposed to tell people that McDonalds is bad for them or that the Cookie Desert at a restaurant is high in calories. I mean, is that really necessary? The argument that people did not know that cigarettes were bad for them or that a Big Mac is unhealthy is pretty interesting to me. I think we all know these things and do not need to have everything we do or every product that is made scrutinized
as such. We have the right to make whatever decisions we want and if each person could focus on simply making good sound decisions based on real facts and knowledge and not a hunch or an accusation, I think some of the rumors on products like Sweet N Low would cease to exist because the gossip would no longer be a hot topic. The mass will always flock to a good argument or a good issue of decision.

I do however welcome the idea of people challenging any new product to the marketplace. That is how the bad products get eliminated from the picture. I simply would prefer the allegations that so easily become common perception be based in scientific fact before becoming so mainstream. The fact that the Sweet N Low product ingredients caused cancer in lab rats is absolutely concerning, but the fact that we as a country simply accuse based on some facts and not all the facts is an alarming trend and can cause significant financial damage to people and products. Many of the restaurants that I visit do not even carry Sweet N Low anymore. What I find comical is when a place like Carl’s Jr. does not carry Sweet N Low because of the unfounded accusations that have been brought forth on the product, when most items on their menu are so unhealthy for people that it really is not funny. It is an oxymoron and we as a society participate in these types of activities constantly.

A prime example is that Saccharin is in the process of being exonerated by the federal government as a potential Carcinogen, but critics still persist and still claim that it could be potentially harmful. This is the type of criticism that I am referencing. How can we have already damaged the name of a product over the past 20 years by claiming that it is a carcinogen and then continue in those accusations and comments after our Federal Government comes in and states the exact opposite? It is good gossip or hot topics. It is unfounded and really pretty slanderous. We as a nation of intelligent people tend to listen to multi-media way too much and take what is said in articles and chat rooms too seriously. We are a nation of impatient individuals and never wait for all the facts to surface before we make final judgments.

We see this type of public guilty verdicts all the time. We saw it with Ben Roethlisberger and we see it with many celebrities and many influential people. We really do not know what Ben did or did not do or what the woman did or did not do, but we know that he is guilty. At least, that is what the media would have us believe. I have to be honest, I fell subject to this type of thought process and then I think about it further and realize that I really do not have all the facts and would not like it much if I was being judged constantly by others based in incomplete information or false accusations and I think that most people would feel the same, so why do we do it to Sweet N Low or Alcohol or Marijuana or any other thing that has a stigma based on incomplete or incorrect information, I will never fully comprehend.

Saccharin has been given a fairly bad name, mostly unjustly, but in the end I believe that the health benefits from sweetened food with fewer calories will be seen. Let’s face the facts and realize that we will all be better off by taking in fewer calories while being able to eat the things we all love. It is hard to believe that people will be able to give up all the things they love. Given
that, it is better to enjoy the items that we all love with fewer calories and less fat. In today’s society we are all focused on becoming healthier and living longer. I think that in order to gain the things we desire we needed the help of modern medicine and modern scientific engineering to continue living within the caloric intakes we need to be at, while enjoying a little of the things we all need in order to enjoy our meals. As with anything, moderation is the key to the success of these products and food substitutes. If we abuse the modern marvels, we are bound to have some sort of health side effect or health issue. We need to educate ourselves properly about the benefits and the side effects or negative health effects of food substitutes and then use those products accordingly.

One of my favorite topics is modern medicines and sports medicine. My father-in-law has been participating in a program at Athletes Performance here in Arizona. At Athletes Performance, they take all the nutritional and training guess work out of the equation and give their patrons what they need to know. They do testing and monitor caloric intakes, caloric expenditures and proper nutrition and training in order to get people in the very best condition for whatever their goals are. I think that is so very interesting to think that athletes get that kind of nutritional and training advice and education. That is the direction that our society is taking us and I feel that we should embrace all the best alternatives and scientific breakthroughs that are beneficial to all mankind. If that be Saccharin or Truvia or any other alternative, we as a nation should embrace those alternatives and use them within reason. We cannot overdose on the product or use products that are known to be harmful. With that being said, we should guard against people that are set in their ambition to attack products and create questions, where questions are really not relevant.

In the next few decades we will have much greater knowledge on food choices, food substitutes, supplementation, training and exercise and human needs. At that time, we will be able to look back on the products that were questioned and determine what those products did for society and how they either set scientific advancement backward or how it helped to bring the scientific advancements of modern science and medicine. All the testing that Saccharin has endured and criticism and question marks will not go to a lost cause, as that testing may lead to a breakthrough discovery or an advancement in society and its understanding of all nutrition and human needs. It is my hope that we will all see that Saccharin was falsely accused and that we can greatly benefit from the use of these products and substitutes as opposed to using higher fat content products of pure sugar. As with anything, it will be the moderation of those products that will help us all to benefit from the perks that these products bring to scientific advancement. Just because a product or substitute is good for use in small doses does not mean that we should use it with everything. This is similar to the benefit that wine can bring to someone’s heart. It has been shown through scientific testing that a glass of red wine can help heart function. I have been around a lot of people who take this finding and apply it to daily wine drinking in excess of a glass and claim that it is good for them. Anything that is over used is not good and can cause toxicity in the body. This is what we need to be careful of.
Conclusion:

Society has a lot of input on whether a product will flourish or diminish. Many substitutes in today's market are being labeled as unhealthy due to minimal scientific evidence. Research has shown that saccharin, one of these substitutes, has harmful effects on rats, but poses no real threat to humans. However, today's media has taken the little evidence to criticize saccharin and blow it out of proportion to make people fearful to use it. Until there is more evidence that it does cause harmful side effects, such as cancer, we should hold back on making such crucial accusations and judgments.
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Prepared For:

Dr. Mancini

Research Paper: Nitroglycerin

Prepared by Mehul Shah

Date Submitted: 04/23/2010
Nitroglycerin

Abstract:

Traditionally when a patient feels chest pain, he/she would have reached for a phone to call paramedics but in today’s world the patient reaches for a tiny white pill instead. This research paper will focus mainly on the effects nitroglycerin has on angina. It will also discuss the pharmacokinetics, mechanism and chemical equation of nitroglycerin. The common dosages and the strengths in which it is provided will also be discussed in the paper. The paper will be summarized by discussing the solution which this drug provides for other serious diseases and author’s opinion about the future of the drug and the direction in which it is heading.

Introduction & Background:

Nitroglycerin is a generic drug which is held at most local pharmacies today. It was originally synthesized by Ascanio Sobrero and later used by Alfred Nobel to discover dynamite. The side-effects of the drug however were not always well known, matter of fact the discovery of the drug’s effects was accidental as the physicians were trying to find cause for heart problems for mine workers. The workers would come to work on Monday complaining about headaches and will go home on Fridays with great health. Some of them were also experiencing heart problems over the weekend and all the sudden started feeling better when they got back to work on Monday. Back in 1860s when the physicians were trying to solve the mystery of heart related problems at a dynamite company they may have discovered the enzyme that is behind dilation of blood vessels. In 1879, the use of sublingual nitroglycerin was discovered which is still used up to this day for angina, chest pain due to lack of oxygen. Nitroglycerin today is available in various forms and strengths. It is today used in order to control hypertension, prevent premature births, osteoporosis, and most importantly congestive heart failure. The drug was approved by FDA in 1938. It is unclear if the production of nitroglycerin was already in use before that. For example, the FDA recently, in 2006, asked two companies, Glenmark Generics of Mahwah, N.J., and Konec Inc. of Tucson, Arizona, to stop production of nitroglycerin because their products are not approved by FDA and could cause harm to patients. If there were companies producing this drug before the approval of nitroglycerin, potential harm could have occurred to patients that decided to take this drug which was not approved at the time. Today, Pfizer Inc. is the only company which is approved by FDA to produce nitroglycerin. There could have been various reasons why the approval of nitroglycerin was not granted to the Glenmark and Konec companies. One of them could have been due to inconsistency of dosage of the drug and another one could be quality of the drug. Since nitroglycerin is critical to one’s body it is important to produce such products with great caution in order to guarantee the safety of the patients. Nitroglycerin is an oily liquid with density of 1.6g/cm at 25°C and is capable of explosion when heated to 218°C.
Manufacturing Nitroglycerin

The IUPAC name for nitroglycerin is propane-1,2,3-triyl trinitrate. The drug is prepared by adding glycerol into the mixture of nitric acid and sulfuric acid. As observed in organic lab the mixture needs to take place under controlled temperature. In the lab this semester, students were asked to run various reactions under iced bath in order to control the rising temperature of the mixture. The same needs to take place when mixing glycerol with nitric acid and sulfuric acid. If the reaction is successful it will generate a yellow colored liquid on top of the mixture which will then need to be poured into a container containing water carefully. In this case the nitroglycerin will be found at the bottom of mixture. The manufacturing factories of nitroglycerin are usually at isolated places where they cause little to no harm to the public surrounding them. The structure of nitroglycerin looks as shown below.
Mechanism of Nitroglycerin:

Once nitroglycerin is taken, it is then able to produce Nitric Oxide (NO) in vascular smooth muscle. NO acts as an intermediate compound and activates the enzyme called guanylate cyclase, which then leads to stimulation synthesis of cyclic guanosine 3',5'-monophosphate. This messenger is then able to activate a series of protein kinase-dependent phosphorylations in the smooth muscle cells, eventually resulting in the dephosphorylation of the myosin light chain of the smooth muscle fiber and the release of calcium ions. The contractile of the smooth muscle is normally dictated by phosphorylated myosin light chain. Therefore, the nitrate is able to induce dephosphorylation of the myosin light chain is able to initiate the cell to release the calcium, which indeed relaxes the smooth muscle cells. In the simpler terms, Nitroglycerin is like a catalyst for the heart. Normally the heart’s job is to pump blood, which is coming in from veins, into arteries against the pressure. As mentioned in the first paragraph, during angina, the heart’s blood flow is interrupted. What nitroglycerin does is that it dilates the veins from which blood is coming from and allows the oxygenated blood to flow where it is needed the most. The drug also lowers the left ventricular systolic wall tension, which lowers the pressure to the arteries and amount of work the heart is doing, which also reduces the further long-term damage to the heart.
Pharmacokinetics:

Nitroglycerin is available to patients in several different routes. Some of the most common routes are oral route (sublingually most common), intravenous route, and topical route. However, there are other ways of taking this medication such as, Extended Release Tablets, Ointment, spray and Patches. This is really critical due to the purpose of the drug which is to prevent further damage to the heart in case of heart-attack. The quickest way of observing the drug is by using it sublingually. Due to the tissue being present under the tongue, sublingual form of nitroglycerin has extremely short half-life of between 1-3 minutes. Another way of taking this drug is by the form of tablet which is also available. Intravenous Route, also known as IV, seems like the most useful way of giving this medication to patients with throat problems or cancer. This allows the hospitals to place an IV on and give the patients the medication needed to prevent heart damage. Last but not least nitroglycerin can also be applied to skin as an ointment.

<table>
<thead>
<tr>
<th>Type of Nitroglycerin</th>
<th>Preparation</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translingual</td>
<td>2-4 minutes</td>
<td>30-60 minutes</td>
</tr>
<tr>
<td>Extended-release capsule</td>
<td>20-45 minutes</td>
<td>8-12 hours</td>
</tr>
<tr>
<td>Formulation</td>
<td>Time to Maximum Effect</td>
<td>Duration of Effect</td>
</tr>
<tr>
<td>------------------</td>
<td>------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Sublingual</td>
<td>1-3 minutes</td>
<td>30 minutes</td>
</tr>
<tr>
<td>Ointment</td>
<td>20-60 minutes</td>
<td>4-8 hours</td>
</tr>
<tr>
<td>Transdermal</td>
<td>40-60 minutes</td>
<td>18-24 hours</td>
</tr>
<tr>
<td>Extended-release</td>
<td>2-3 minutes</td>
<td>5 hours</td>
</tr>
</tbody>
</table>

Patches strengths available in market:
- 0.2mg, 0.4mg, 0.1mg, 0.6mg, and 0.8mg

Capsule Strengths available in market:
- 2.5mg, 6.5mg, 9.0mg

Tablet Strengths available in market:
- 2.0mg and 3.0mg

Sublingual Tablets available:
- 0.3mg, 0.4mg, and 0.6mg

Source: Google Image
Nitroglycerin and Diseases:

Nitroglycerin is used for various diseases. One of them is treatment of angina. As discussed before there are various ways to get nitroglycerin in a human body. Since the effects of the drug throughout the page was mainly focused on angina, in this section the main focus of the drug is put on how patients are asked to take nitroglycerin and actions they are asked to take upon the effect of the drug for angina. When focusing on sublingual route, the patient is asked to take one tablet by mouth onset of angina. The patients that use nitroglycerin frequently for chest pains are asked to repeat the dose up to three times every fifteen minutes in order to control the chest pain. However, physicians today do advise new users to call 911 immediately after the first dose if the pain worsens or the effect of the drug is minimal to none. The drug can also be used to control hypertension during anesthesia. The surgeons can use nitroglycerin during severe conditions such as high pulmonary hypertension, postoperative hypertension, unstable angina, and severe hypertension. The duration of the drug via IV is not long therefore, the drug is given at a set rate every minute. The common dose via IV is 5mcg per minute every 3-5 minutes. A study was done to inquire the effects of nitroglycerin on treatment of pain caused by hemorrhoids and fissures. The ointment form of nitroglycerin showed to relax the internal muscle and improved the flow of blood to anal tissues which could lead to the healing or eliminate the pain caused by hemorrhoids and fissures. However, the FDA did not approve the use of nitroglycerin for such diseases. The drug has also been recently acknowledged to help with bone thinning, which often leads to osteoporosis; the drug is known to keep the body from reabsorbing bones and delaying the thinning of the bone. The drug has also been in headlines as the newest solution to prevent premature births. The study suggests the use of nitroglycerin during pregnancy may be able to prevent cerebral palsy. About two to three children over the age of three out of one thousand have cerebral palsy, which cannot be detected before the age of three.
Maximum Dose Limits

There are various dosages available for nitroglycerin in many different forms. However standards are set in order to protect the patient when it comes to the limit of the dosage per patient. The dose limits are divided in three different criteria as they vary by patients’ ages. However, there is no such limit for adult and elderly users due to the variation of treatments being offered to patients with critical heart conditions. However for children, there is the maximum dose of 5 mcg/kg/min.

Conclusion:

Nitroglycerin has been around for very long time and as discussed the actual impact of the drug was not recognized until over a century ago. The drug is commonly known for its effect on angina, however as stated in this case study it is not just limited to angina it has significant impact on other diseases which the science world is just beginning to explore. The price of nitroglycerin is fair; selling at the local Fry’s pharmacy for $8.99 for twenty tablets. As the recent research shows, in the future we can expect to see further uses of this drug as it is extremely effective in terms of relaxing smooth muscles and relieving pain up to certain extent. While the prices of health care are continuously rising, nitroglycerin acts as a critical drug to many heart patients as they try to avoid damaging their hearts further. It currently also serves a life saver in terms of immediate solution to a critical heart situation. It is to be concluded that nitroglycerin will lower the overall health care costs of the governments since most heart patients, usually seniors, will not be reaching for their phones but would rather be reaching for their pills in order to stay out of uncomfortable hospitals and away from expensive bills.
Cited References


4. Ignarro L J. After 130 Years, the molecular mechanism of action of nitroglycerin is revealed. [editorial] Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of California [serial on the Internet]. 2002 June 11 [cited 2010 Apr. 21];(132271799):2. Available from: http://www.pnas.org/content/99/12/7816.full


8. Science news. Dynamite discovery on nitroglycerin - Biomedicine - research indicates


A. Nitric Oxide is a small, diffusible, and transient molecule produced in mammals from the amino acid arginine by three nitric oxide synthase (NOS) enzymes.

B. Intravenous Route: A path by which drugs and fluid are brought into the body, commonly known as IV.

C. Osteoporosis is thinning of the bone or loss of the bone over long period of time, which normally occurs in women during or after menopause.
The Inauspicious Mind
Learning To Overcome the Complexity of Schizophrenia

Prepared for
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Organic Chemistry 236

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March 8, 2010
Abstract

Schizophrenia can be a debilitating disease that can be a burden to not only an individual but family and friends as well. The curious disorder that is schizophrenia has been a mystery to doctors and psychologists since the origin of the disorder. The key to solving this mystery is researching how to best attack the problem. However, in order to do this the problem must be understood. This paper details fine points of the disorder and how new research is leading toward more permanent results through psychopharmacology.

Introduction

Schizophrenia is best described as “a disturbance that lasts for at least six months and includes at least one month of active-phase symptoms” (1). In lemons terms, a schizophrenic is living in an alternate universe, their mind, while dealing with the same everyday life issues that all people do. Getting through the day can be quite the challenge for a lot of people without the added pressures and stress of separating fiction from reality. Many have heard of schizophrenia but what does the average person really know about the mental disorder? Some simply think that schizophrenics are crazy and belong in a mental institute. While others think they are dangerous and should not be allowed out in the world with the rest of society, fearing that at any moment they could have a “mental episode.” The reality is people tend to fear what they can’t understand. The trouble is how can anyone understand something as intricate as schizophrenia? The quick answer is they honestly can’t. However, after dispelling the myths and realizing how life is for schizophrenics, society can learn that there isn’t much to fear after all.

Much has been done to allow schizophrenics to get back their lives and live among society. Within a rather short time, those studying about this very atypical disease have discovered many new ways to help people cope with schizophrenia. There have actually even been discussions of a cure being available by 2013 (2). At this time schizophrenics must depend on the advancements in the pharmaceutical world to overcome the difficulties their mind bestows upon them.

History of the Illness

Historically, schizophrenia is a relatively new disease that has only been known as a mental disorder for a little more than a century. Arnold Pick, a professor of psychiatry, first discovered it in 1891. He referred to it as “dementia praecox” which is a Latin term for premature dementia. His works and studies of the disease did not achieve all that much; however, they did intrigue German psychiatrist Emil Kraepelin on his path to unlocking a lot of what we know today (3).

In earlier centuries, certain South American cultures would see a schizophrenic as being blessed or as if they possessed the powers to be visited by the gods. In these situations these people were anointed and lived lives of power. In other cultures they
were said to be possessed by devils, and therefore shunned from society, if not killed. In most western societies, the inability and ignorance to understand what the “confused” were going through led to banishment into asylums, and they were left to rot. Those lucky enough to not be locked up in asylums were forced to stay in their homes and ignored by society (1).

Kraepelin was able to help displace these impractical and rather immoral acts of humanity as he helped define and determine what is now known as schizophrenia. According to Kraepelin, “it is referred to as a chronic, deteriorating psychotic disorder characterized by rapid cognitive disintegration.” From the start of his work, he thought of dementia praecox as a “progressively degenerating disease” in which no one could ever recover. After 20 years or so of ongoing research, he soon realized he might have been a little premature with that prognosis. Realizing that although minor defects will always remain, there are things that can be done to improve and develop a schizophrenic’s life (1).

Who’s Affected

Schizophrenia is a disorder that is rather difficult to truly interpret by its abstract definition alone. No one really knows exactly what it is, which makes it that much harder to find cures and treatments for those who suffer. What is known is that schizophrenia is a mental illness that affects one in every 100, more than any other mental disorder (2). Twenty percent of the world’s population will develop a mental illness at some point in their life. The disease most often strikes in the teenage years to the early adulthood (16-30), but has been found in children as early as five (1). It is very rare that a person develops symptoms any later than forty, and some aspects will last the individual a lifetime (3).

Schizophrenia has not been known to develop in any one sex, ethnicity, or race than the other. As far as researchers can tell, anyone is susceptible to the disease at any time in the earlier phases of life. A lot of the researchers have begun to study genetics to see if there is any correlation. According to the DSM-IV, first degree biological relatives with schizophrenia are ten times more likely than the general population to be diagnosed. If a grandparent, aunt, uncle or any other second degree relative has schizophrenia, the risk factor is increased slightly to 3%. If both parents are schizophrenic, then the occurrence will increase to 40%. When being compared amongst twins, identical twins, where one has it, the other is 40% likely to develop whereas fraternal twins are only 10-15% as likely. Researchers have concluded that although there is some proof that genetics plays a role, there is not yet enough for a conclusive determination of a cause. It is important to know that children do not inherit the actual disorder, just become more vulnerable and therefore cannot be ruled a cause (1).

Types of Schizophrenia

There are five subtypes of schizophrenia that have been identified by psychiatrists: paranoid type, disorganized type, catatonic type, undifferentiated type, and residual type. The first and most well-known form is the paranoid schizophrenic; the key for this type is
the presence of delusions and auditory hallucinations. These delusions may be limitless and varied, but mainly are organized in a current and reoccurring theme. A person with paranoid schizophrenia is more apt to anger, anxiety, and argues frequently. The second form is the disorganized Schizophrenic; the essential component for this type is disorganized speech and behavior. The individual will also exhibit long stands of flat or inappropriate emotional displays, while at other times displays moments of goofiness or laughter during discussions about a serious topic or something completely unrelated. They also have problems with everyday activities such as dressing, showering, or preparing a meal. The person may have hallucinations; however, they are very rare and not persistent. They may tend to show off odd facial expressions as a little child would and thought processes may become very difficult. The third form is the catatonic schizophrenic; the main focus for this type is by a psychomotor disturbance. The catatonic schizophrenic has uncontrolable physical movements of their body. Stupor or rigid postures are good examples of this. There is also evidence of echolalia, the parrot-like and senseless repetition of a word or phrase that they just heard, and echopraxia, the repetition of body movement. The fourth form is the undifferentiated schizophrenia; this type is defined by the medical version of schizophrenia but doesn’t fit in any of the previous three subtypes. There is still a lot to be learned about this form. The final form is the residual schizophrenia; in this final form, the person has experienced some sort of schizophrenic episode, but currently shows no significant signs. There still exists evidence of schizophrenic behavior such as a flatness emotion and expression. The person may also have strange beliefs or behavior and attribute speech deficiencies (1,3).

**Categorizing Symptoms**

Psychiatrists and researchers have developed a system they use to compare symptoms of a schizophrenic. They have coined the usage of positive and negative to better understand the range of schizophrenic experiences. When discussing positive and negative symptoms, it is important to suspend the typical definitions of the terms. When looking at positive and negative, think of it not as good and bad, but in the terms of positive, as to symptoms that are progressively worsening, and negative as to do with less serious issues. One of the more common positive symptoms includes ‘grandiosity’ where a person believes that they are a descendant of someone great like Albert Einstein or even that they will become Einstein. Other symptoms include the idea that they can read minds or even control others’ minds. Often times they will hear voices in their heads, sometimes nice and sometimes overly critical. A positive natured schizophrenic may be seen wearing five or six coats in the middle of a hot summer day, or wearing a dress on top of another dress. Also they can develop a form of turrets where they can be seen screaming or swearing at random times. On the other side of the spectrum, negative type schizophrenics have much more mellow forms like alogia, going long periods of time with very little to no speech. Many times they just become completely flat and almost lifeless, showing no emotion for days. Avolition is the major sign of negative symptoms and occurs when a person begins to show long term inability to initiate and continue goal-oriented activities (1).
Life with Schizophrenia

Living with schizophrenia is a difficult and strenuous task not only for those with the illness, but their families and caregivers as well. As discussed earlier, a schizophrenic can go through many different phases of life including many different peaks and valleys along the emotional scale. Many suffer from severe depression, which makes the high suicide rate more understandable. For them the idea of never being able to tell what is real or fiction, never waking up from that dream that chases you, feels like it’s the only way out. The whole situation just brings chaos into the house. Parents experience many emotions often blaming themselves when there is nothing they could have done to prevent the situation. Other members of the family may take the ashamed role and hide the disease for fear of ridicule by the public. Other issues arise such as denial, guilt, fear, and grief. Exhaustion sets in and plays a huge role in families. Working so hard with their sick child leads them to ignore their own health by a loss of sleep or appetite. Some become angry and bitter and think “what did I do to deserve this” or “why my family.” Siblings may think of it as an act to get attention and feel resentment towards their sibling. Often times it becomes rather burdensome on the schizophrenic to live amongst society. They become so ill; they may lose their job or have to drop out of school. It can become so bad that they become trapped in the fantasy world and forget to do simple things like brush their teeth. It becomes very expensive for the schizophrenic to get through each day. They are unable to work on a regular basis and are faced with the increasingly high rate of medical bills (1, 3).

Treatment

Searching for treatment to help out the schizophrenic community has turned out to be a very difficult task. As alluded to before, not that much is known about the disease, so finding a cure for an unknown becomes difficult. Instead, research has leaned toward treating the disease and focusing on helping the schizophrenic live as a normal, functioning part of society. Over the years many different types of treatments have been tested; some have been mildly successful while others have proven to work over time. In the earlier days, a popular type of treatment was electro-shock treatment; shock waves would be sent through the brain with the idea that neurons in the brain would be reset. Although proven successful in a few cases, it has a high rate of negative side effects like increased depression and memory loss. Lobotomy is another form of medical procedure that has been used in severe cases, but once again the harmful side effects have brought this procedure to extinction. The more popular forms of treatment are those of therapy, psychopharmacology, and behavior modification. These forms of treatment, however popular, are extremely expensive for all those involved. The rising cost for medication and psychiatry can also have a strong affect on the patient themselves, with all the added stress of bills piling up. The National Institute for mental health estimates that the total cost of schizophrenia is between 30 to 65 billion dollars (2,1).

In fact psychologists have studied and determined that many forms of therapy can be successful. In most cases using more than one form of therapy will increase the odds.
The most popular form is a one-on-one session with a psychiatrist; this allows the patient to share what is going on inside their mind and decrease stress. Another more popular setting is the family session; the patient shares what is going on, their feelings as well as gets the family involved. The psychiatrist can provide good advice for the family on how they can help at home as well as help ease their own stress. Other ways include group settings, similar to those of addiction, where a psychologist will sit with a group of schizophrenics and they can share stories. It is important that they remain on a very strict and tight schedule with these sessions in order to prevent relapses (1).

Behavior modification is the least used of the three most popular forms of treatment, but is quite effective. The purpose of this treatment is to retrain the mind for more positive production. Ivan Pavlov, a Russian physiologist, who accidentally developed the basic principles of classical conditioning, first introduced it in the early twentieth century. The idea was to change a reflex to that of a stimulus other than the original. This was proven in an experiment where dogs began salivating at times when they weren’t supposed to. Pavlov changed the dogs in a way so that he could introduce a stimulus (in this case a bell) and make the dogs respond to the stimulus in the same way they would have to the other stimulus. The same principles have been applied to schizophrenics where they are trained based on a certain stimulus to help them through the day. Basically, get their focus back on the tasks at hand.

Psychopharmacology is the use of drugs to control or relieve the symptoms of psychological disorders. It is the most widely used treatment for schizophrenics. Psychopharmacologists must stay current with all the up to date studies due to the complexities of the drugs. They need to have a firm grasp on pharmacokinetics and pharmacodynamics, which are essentially how the drugs react in the body. The rather extensive study has to be handled delicately keeping an eye on how drugs react with other drugs, how long it reacts in the body, and how it affects genes. For this reason a psychopharmacologists must pass a test every five years in order to continue in their field (4). Recent studies have lead to the findings of the particular neurotransmitters in the brain that affect schizophrenics. It is this that causes psychopharmacologists to develop medications to attack the particular dopamine receptors. The most commonly prescribed drugs are Stelazine, Haldol Oral, Trilafon Oral, and Clozaril Oral (5).

Stelazine is a drug made up of trifluoperazine hydrochloride (C21H24F3N5S-2HCl). Trifluoperazine is also known as, 10-[3-(4-methylpiperazin-1-yl)propyl]-2-trifluoromethylphenothiazine, according the IUPAC.
It's used by schizophrenics usually in a concentrate form (7). The drug is designed to work by attacking the $D_1$ and $D_2$ dopamine receptors in the brain. The actions of these chemicals change and allow the schizophrenic to be free of anxiety. However, it does not treat for dementia and hallucinations. Unfortunately, trifluoperazine does not react well with many other medications and especially alcohol. Stelazine has many side effects such as hives, seizures, joint pain, slowing of the heart rate, uncontrollable twitching, pale-bruised-rashing of the skin and nausea to name a few. It is important not to be exposed to high volumes of sunlight or any ultraviolet radiation because of the reaction that takes place with the skin (8).

**Figure 2**

Sagittal section of human brain showing the dopaminergic pathways involved in the actions of antipsychotic drugs (see text for further information).

Haldol Oral is another drug that is used for the treatment of schizophrenic disorders. Haldol is primarily made up of haloperidol ($C_{21}H_{23}ClFNO_2$) or by

![Chemical Structure of Haloperidol](image)

**Figure 3**

IUPAC nomenclature as 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidyl]-1-(4-fluorophenyl)-butan-1-one. Unlike stelazine its primary use is for diminishing dementia and hallucinations. It also can help eliminate disorganized thinking like turrets mentioned
earlier. Like stelazine it is primarily taken in concentrate liquid form orally. The benefit to haldol is it can be taken with many more pharmaceuticals than stelazine with low risk of counter reactions. The side effects are relatively common for drugs of this nature and they include uncontrollable movements, dizziness, drowsiness, low blood pressure and other minor set-backs. However, haldol does react negatively to alcohol, and cigarette smoking may decrease its effectiveness (11).

Trilafon is primarily made up of perphenazine (C$_{21}$H$_{26}$ClN$_{3}$OS) and is similar in affect to stelazine. The IUPAC is also known as 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl) propyl]piperazin-1-yl]ethanol.

![Figure 4](image_url)

Trilafon can cause severe drowsiness and should especially be avoided with alcohol or any other barbiturates. All major side effects are the same as stelazine. Perphenazine does not react well with other drugs prescribed or over the counter and should be carefully monitored if drugs are consumed (13).

Clozaril is primarily prescribed to younger adults usually between the ages of 13 and 17. It is also known as clozapine (C$_{18}$H$_{19}$ClN$_{4}$) or according to IUPAC 8-chloro-11-(4-methylpiperazin-1-yl)-5H-dibenzo[b,e][1,4]diazepine.

![Figure 5](image_url)

Clozaril has a very high dependency risk and should be monitored. Clozaril is usually prescribed in patients who don’t respond to other schizophrenic antipsychotics because it has a high risk of agranulocytosis. Agranulocytosis is a serious life threatening event. Researchers still don’t know quite how this mechanism works which causes even more of a concern when combined with other drugs; it increases the risk of bone marrow deficiencies. Clozaril works by being metabolized through the liver and received by the enzymes CYP3A4, CPY1A2, CPY2D6. If other drugs are consumed through these enzymes, the end result can be an overdose which significantly will increase the side effects. These side effects can include such events as seizures, cardiac arrest, hepatitis,
ulcers, amnesia, hypothermia and vertigo just to list a few of many. For these reasons clozaril should only be used in severely ill patients with professional guidance (15).

Pharmacologists admit that it is a trial and error guess on which medication they prescribe. Several other medication including thorazine, abilify, geodon, seroquel, and navane are also often prescribed (5). In most cases, they will start a patient off with one medication that is closest to the symptoms they can determine; they will monitor the success and more often than not will have to try another form. This process is repeated until they find one that best suits each individual patient. These medications do not come without their consequences; it is crucial the patient refrain from any sort of drug use and/or drinking. Most narcotics or barbiturates mixed with the medication can worsen the hallucinations and create very intense delusions. Even cold medicine or any over the counter drug should never be taken without permission from their doctor. The unfortunate part is the schizophrenic will also start feeling better and like most people, quit taking their medication too early. Eighty percent of all patients who stop taking their medication will relapse within two years (3). However, only forty percent of those who continue to stay on their medication will relapse at all (1). In addition to medication, those who took high amounts of vitamins showed a better prognosis than those who did not (1,3).

Conclusion

Overall, schizophrenia is a disturbing and frustrating illness but due to its growing numbers, there is hope. People, unlike once before, can rejoin society as a strong working force. There is no need for people to fear them like they have throughout time. Families can go back to having a healthy life without worry and very little stress. Whether the schizophrenic has catatonic or paranoid forms, treatments have been practiced and solutions have been set in place. These treatments have diminished the occurrences of such positive symptoms as turrets and negative symptoms as algolia and depression. In my opinion using a mixture of treatments and pharmacology can make the person healthier than they ever thought possible. Making sure to take their medication and showing up to therapy sessions will lead to a full recovery. As of now, twenty-five percent of all schizophrenics will successfully recover, and another fifty percent will recover partially, meaning enough to prevent hospitalization (1,2). The development and understanding of how these drugs act with each other and in the mind and body will only increase with time. The research into the brain and how the dopamine receptors work will only increase these already positive signs. As the development of pharmacology is advanced and new techniques are developed, more hope lye ahead.
References

Narcolepsy

Keerat Singh
4/23/10
Abstract

Narcolepsy is a serious chronic neurological sleep disorder that causes excessive sleepiness and daytime sleep attacks. Like any other disorder, there are many symptoms of narcolepsy. There are not many options for treatment, except some therapy, and taking prescription drugs can control sleep attacks. Not much is known about the causes of narcolepsy, but research has shown that it is related to the functionality of the brain and it is also related to the genes the person possesses.

Introduction

Imagine falling asleep behind the wheel or falling asleep while having a conversation with someone. People with narcolepsy go through these dangerous and awkward situations almost every day. Patients with narcolepsy can put their lives and sometimes, other people’s lives in danger. The sleep attacks that patients with narcolepsy suffer can occur anytime during the day with no warning. Narcolepsy causes frustration and depression in a person’s life, which not only affects the patient, but it also affects the people who are close to the patient. Usually the sleep attacks last from a few seconds to a few minutes, and very rarely they can last up to an hour. Other than the sleep attacks, patients with narcolepsy suffer from cataplexy, vivid hallucinations, and brief paralysis at the beginning or the end of sleep. Many people believe that patients with narcolepsy spend a greater portion of their time asleep during a 24-hour period than do normal sleepers, but narcolepsy causes patients to be awake frequently while sleeping at night. The frequent awakenings at night balance out with the time when patients are asleep during the day, meaning that patients with narcolepsy get the same amount of sleep as people without narcolepsy. Scientists believe that narcolepsy is caused by an irregular process in the brain that affects the Rapid Eye Movement (REM) sleep. A normal sleep cycle is 100-110 minutes long, beginning with NREM sleep, which proceeds into the REM sleep after 80-100 minutes. People who have narcolepsy enter the REM sleep cycle frequently and narcolepsy patients can enter the REM sleep cycle in just a few minutes. However, narcolepsy is not rare; it is one of the most unrecognized disorders in the world, and is expected to affect 1 out of 2000 Americans. Narcolepsy appears all over the world, in all races and it affects males and females equally.
Symptoms and Biological Applications

Other than the frequent sleep attacks, patients with narcolepsy also suffer from cataplexy, sleep paralysis and hallucinations. Cataplexy is a muscular weakness that can range from weak attacks, like dropping of the jaw and weakness in the knees, to major attacks like a total collapse of the body and slurred speech. Cataplectic attacks can occur anytime during the awake period, but in many cases, they can be misunderstood for a seizure disorder. Most of the time, cataplectic attacks are triggered by sudden and strong emotions such as fear, anger, and stress, but mostly these attacks are caused by humor. Scientists believe that humor plays a major role in the cataplectic attacks because when an average person sees a humorous image, the activity of the frontal lobe and the hypothalamus is increased. In contrast to normal brain activity, when a person with narcolepsy sees a humorous image, the activation of those brain areas is greatly increased and the increased activity occurs very quickly. If the brain is observed in more detail, when a person finds something humorous, the amygdala and hypothalamus become activated. The activation of the hypothalamus is particularly interesting because it plays a role in sleep regulation, which depends on proper levels of hypocretin in the brain. Hypocretin is a neuropeptide hormone that promotes wakefulness. Patients with narcolepsy have improper levels of hypocretin, causing impaired sleep cycles.

Hypocretin

FIGURE 2

Sleep paralysis is common in narcolepsy patients. Sleep paralysis is a condition in which a person is conscious, but unable to move the body because of fear, and it may occur only once or several times during the night. Even though it was believed that sleep paralysis was related to some kind of evil presence, research shows that in most cases, the body is not moving smoothly through the stages of sleep. Rarely, the evil presence may seem to attack the patients in their sleep, exerting some pressure on their chests and strangling them. When a person sleeps, the brain sends signals to inhibit any muscle contraction and sometimes a person becomes conscious before the brain can send muscle contraction signals, resulting in paralysis of muscles. Sleep paralysis is related to the mechanism of the brainstem and the vestibular and oculomotor neurons, which prevent body movements during REM sleep. These neurons are necessary in order to prevent any body movement while dreaming. Sleep paralysis occurs when the brain is awakened from a REM state to a fully awake state, but with the bodily paralysis still occurring. The consciousness in the paralysis state causes a person to be fully aware of
his/her surroundings, but unable to move. This state of sleep paralysis occurs for no more than 2 minutes before the person goes back to REM sleep, or is fully awake. Research has shown that hallucinations also accompany sleep paralysis. Scientists have suggested that sleep paralysis may be linked to the postsynaptic inhibition of motor neurons in the pons region of the brain. Low levels of melatonin are involved in sleep paralysis, as the levels may stop the depolarization currents in the nerves, which prevents the stimulation of muscles. Various studies have suggested that most people will experience sleep paralysis at least once or twice in their lifetime.

Another common symptom in narcolepsy patients is hallucinations, which are false perceptions of objects or events. People that suffer from hallucinations can see, hear, smell, and even taste something that is not really there. This misinterpretation is usually caused by the changes in the brain that occur because of the disease. Hallucinations can cause patients to see or hear things that are imaginary. For example, a person can see his/her face on a wall, or see insects crawling on his/her hands. Auditory and visual hallucinations are related to different parts of the human brain. Auditory hallucinations are related to the temporal lobe lesions, although the frontal and parietal are also involved. The visual hallucinations are related to the occipital lobe of the brain. The olfactory hallucination is related to all of the lobes, mainly temporal, but the frontal and the parietal lobes are also related to it. Though certain types of hallucinations are related to particular lobes of the brain, these hallucinations can also be related to adjacent or distant lobes.

![Diagram of brain lobes]  
*FIGURE 3*

**Treatment**

There are few options when it comes to treating narcolepsy. A combination of therapy, counseling and medication can be used to control the sleep attacks and other narcolepsy symptoms. Narcolepsy patients can suffer from depression, which causes them to withdraw from others. One of the best ways to treat this disorder is to get therapy from a psychologist who can help the patient cope with the effects of narcolepsy. People who cannot afford to go to psychologists can carry out some natural therapy themselves. For example, patients can practice getting a sufficient amount of
sleep every night and taking short naps throughout the day. The necessity of obtaining proper amount of sleep suggests that patients with narcolepsy should stay away from alcohol and shift work. Short naps can make patients feel refreshed, so it has been suggested that people with narcolepsy schedule naps during the day so they can combat any excessive sleep they might experience during the day. Usually, these short naps should be taken after lunch and once in the evening. A proper diet and exercise are also recommended for narcolepsy patients, meaning that they should stay away from alcohol and caffeine as much as possible. Eating or drinking right before going to bed is strongly discouraged because the food or drink might contain caffeine, which might make it hard for the patient to fall asleep. Quality exercise is also suggested to patients because it plays a major part in getting a good night’s sleep. Exercising helps to stimulate the brain, and it can also act as a stress reliever. Patients should stick to a sleep cycle, whether it is going to bed at a certain time, or waking up in the morning at a certain time. Six to eight hours of sleep is suggested to the patients with narcolepsy.

Another way to control the symptoms of narcolepsy is by taking prescribed medications like Ritalin and Modafinil. Ritalin is a central nervous system stimulant that affects the brain and nerves that are connected to hyperactivity and impulse control. Ritalin should be taken at least 30 minutes before a meal, and it can be taken in the form of a capsule or a tablet. The tablet should be swallowed as a whole, and it should not be crushed or chewed. The tablet form of Ritalin is meant to release the medicine slowly in the body, and if it is broken the medicine might release too much of the methylphenidate. The capsule form of the Ritalin, however, can be taken by opening the capsule. It is believed that Ritalin works on the neurotransmitter dopamine, and it resembles the stimulants of cocaine. Some of the side effects of Ritalin include: loss of appetite, vomiting, headaches and changes in heart rate. People with Attention Deficit Hyperactivity Disorder (ADHD) also take Ritalin. ADHD patients have low levels of dopamine, which helps them control their behavior. Ritalin increases the level of dopamine in the brain, which helps the patients with ADHD to focus, filter out any distractions, and make decisions based on reason rather than emotions.

**Ritalin molecular structure**

![Ritalin molecular structure](image-url)
Another effective pharmaceutical drug that can be taken by patients suffering from narcolepsy is Modafinil. This drug is a wakefulness-promoting agent and it is a racemic compound. Some of the agents that act as wakefulness agents are amphetamine and methylphenidate\textsuperscript{12}. Modafinil works by changing the amounts of certain natural substances in the area of the brain that controls sleep and wakefulness. The medication is usually taken once a day with or without food, and if the medication is being used to help treat narcolepsy, it is taken in the morning\textsuperscript{12}. The doses should be taken at the same time every day and the time should only be changed after talking to a doctor\textsuperscript{12}. As mentioned earlier, there are no medications that can cure narcolepsy totally, and Modafinil is another example of a drug that can help decrease sleepiness. Some of the side effects of Modafinil include: dizziness, headaches, dry mouth, heartburn and constipation\textsuperscript{12}. If a regular dose is missed, the patient should wait until the next time the medication is supposed to be taken\textsuperscript{12}. If Modafinil is taken very late during the workday, it might be hard to go to sleep\textsuperscript{12}. The mechanism of action for this medication is unknown, but tests have been done on animals, which show that the drug acts on the areas of the brain involved in sleep/wake periods\textsuperscript{13}. The animal study shows that Modafinil increases activity in animals without causing agitation\textsuperscript{13}. Modafinil is rapidly absorbed after consumption, and it reaches its peak in about 2 hours\textsuperscript{13}.

structure of modafinil

![Structure of Modafinil](image)

FIGURE 5

Support groups

People who are diagnosed with narcolepsy face many challenges in their daily lives, which may cause serious depression or even fatal suicide thoughts. Studies that have been done on narcolepsy, suggest that people with this disorder should join some kind of a support group. Joining support groups helps the patients cope with their problems and the support groups in providing a positive view at life. One of the major reasons for joining a support group is the shared experience it can provide. Studies show that when patients meet others who have suffered with narcolepsy, they are encouraged\textsuperscript{15}. Patients feel better about themselves when they know that they are not the only ones in the world who suffer from this disorder. Another big reason to join a support group is
that it serves as a source of information\textsuperscript{15}. Patients who suffer from narcolepsy are able to expand their knowledge about their disorder by joining a support group because they are dealing with people who are going through the same disorder\textsuperscript{15}. Finally, joining a support group can help make new friends, and by making new friends, patients have somebody they can talk to about narcolepsy.

\textbf{Conclusion}

Narcolepsy is a serious neurological disorder that affects the lives of many people around the world. It is a rare, but ignored disorder as it affects 1 out of every 2000 people in the United States. Narcolepsy is one of the most dangerous disorders in the world because sleep attacks can occur any place at anytime. Besides the sleep attacks, patients with narcolepsy also suffer from cataplexy, sleep paralysis and hallucinations. Narcolepsy is not a curable disorder, but the symptoms can be controlled by a combination of therapy and drugs. The safest way to control the symptoms is by taking some natural steps. Some examples of natural healing include: taking short naps throughout the day, avoiding caffeine and alcohol and exercising daily. If narcolepsy patients try to take medication for their symptoms, they have to make sure that they take precautions on the consumption of the drug. Narcolepsy is also related with the stages of sleep a person goes through at night. An average person takes about 80-100 minutes before entering the REM sleep, but a person with narcolepsy can enter the REM in just a few minutes. Studies have shown that joining a support group can help patients deal with their disorder. Some of the advantages of joining a support group are: Shared experience, social interaction and finally, support groups can serve as sources of information about narcolepsy. Considering the seriousness of this disorder, proper actions should be taken to find more ways to cure Narcolepsy.
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Rare Bleeding Disorders: Hemophilia
Ian Strauss
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Bleeding disorders are rare and there are many of them published in medical journals, and amongst the most popular is Hemophilia. Hemophilia is one of the rarest bleeding disorders known to man. Scientists have studied its genetics for thousands of years and figured out how to diagnose the disease and even more specifically who it affects. Signs and symptoms of the disease could be a deadly warning. Even a treatment has been found, with a few tips on how to cope with living with the disease.

Its human nature for people to fall down and cut themselves, and when they do, they bleed. The body’s natural instinct is to direct attention to the wounded area and begin healing it. Usually within a few minutes the cut has stopped bleeding and all is back to normal. This is because the body’s wound healing mechanism is partly in the blood. It’s called the blood clotting system. Inside the blood are special proteins known as clotting factors. These proteins work with platelets to help the blood clot. Platelets are a huge component of the blood system. Platelets are small blood cell fragments that form in the bone marrow—a sponge-like tissue in the bones.

(18) When identifying clotting factors Roman numerals are used. These clotting factors are special because they are what allow an injured blood vessel to heal when an injury has occurred. Coagulation is the last step in the clotting process. A net is created over the torn blood vessel and the bleeding is stopped. Clotting is the process by which your blood changes from a liquid to a solid state in order to stop bleeding.

However, there are rare bleeding disorders that disrupt this clotting process and amongst the most common is Hemophilia. Hemophilia is a rare bleeding disorder in which your blood doesn’t clot normally. (18) The condition known as hemophilia has been recognized for thousands of years. About 18,000 people in the U.S. have hemophilia. Each year, about 400 babies are born with the disorder. (13) Hemophilia is a disorder that causes coagulation time to be greatly lengthened and prolonged. The reason for this is because there is a deficiency in the clotting factors, particularly factors VIII and IX that cause the blood in a patient with hemophilia to not clot properly. Having hemophilia might cause a person to bleed for longer periods of time after an extensive injury, especially a trauma. Internal bleeding, particularly from the knees, ankles
and elbows is highly common because of the joints. Often the bleeding from a hemophilia patient can damage the internal organs and be life threatening.

There are two types of hemophilia but both are equally as dangerous and require the same amount of care and precaution. Hemophilia A is the first type. It is the most common type of hemophilia. It is also commonly referred to as Factor VII deficiency or classic hemophilia. People that have the disease are six times more likely to have this disease than the second type. The second type of hemophilia is Hemophilia B. Hemophilia B, also has alternate names. It can be referred to as Factor IX deficiency or Christmas disease. It was originally named “Christmas disease” for the first person diagnosed with the disorder back in 1952. (9) People with an unusual form of hemophilia B, known as hemophilia B Leyden, experience episodes of excessive bleeding in childhood, but have few bleeding problems after puberty. (7) Hemophilia is categorized into three different factor levels. The first level of Hemophilia is mild. The second level is moderate, and the final level is severe. For both Hemophilia A and B when a person has mild hemophilia they usually have factor levels that range between 6% and 49%. For these people hemophilia is usually only a problem after a serious injury has occurred, resulting in a trauma or if that person has just had surgery. In many cases, mild hemophilia is not discovered until an injury, surgery or tooth extraction results in unusual bleeding. The first episode may not occur until adulthood. (9) Roughly 15% of people with hemophilia have moderate hemophilia. Now a patient with hemophilia will not necessarily bleed harder or faster than someone who does not have the disease but they will tend to bleed much longer. When the bleeding does not stop for a long period of time in a hemophilia patient it is known as a “bleeding episode”. A patient with moderate hemophilia will almost always tend to have bleeding episodes after an injury. They may also experience occasional bleeding episodes without obvious cause. These are called “spontaneous bleeding episodes”. (9) If a patient has severe hemophilia which about 60% of the hemophilia population does, they will experience bleeding episodes after an injury and very frequent spontaneous bleeding episodes; these will often leak into the joints and muscles.

Hemophilia is inherited in an X-linked recessive pattern. (5) The disease is considered to be X-linked due to the fact that the gene mutation that causes it is located on the X chromosome. The X chromosome is one of two sex chromosomes. Females have two X chromosomes and males only have one X chromosome. If one gene is mutated or altered a female has the second X chromosome as a backup, however the male does not have that luxury and therefore it only takes one mutated or altered gene in the X chromosome for the male to get the disease. So due to the fact that both hemophilia A and hemophilia B are X-linked disorders, they are seen primarily in men. Hemophilia can be inherited by boys only via the mother since the mother gives the X chromosome. 80% of the time hemophilia is given to the male because the mother has passed on a mutated X chromosome. However the other 20% of the time hemophilia can be inherited even if the mother does not pass on a mutated X chromosome. This occurs when the gene mutates during the production of the egg or during early development of the embryo. Even though
females do inherit the mutated Factor gene, it is extremely rare that they ever develop hemophilia. It is more common that they pass it on to their own children. Only about 10% percent of women that carry the mutated Factor gene actually experience bleeding problems. There are only four possible outcomes for the baby of a female who possesses a mutated X chromosome. These four possibilities are repeated for each and every pregnancy:
1. A girl who is not a carrier
2. A girl who is a carrier
3. A boy without hemophilia
4. A boy with hemophilia

One in 10,000 males is born with deficiency or dysfunction of the factor VIII molecule. (16) That’s the same as Hemophilia A. Factor IX deficiency or dysfunction occurs in 1 in 100,000 male births. (16) That’s the same as Hemophilia B.

When diagnosing hemophilia several tests must be performed to narrow down the exact cause of the problem. Von Willebrand,
Dysfibrinogenemia,
Hypofibrinogenemia,
Thrombocytopenia
and Bernard-Soulier
Syndrome are all very closely related diseases to hemophilia and must be ruled out. Among the special tests are the coagulation tests. Coagulation factor tests may be ordered when someone is experiencing excessive bleeding or bruising or has a prolonged “Prothrombin Time (PT)” or “Partial Thromboplastin Time (PTT)” (2). These tests are used as screening tools to determine whether one has a coagulation problem. (2) Factor testing is often done when an inherited factor deficiency is suspected, especially when bleeding episodes have been occurring. The tests are even more necessary when the bleeding episodes begin early in life. The doctor will often take a family history and medical background to reveal if the patient or anyone in the family has any history of frequent bleeding episodes or bruising that might seem abnormal. Properly diagnosing will require a physical exam and several blood tests. Blood tests are particularly important in these circumstances because they help to:

1. Determine how long it takes the patient’s blood to clot
2. Whether the patient’s blood has low levels of any of the clotting Factors
3. Whether one of the clotting Factors is completely missing from the patient’s blood

The blood tests will determine whether the patient has hemophilia, what type, and the severity. The most important test and the last test is the Factor activity test. This test determines how well a Factor performs relative to that of an unaffected person. (2) For someone who is considered normal they would have a fully functional Factor that has 100% activity and is fully active. A non functional Factor has 0% of normal activity. The amount of activity determines the severity of the disorder. (2) For people with hemophilia A they have low Factor VIII activity, while people with hemophilia B have low Factor B activity. Genetic testing is also available for the Factor VIII gene and the Factor IX gene. Genetic testing of the Factor VIII gene finds a disease-causing mutation in up to 98 percent of individuals who have hemophilia A. Genetic testing of the Factor IX gene finds disease-causing mutations in more than 99 percent of individuals who have hemophilia B. (5) Usually when genetic testing is done the purpose is to find out if a pregnant female that has a known genetic mutation on one of her X chromosomes is going to give birth to a child with hemophilia. Patients who are diagnosed with severe hemophilia generally are diagnosed shortly after birth because of an extensive “cephalhematoma” (16) or a profuse amount of bleeding at circumcision. Hemophilia is diagnosed at an average age of 9 months, and almost always by age 2. If your child has heavy bleeding that can’t be stopped after an injury, call 911 or your local emergency number or go to an emergency room. (10) It is not always the case that hemophilia is found in young babies. Young children with moderate hemophilia may not start to bleed until they begin walking or crawling. Individuals with mild hemophilia may not even be diagnosed until they are adolescents or even young adults.

There are key signs and symptoms of hemophilia. Some symptoms are noticeable to the naked eye and others are not. The most common signs are excessive bleeding and easy bruising. Depending on the severity of the disease the bleeding may be more subtle or more rapid. Children who have mild hemophilia may not have symptoms unless they have excessive bleeding from a dental procedure, an accident, or surgery. (18) Bleeding can be extremely profuse after circumcision for young infant males with severe hemophilia. Bleeding can occur on the surface of the skin known as external bleeding but it can also occur in the body’s inner organs, which is known as internal bleeding. Internal bleeding is often much harder to recognize. There are key signs of external bleeding they include:

1. Bleeding in the mouth from a cut or bite or from cutting or losing a tooth
2. Nosebleeds for no obvious reason
3. Heavy bleeding from a minor cut
4. Bleeding from a cut that resumes after stopping for a short time

There are also key signs to recognize internal bleeding and they include:

1. Blood in the urine (from bleeding in the kidneys or bladder)
2. Blood in the stool (from bleeding in the intestines or stomach).

Excessive bleeding in the joints is another sign of hemophilia. Though this is difficult to recognize it can be very painful. This is another common form of internal bleeding. When blood
leaks into the knees, elbows, and other joints of the body it sits and over time the joints become swollen and enflamed. The joints become extremely tight and hot to the touch for someone with hemophilia. The bones are partly held together by a joint capsule. The joint capsule has a lining called synovium with many capillaries (small blood vessels). It makes a slippery, oily fluid that helps the joint move easily. (1) When the capillaries in the synovium are injured they begin to bleed. There is usually no clear reason why the bleeding starts, especially in people with severe hemophilia. If the joint isn’t treated, permanent joint damage can occur. Internal bleeding in the brain is a very serious complication of hemophilia that can happen after a simple bump on the head or a more serious injury. (18) The signs and symptoms include:

1. Long-lasting, painful headaches or neck pain or stiffness
2. Repeated vomiting
3. Sleepiness or changes in behavior
4. Sudden weakness or clumsiness of the arms or legs or problems walking
5. Double vision
6. Convulsions or seizures

The most feared complications and signs of hemophilia are oropharyngeal (throat) and central nervous system bleeding. Intubation is often required to maintain an open airway when the throat becomes filled with blood. A tube is placed down the throat so that an airway can be opened and maintained.

Living with hemophilia stretches out beyond just you. If your child has it there are a number of things to prepare for. Expect emotional, financial and social ties as you adjust to the situation of living with a child that has hemophilia. Take the time to go to classes and learn Young children need to be taught that the disease isn’t their fault. Young children will need to have a closer eye kept on them. They have a tendency to get into trouble. Toddlers need to wear helmets, knee pads and arm pads when riding tricycles and bicycles. Safety belts and straps should be worn at all times to protect toddlers from falls. Remove or pad furniture with sharp objects. Finally always check outdoor play equipment for hazards that could cause bleeding. Physical activity helps keep muscles flexible, strengthens joints, and helps maintain a healthy weight. When the child is an infant it is always safest to put bumper pads on his crib. Children and adults who have hemophilia should get physical activity regularly, but they may have limits on what they can do safely. (18) Mild hemophilia is at a low enough degree that person with the disease can play contact sports however when someone has severe hemophilia contact sports should always be avoided. There is too much risk for bleeding. Some safe physical activities that are recommended are swimming, golf, biking with a helmet, and walking. When it comes to the psychological aspects of the disease and living with it psychologists have found that, a toddler may not tell his or her parents about an injury that resulted from doing something that wasn't allowed (i.e., riding a bike without a helmet, jumping on the furniture, running in the house, etc. Most kids, though, will discover that seeking prompt treatment is better than waiting until pain and swelling become unbearable. (12) When a child has hemophilia he or she is generally able to tell when there has been a bleed. They will most often describe it as bubbly or tingly in their joint. As a parent it will feel warm to the touch. That is a good indicator. Encouraging children to tell the parent when they feel a bleed is the right thing to do. Never tell the child to hide his or her bleeding episodes. That could only lead to serious damage. Doctors also recommend splinting an affected joint for a short period of time and then applying ice to decrease inflammation, promote clotting, and
relieve pain. (12) When a child has a bleed it must be treated quickly and promptly. Prolonged bleeding will cause joint disorders. Extreme advances have been made in the treatment of hemophilia and most patients can now live long full productive lives.

To treat hemophilia the missing or deficient Factor VIII for hemophilia A must be artificially replaced and to treat hemophilia B the missing or deficient Factor IX must be artificially replaced into the body so that the clotting system can form to complete itself. However in a hemophilia patient there are certain drugs that can and can not be taken. It is recommended that when a bleed occurs that is not to serious more commonly in a child, that acetaminophen such as Tylenol be given as a pain reliever. Some medicines however will cause an increased chance in bleeding and therefore a patient with hemophilia should not take aspirin and other medicines that contain salicylates. Ibuprofen, naproxen, and some other nonsteroidal anti-inflammatory medicines should be kept away from.

To help treat hemophilia plasma has a major role in helping. Plasma products enriched in Factor VIII have revolutionized the care of hemophilia patients, reduced the degree of orthopedic deformity and permitted virtually any form of elective emergency surgery. (16) The most current treatment is Factor concentrates that are virally inactivated or recombinant. The idea to helping treat hemophilia is to artificially replace the Factor that is missing. So by using rapid Factor replacement is the key to effective therapy. Patients with severe hemophilia often infuse low doses of prophylactic Factor on a regular basis and boost their dose or the frequency of infusion when they sense internal bleeding, sustain trauma, or undergo dental procedures. (1) The way it works is patients are slowly administered Factor VII for hemophilia A or Factor IX for
hemophilia B through an IV drip or are given an injection into the vein. Clotting factor concentrates can be made from human blood that has been treated to prevent the spread of diseases, such as hepatitis. With the current methods of screening and treating donated blood, the risk of getting an infectious disease from human clotting factors is very small. (18) Replacement therapy may be received on a regular basis to prevent bleeding for some patients. This is known as “prophylactic” or “preventive” therapy. Other patients only need the therapy on a much broader basis, when bleeding occurs. The use of the treatment on an as needed basis is known as “demand therapy”. A majority of patients with hemophilia require factor infusions. Despite hemophilia being a treatable disease there are still many complications that can arise from the disease. A person living with the disease is often at risk for serious illness, or catching another potential deadly disease. Most hemophilia patients have had multiple episodes of hepatitis, and a majority have elevated hepatocellular enzyme levels and abnormalities on liver biopsy. (16) Certain patients have been known to have been completely cured of the disease after having a liver transplant. Hemophilia patients are at high risk for AIDS because the clotting Factor infusions that they receive are retained from other human blood products. They can tend to present with a full range of AIDS related symptoms. Although up to 50% of multiply transfused hemophiliacs are HIV-positive and many have clinical AIDS, the advances in Factor VIII concentrate production should prevent future HIV infection. (16)

After completely and thoroughly researching this topic it has really put me in a position where I have to take a step back and just thank my lucky stars that I am in the position that I am in today. These people that I have read and learned about have to live a life that I don’t feel I could imagine waking up to each day. Not playing sports as a kid, wearing pads everywhere you go and having that thought in the back of your mind, wondering if your constantly going to have a limb spontaneously start bleeding and swelling internally is to much for me to handle. In my opinion hemophilia is one of the worst imaginable diseases known to man. It’s amazing the medical advances that scientists have come up with but in all honesty I don’t think we’ve come far enough. The people that have to live with this disease will never truly know how it feels to be normal because they are always in constant worry. I’ve spent the past two years working in an Emergency Room and I’ve never seen a patient present with hemophilia. The disease is very rare there is no question but the fact of the matter is, it’s still out there and it doesn’t really have a cure. Unfortunately as of right now there isn’t much we can do about it. There appear to be some great medical breakthroughs on the horizon and for right now we just have to watch. I feel it’s truly important to teach your kids that have this disease or that have the potential of giving off that genetically altered chromosome, that hemophilia is a possibility. It’s rare but it’s no joke.
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Macromolecules of Life

Sina Velayati

April 21, 2010
Abstract

All the living organisms are composed of one or more cells. These cells carry out all of the biological processes which are vital for living organisms to stay alive. To understand these complex processes, it is essential to study and know the four macromolecules that cells are made of. This paper tries to introduce and explain the properties and functions of carbohydrates, nucleic acids, proteins, and lipids, the four macromolecules of life.

Introduction

Billions of years ago, the universe was formed by a big explosion which is known as the Big Bang. At the beginning of this event, the universe was very hot and small, but over time, it cooled down and more explosions happened and eventually resulted in forming hydrogen and helium. These basic elements joined together, and over billions of years, stars and planets were created.

The earth was formed about 4.5 billion years ago, when molten rocks cooled down and formed the solid outer crust. As it cooled down, the water vapor was condensed to liquid form and at the same time clouds were formed and resulted in a lot of rain. The consequence of these processes was forming of the oceans on the surface of the earth. It is believed that life began in the oceans about 3.5 billion years ago. Bacteria and Archaea were the initial forms of life on the earth which could survive the harsh conditions and toxic atmosphere that existed at that time. By the evolution of the photosynthesis processes in some types of organisms, such as cyanobacteria, the oxygen was introduced to the environment. The accumulation of oxygen in the atmosphere let the other forms of life to begin on the planet, and through the evolutionary mechanisms the diversity of life has been created.

Today, millions of species are living on the earth, including unicellular, multi cellular, prokaryotic, and eukaryotic organisms which exhibit very different life styles, but all these living organisms have one characteristic in common. They are made of cells. The cell is the basic structure of life. What are the cells made of? How do they function? To answer these questions and have a better understanding of how the very complicated processes of life occur, it is essential to know the structure and functions of four macromolecules of life, including carbohydrates, nucleic acids, proteins, and lipids. These macromolecules are the building blocks of all living organisms and are synthesized and used by them on a daily basis. In the next pages, the structure and important functions of these macromolecules will be discussed.

Carbohydrates

One of the four types of these macromolecules is carbohydrate, which is composed of carbon, hydrogen, and oxygen. The ratio of these atoms in a monosaccharide molecule follows a simple formula: \((\text{C}_n\text{H}_{2n}\text{O}_n)\). \(n\) is the number of carbon atoms in the formula. There are three different types of carbohydrates, including monosaccharides, disaccharides, and polysaccharides. Monosaccharides are known as simple sugars. The number of carbon atoms varies from three to seven carbon atoms in a simple sugar. There are three important monosaccharide molecules that play key roles in biological processes of living organisms, including glucose, fructose, and galactose. All of them are composed of six carbon atoms. Fructose and galactose are the isomers of glucose. Isomers have the same molecular formula, but they differ in the structure or
the orientation of the atoms in the space. The molecular formula of these compounds is C6H12O6. Although they have the same molecular formula, their characteristics differ from each other because of the structural differences\(^1\).

Disaccharides are another type of carbohydrates, which are composed of two monosaccharide molecules connected to each other. Sucrose is one of the disaccharides that is produced and consumed by living organisms. It is made when one molecule of glucose is connected to a molecule of fructose. Another type of disaccharides is lactose which contains one molecule of glucose connected to one molecule of galactose. When two molecules of glucose are attached to each other, they produce another type of disaccharides known as maltose\(^1\).

The third type of carbohydrate is called polysaccharides, which are polymers that contain several monosaccharide molecules, all connected to each other. Starch is a polysaccharide composed of many molecules of glucose. Other examples of polysaccharides include cellulose, chitin, and glycogen which are found in many living organisms and play many important key roles\(^1\).

One of the most important functions of carbohydrates is to provide energy to the bodies of organisms. The C-H bonds in carbohydrates store a lot of chemical energy, which can be released by chemical processes through metabolism. Glucose is the most important simple sugar which is converted by cells to provide energy to the bodies of living organisms\(^1\). "The health and functioning of every cell in the body depends on energy provided by glucose, but the brain is especially dependent on a stable and constant supply to sustain its function."\(^3\)
Plants are one type of the organisms that carry out photosynthesis on the earth. The major product of this process is sucrose which is a disaccharide, and it is available in large amounts in many fruits and vegetables. Sucrose is the most common sugar that humans consume as food.

Lactose which is another type of disaccharides can be found in milk. It contains a lot of energy that can be provided to the body when it is consumed. "Lactose digests slowly, affording an extended energy supply to the human body. In addition, the slower digestion rate of milk sugars allows the body to absorb a higher level of minerals such as calcium, magnesium, and zinc."

Polysaccharides, which are composed of many monosaccharides, provide two important functions to living organisms. Some of them play structural roles, such as chitin and cellulose, and the others function as energy storage, including starch and glycogen. Cellulose is used by plants as the cell wall because it has a very tough structure which can protect their cells. Also, it has the ability to allow water and other solutes pass it into and out of the cell. Chitin functions in the same way for other organisms. For example, cell walls of most fungi are made of chitin. Also, it can be found in the exoskeleton structure of many arthropods.

Polysaccharides, such as starch and glycogen, are the main polymers which are used by plants and animals, respectively, for storage of energy in their cells. "Polysaccharides make ideal storage molecules for energy for a number of reasons: a) they are large, this makes them insoluble in water and therefore they exert no osmotic or chemical effect on the cell; b) they fold into compact shapes; c) they are easily converted into required sugars when needed."

Nucleic acids

Another important type of macromolecules which is found in living organism’s cells is nucleic acid. All polymers are composed of smaller subunits which are called monomers. The monomers of nucleic acids are called nucleotides. These monomers are generally composed of three elements: a sugar composed of five carbons, an organic nitrogenous base, and a phosphate group. These monomers are attached to each other by a phosphodiester bond which is a bonding between the phosphate group and hydroxyl group on the five-carbon sugar. The nitrogenous bases are composed of two different types: purines and pyrimidines. Purines are composed of two rings connected to each other, including adenine and guanine. Pyrimidines are smaller molecules and consist of only one ring, including cytosine, thymine, and uracil.
There are two types of nucleic acids found in living organisms: deoxyribonucleic acid (DNA), and ribonucleic acid (RNA). DNA is a double stranded molecule which has five-carbon sugar deoxyribose in its structure. Thymine can be found only in DNA structure. RNA is another type of nucleic acids which has five-carbon sugar ribose in its structure, and is a single stranded molecule. Nitrogenous base, uracil, is only seen in the RNA molecules. Each strand consists of five-carbon sugars and phosphate groups connected to each other as the backbone of the molecule, and nitrogenous bases protrude from this backbone structure. Two strands of the DNA molecule are bonded to each other by hydrogen bonds between nitrogenous bases. Only specific combinations of nitrogenous bases are allowed. Adenine can make bonds only with thymine or uracil, and cytosine can make bonds only with guanine. It results in a spiral shape which is called double helix.

DNA is the hereditary molecule which encodes the proteins necessary for living organisms. DNA molecules and proteins are combined together in a very condensed form which is called chromosome. In eukaryotic cells, the chromosomes have a linear shape and are located in the nucleus; on the other hand, in prokaryotic cells, the chromosomes have a circular shape. Each time a cell divides to produce another cell, DNA molecules make an identical copies of themselves by a process which is called replication, as a result, the genetic information are transferred to the new cells.

The flow of information in a cell follows a specific direction. A DNA molecule makes a RNA copy of itself, and the RNA molecule is used by ribosome to make proteins by connecting specific amino acids based on RNA information. The first step is called transcription, and the second step is known as translation. The DNA molecule encodes information for protein synthesis by using specific sequences of four nitrogenous bases. Each sequence, which is called a codon, consists of three nucleotides, and determines a specific amino acid. "DNA codes for protein synthesis by first coding for RNA. First, the DNA code is transcribed to RNA code, which is still in the "language" of nitrogenous bases, except that adenine on the DNA pairs with uracil (in place of thymine) on the RNA. The RNA code is then translated to protein code, which is a different "language." This process involves ribosomes and two kinds of RNA: mRNA and tRNA. The mRNA codes for the gene in question and is copied off the DNA, while tRNA matches a specific group of nucleotides with a specific amino acid. A "unit" of three nucleotides
on the tRNA codes for one amino acid. Each of these “units” is called an anticodon. These match up with corresponding three-nucleotide sequences on the mRNA called codons, and in this manner the amino acids are organized into the correct sequence to build a protein. The ribosome works with the mRNA and tRNA to hook the amino acids together to form a protein. 8

Mutation is an important concept associated with DNA molecules. Mutations are changes in the DNA sequences. They can occur in a single base of the DNA molecule or in a larger segment which includes several bases. Mutations can occur in different ways. For instance, if one of the parents has a mutation, it can be inherited to the offspring. Also, when a cell divides and the DNA makes a copy of itself, mistakes can be made in the replication process, which eventually can result in mutation. In addition, some environmental factors, such as ultraviolet light, can contribute to gene mutations as well. Some mutations happen at higher rates, but some of them are very rare. Those mutations that are seen in more than one percent of the population are called polymorphisms. For instance, differences in types of hair, eye color, and blood type are the results of polymorphisms. On the other hand, some of these polymorphisms can cause diseases and disorders in population, such as down syndrome, hemophilia, sickle cell anemia, and phenylketonuria 1.

Proteins

The next group of biological macromolecules that serve very important functions to the living organisms is protein. Proteins are polymers of amino acids. Each amino acid is composed of an amino group and a carboxylic group. There are twenty different amino acids found in nature, which differ in the type of R group that is bonded to the central carbon atom on the molecule. These amino acid monomers can be arranged in many different orders in a linear structure, which results in different protein molecules with different functions. Most of the amino acids are chiral compounds which can have two enantiomeric forms, but only the L enantiomers are found in proteins and recognized by living organisms. Depending on the nature of the R groups, the amino acids can exhibit very different properties and functions. For example, they can be polar or nonpolar based on the type of the R group attached to them. In addition, the shape of the protein molecule can be affected depending on the nature of the R groups. The amino acids are attached to each other by peptide bonds in long chains which are called polypeptides, and proteins are composed of one or more of these polypeptide chains 1.
As a matter of fact, function of a protein depends on its shape. In the structure of the majority of proteins, the nonpolar amino acids form the internal structure of the molecule; on the other hand, polar and charged amino acids are found on the surface of the proteins. Nonpolar amino acids are hydrophobic, and the interaction between these monomers and water, which are polar molecules, results in aggregation of them into the interior portion of the protein molecule. In contrast, charged and polar amino acids are hydrophilic; as a result, they aggregate on the surface of proteins which is in contact with water.

The final shape and structure of proteins can be explained based on a process which is composed of four levels, including primary, secondary, tertiary, and quaternary structures.

The primary structure of a protein shows the order of the amino acids which form the long linear chains of polypeptides. Any amino acids can occupy any positions in the chain which results in a great diversity of proteins.

Secondary structure contains the regions of proteins which are organized into alpha-helices or beta-shaped sheets. The hydrogen bonds are responsible for folding the proteins into these structures.

The tertiary structure of a protein determines the positions of these secondary structures in the space, which results in the overall three dimensional shape of the molecule. The interactions between the R groups on different amino acids are the forces that hold the tertiary structure of the proteins. These forces include hydrogen bonds, van der waals interactions, ionic bonds, and disulfide bonds.

Most of the proteins are composed of more than one polypeptide chains. The arrangement of these polypeptide subunits determines the quaternary structure of the proteins.

Proteins can be unfolded under environmental stresses, including PH changes and temperature shocks, by a process which is called denaturation. The folding or refolding process of a protein molecule to its final shape is facilitated by other proteins which are called chaperone proteins. These molecules are grouped to many subunits and can be found in any organisms. “Heat-shock proteins (Hsps) are molecular chaperones that are induced when organisms are exposed to high temperatures and other stresses. These stresses cause proteins to unfold and potentially aggregate, thereby creating a protein-folding crisis in the cell. Hsp chaperones help the cell cope with this crisis by binding different types of folding intermediates and interacting with them in different ways.”

Proteins are involved in many different functions in all types of cells. A few examples of protein functions include antibodies, enzymes, hormones, and transport activities. Antibodies
are proteins that help living organisms to identify and recognize antigens, and neutralize them. These antigens include viruses, microbes, bacteria, and parasites. Enzymes are proteins which help the biochemical reactions to proceed faster; without enzymes, many of the reactions that play vital roles in cells would stop or proceed at very slow rates. As a result, enzymes can be mentioned as the catalysts of biochemical reactions. "Alcohol dehydrogenase catalyzes the first step in the metabolism of ethyl alcohol, converting it to ethanol (acetaldehyde) by an enzyme-catalyzed oxidation reaction. Ethanal, or acetaldehyde, is the compound responsible for many of the unpleasant symptoms of a hangover." 

Hormones are another important type of proteins that regulate and coordinate the activities of living organism cells. "Growth hormone is one key growth signal released from the pituitary, a pea-sized gland located at the base of the brain. Lack of this hormone in children can cause them to remain shorter than average, while in its excess they may grow taller than most. Growth hormone continues its work in adults, playing an important role in repair and maintenance of different tissues in the body."

Transport proteins help with the movement of certain molecules within the body. "Hemoglobin is another example. It carries oxygen from the lungs to the tissue. Myoglobin performs a similar function in muscle tissue, taking oxygen from the hemoglobin in the blood and storing it or carrying it around until needed by the muscle cells."

Lipids

The last group of macromolecules that will be discussed includes lipids. They are composed of two components, including fatty acid and glycerol. Fatty acids consist of long chains of hydrocarbons and carboxylic groups. The other component, glycerol, is composed of three carbons with one OH group attached to each carbon. In the structure of a lipid molecule, these fatty acids are attached to the three carbons by ester linkages which are the results of dehydration reactions. The final structure is known as triglyceride. The attached fatty acids can be identical or can have different structures. When these hydrocarbon chains contain carbon-carbon double bonds, they are called unsaturated lipids; on the other hand, saturated fats only consist of carbon-carbon single bonds. Saturated lipids are usually solid at room temperature because they have higher melting points based on their structures.

![Glycerol]
As it has been mentioned, lipids have long chains of hydrocarbon in their structure. These portions of the fat molecules are nonpolar, because the carbon and hydrogen electronegativities are almost the same. As a result, the solubility of the lipids in the water decreases drastically because of the presence of these nonpolar components. In addition, due to large number of carbon-hydrogen bonds in their structure, fats are capable for storing energy. When the food intake is more than what is burned by daily activity, it will be converted to the fats and deposited at specific locations, which results in gaining weight1.

Phospholipids form a specific group of fats with one special function; they are the main component of cell membranes. Phospholipids have the same structure like the lipids, except that one of the fatty acids is replaced with a phosphate group which is attached to a charged organic portion. The phosphate group and organic molecule which is connected to it form the hydrophilic component of the molecule, but the hydrocarbon tails are nonpolar. These characteristics are essential to form the bilayer structure of the cell membrane. Due to interactions between phospholipids and water molecules, the hydrophobic tails are arranged inside the bilayer structure, and the hydrophilic phosphate heads are directed outward where they are in contact with water molecules1. "The phosphate group along with the glycerol group make the head of the phospholipid hydrophilic, whereas the fatty acid tail is hydrophobic. Thus phospholipids are amphipathic; water loving and water hating. When phospholipids are in an aqueous solution they will self assemble into micelles or bilayers, structures that exclude water molecules from the hydrophobic tails while keeping the hydrophilic head in contact with the aqueous solution.15"

The only polar molecule that can pass through the cell membrane structure is water. To make the transfer of the other polar molecules and ions possible, proteins are embedded in the cell membrane, which act as carriers and ion channels1. "The lipid bilayer is the main fabric of the membrane, and its structure creates a semi-permeable membrane. The hydrophobic core impedes the diffusion of hydrophilic structures, such as ions and polar molecules but allows hydrophobic molecules, which can dissolve in the membrane, cross it with ease. Proteins determine most of the membrane's specific functions.15"
As it has been discussed, proteins contain nonpolar and polar amino acids. The nonpolar part is attached to the nonpolar tails of the cell membrane, and the polar portion is exposed to the surface of bilayer structure which is in contact with water\textsuperscript{1}.

Conclusion

The major molecules on which life depends have been introduced and discussed in this paper. All of them are polymers of many smaller units known as monomers. Carbohydrates are the main source of food, and also, they are used for protection in the cell walls of the plants. The genetic materials, nucleic acids, are the building blocks of DNA and RNA molecules. Proteins have numerous functions for each living organism. Finally, lipids, which are found in the structure of the cell membrane, facilitate the exchange of material with surrounding environment. The properties of these building blocks, the way they interact with each other, and the reactions they undergo, only can be explained by the study of organic chemistry. In fact, biology and organic chemistry are in a very close relationship with each other, and it is essential to have a good understanding of chemistry to be able to learn biology.
Works Cited

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The True Case of Benjamin Button:
Hutchinson-Gilford Progeria Syndrome

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Organic Chemistry 236
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Abstract

Progeria is a rare disorder that affects children and is caused by mutation on the LMNA gene causing atypical nuclear shapes. Clinical manifestations are very similar to that of an aging adult. Children with this disorder have a very short life expectancy, averaging 13 years old. Pathophysiology, clinical manifestations, diagnosis, treatment options, and current research are discussed.

Background

In the 1920’s F. Scott Fitzgerald wrote a short story titled “The Curious Case of Benjamin Button”, which was inspired to produce the recent movie. The story is about a child born as an old man who ages backwards⁴. There has been some speculation that Fitzgerald used Hutchinson-Gilford progeria syndrome as the basis for the young character of Benjamin Button. This disorder was used as an inspiration for the makeup of the young Benjamin Button for the movie. Other movies have characters different forms progeria include “The Three Wishes of Billy Grier”, “Jack”, and “The Hunger” ⁵.

Hutchinson-Gilford progeria syndrome (HGPS) is a genetic disorder that affects the skin, musculoskeletal system, and vasculature⁶. This disorder is extremely rare, only 130 cases of progeria have been documented since 1886⁷; the estimated incidence of this rare disorder is one in eight million births⁸. According to Sarkar, PK and Shinton, RA⁹, the first patient with HGPS was documented by Jonathan Hutchinson and Gilford as a 3.5-year-old boy who had the “appearance of an old man.”

The name “progeria” was proposed by Gilford in 1904 and was derived from the Greek word geras, meaning old age. This disorder causes children to age prematurely, however, the child may appear normal at birth but within a year signs and symptoms start to manifest. Children with this rare disorder have a very short life expectancy of averaging 13 years with a range of 7-27 years old⁴.

Pathophysiology

Before discussing the biological pathophysiology of HGPS, the definition of aging must first be established. In general, aging is considered a developmental process that begins with birth and ends with death. As the cells age they die at an increased rate. There are several theories of aging, below is a table that list all the theories of aging⁵. The genetic-molecular theory will be used and the definition for aging for this discussion.
Table 2  Theories of aging (modified from ref 22, 27, 56)

<table>
<thead>
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<th>Type of theory</th>
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| Genetic-molecular | Codon restriction: accuracy of DNA-mRNA impaired  
|                  | Searle's theory: accuracy of mRNA-protein impaired  
|                  | Gene regulation: post-reproductive changes in gene expression  
|                  | Genetic mutation: radiation damage to DNA  
|                  | Wear and tear: with age the body wears out and dies  
|                  | Age pigments: lipofuscin deposits as a primary cause of aging  
|                  | Free radicals: lead to cell damage and thus aging  
|                  | Crucial linking: increased cross-linking of DNA leading to irreversible damage to DNA and  
|                  | senescence  
| Evolutionary     | Whole range of species-specific variations in lifespan  
| Disposable soma  | Balance between energy investment in reproduction and maintenance  
| System level     | Nervous system: control of a "biological clock" controls development through neural and  
|                  | hormonal mechanisms  
| Age changes      | Immune control: thymic gland or "immunological clock" leading to cell destruction due to  
|                  | failure to recognize self  
|                  | Changes occurring throughout the whole lifespan, often involving deterioration of an  
|                  | anatomical/physiological nature  

De novo point mutations in the lamin A or LMNA gene on chromosome 1q have been found in almost all patients with HGPS®. According to Shah, K and Kaiser, HW, "the LMNA gene encodes the nuclear A-type lamins, which are type V intermediate filament proteins that localize to the cell nucleus and form the nuclear lamina, a structure that supports the nuclear envelope. They are important in maintaining nuclear stability and organizing nuclear chromatin. The nuclear lamins may also play a role in regulating gene expression, DNA synthesis, and DNA repair."

The most common LMNA mutation found in HGPS patients involves a C→T transition at nucleotide 1824. This type of substitution activates a cryptic splice donor site at exon 11 which causes a base pair deletion and an abridged lamin A protein known as progerin. The abridge progerin prevents the normal assembly of nuclear lamins. After the translation phase of replication, the mutant progerin will go through normal farnesylation, after which step the farnesylated preprogerin protein are then integrated to the nuclear membrane. Since the mutant protein does not have an important posttranslational processing signal that is required for cleavage of the preprogerin protein, prelamin A cannot be formed from the nuclear membrane; the mutant protein can only form an insoluble cytoplasmic protein. In the absence of lamin A in the nuclear lamina, the nuclei shows atypical nuclear shapes and blebbing which may further progress to abnormal chromosome segregation and delayed mitosis in patients with HGPS1.

Autosomal dominate mutations in the LMNA gene are found to be responsible for most cases, but autosomal recessive transmission have also been confirmed in cases with affected siblings born to consanguineous carrier parents that are unaffected by this disorder1.

This disorder is rare because affected patients die before reproductive age, so in theory every case is a new mutation which means the mutation must be specifically targeted to produce the phenotype of that new mutation. The cause of how these events are producing the clinical phenotype of HGPS is not fully understood. Several theories have been developed to explain the clinical phenotype such as the deformed nuclear membrane may be more susceptible to mechanical damage leading to increased cell death, disruption of chromatin or protein binding to
the nuclear lamina causes less control in gene expression, the nuclear lamina plays a role in DNA replication and repair; fibroblasts s have shown evidence of unrepaird DNA damage supporting this theory.

As shown by Korf, there are 12 exons in the LMNA gene and normal splicing produces a normal lamin A. In most patients with HGPS a cryptic splice donor is activated and 150 bases from the messenger RNA are deleted, producing progerin.

The following figure depicts lamin A-processing defects in laminopathies.

![Diagram of lamin A processing](image)

**Figure 1** Lamin A processing defects in laminopathies. Mutation of lamin A from the precursor prelamin A requires several events: farnesylation of the carboxy terminus, cleavage of the three carboxy-terminal amino acids, carboxymethylation of the farnesylated cysteine and cleavage of the 13 terminal serine acids (red cylinder) by the endoprotease Zmpste24. In cells from Zmpste24-deicient mice, an unprocessed lamin A intermediate containing the farnesylated carboxy terminus accumulates and no mature lamin A is generated. In HGPS cells, the cleavage site for FASE1 (yellow line) is absent because of an internal deletion, and a noncleavable truncated lamin A is synthesized. The presence of these dominant negative, farnesylated intermediates alters the nuclear lamin scaffold and leads to defective recruitment of DNA repair factors (green). As a result, unrepaired damage sites (arrows) accumulate in the nucleus, causing genome instability, as observed by Lin et al.
Clinical Manifestations

The clinical manifestations of HGPS are closely associated with the progression of an aging adult. During infancy the manifestations are short stature with low body weight for height, incomplete sexual maturation, osteoporosis and pathologic fractures, feeding difficulties, delayed dentition, low-frequency conductive hearing loss, hypertension, prolonged prothrombin time, elevated platelet count, and elevated phosphorous levels.

Physical characteristics of skin and hair include sclerodermatous skin changes (indurated, shiny, inelastic skin); prominent scalp veins; loss of subcutaneous fat causing generalized lipodystrophy with loose, wrinkled skin; hyperpigmentation in sun-exposed areas; hair loss; dystrophic nails; hypertrophic scars; hypoplastic nipples. Facial features includes protruding ear with absent lobes, beaked nose, thin lips with cyanosis, prominent eyes, frontal and parietal bossing with pseudohydrocephaly, midface hypoplasia, and larger anterior fontanel. Musculoskeletal abnormalities include but are not limited to thin limbs with prominent joints, joint contractures, pyriform (pear-shaped) thorax with dystrophic clavicles, and bilateral hip dislocations. Children with HGPS show all the physical characteristics of aging but they do not typically exhibit other characteristics of aging such as Alzheimer's, neurosensory decline, cataracts, type 2 diabetes, or cancer because these disorders are caused by a mechanism and are not related to tissue regulation.

Other manifestations of this disorder, that are most often the cause of death in these patients, are cardiovascular and cerebrovascular complications. Cardiovascular complications include myocardial infarction, congestive heart failure, interstitial fibrosis, diffuse myocardial fibrosis, progressive artherosclerosis, and calcification of mitral and/or aortic valves. Cerebrovascular complications are often times a result of the cardiovascular complications and can include stroke both infarction and hemorrhagic, subdural hematoma, and seizures.

Diagnosis

There is not a definitive test that confirms the diagnosis of HGPS. Typically several tests in combination with physical manifestations are what lead to the diagnosis of HGPS. However, with the discovery of the genetic mutation that typically causes HGPS, genetic testing for the LMNA mutations may also be used as a diagnostic test in suspected cases.

Laboratory tests used to support the diagnosis of HGPS include high density lipoprotein levels which would typically be low in someone with HGPS because low levels are typically associated with atherosclerotic disease and the other. The last laboratory study that is used is hyaluronic acid exaction in the urine, this however is not considered diagnostic but it is found in many patients with HGPS.
Some imaging studies may be done on the skull, thorax, long bones, and phalanges to confirm additional diagnosis of osteopenia,acroosteolysis (bone resorption in the phalanges and distal clavicles), coxa valga, “fish mouth” vertebral bodies, avascular necrosis of the femoral head, and a brain magnetic resonance angiography my identify occlusive disease. These imaging studies do not give a definitive diagnosis for HGPS, but they help confirm the diagnosis in conjunction with physical manifestations present³. As one can see, based off of the available diagnostic test available the diagnosis of HGPS is difficult to make.

Treatment

Currently there is no effective treatment or cure for HGPS, there are several studies being conducted on treatment options such as stem cell therapy, which will be discussed in the next section, and some medications. Typically the symptoms are treated and monitored carefully to help prevent further deterioration and hopefully prolong the life span and increase the quality of living of the child.

Interventions that are commonly used include monitoring for cardiovascular and cerebrovascular disease. Drastic interventions such as coronary artery bypass surgery or an angioplasty may be needed with the progression of cardiovascular disease that is very common with this disease². Physical and/or occupational therapy to help maintain a normal lifestyle by preventing joint stiffness and dietitians may be utilized to ensure adequate nutritional intake by including high-calorie dietary supplements and utilizing a feeding tube if necessary.

There are a handful of medications that are used to help treat the symptoms of HGPS and hopefully help prolong the lifespan of the child. One commonly used medication is Aspirin (acetylsalicylic acid). Typically 81-325 mg of aspirin is prescribed to be given daily as prophylaxis to help prevent heart attacks and stroke. This aspirin works by inhibiting platelet coagulation and in turn prevents blood clots from forming. Shown to the right is the structural formula of aspirin. This molecule is in a family of chemicals known as salicylates which contain salicylic acid. Aspirin, in short, works by blocking cyclooxygenase which in turn blocks certain prostaglandins that make platelets clump or coagulate together which can block arteries in the heart or brain and decreasing the available blood supply to that organ¹⁰. There are side effects to taking aspirin that can be life threatening if not treated in a timely manner such as internal bleeding which most commonly manifests itself as a gastrointestinal bleed. Since aspirin can be caustic to the stomach it is recommended that it be taken with food to help reduce the risk of stomach irritation and often times patients may be placed on a medication such as Protonix in conjunction with aspirin therapy to help prevent stomach ulcers from forming and therefore
reducing the risk of a gastrointestinal bleed. It is important to note that aspirin has a long half-life, or remains in the body for a long time; if a patient is having surgery and/or some minor procedures it is recommended that patients stop taking aspirin typically 2 weeks before to reduce the risk of post procedure bleeding. There are other drugs currently on the market that inhibit platelet coagulation such as Plavix, but aspirin is typically the starting drug due to its low cost and general effectiveness.

According to Mayo Clinic², drugs called farnesyltransferase inhibitors (FTIs) are showing promising results in correcting cell defects that are responsible for causing HGPS. This drug is typically used to treat cancer and is still in human clinical trials currently. Farnesyltransferase inhibitors have shown a decrease in nuclear misshapen which is key is the progression of this disease. The FTI promotes the release of preprogerin from the membrane of the nucleus which in turn incorporates it correctly to the nuclear lamina (refer to Pathophysiology section). When it is incorporated correctly, the structural and functional nuclear defects are corrected¹. In one study conducted on mice it showed that early therapy (at 4 weeks of age) proved to be effective in improving body weight, prevention of adipose tissue loss, increase bone mineralization resulting in fewer fractures⁹. The results are promising, however if therapy is required to start at an early age it may not be an effective drug because HGPS can be difficult to diagnosis, especially for children under one year of age.

Pravastatin is an antihyperlipidemic agent that could be used in HGPS to help decrease the risk of a cerebrovascular accident and it is also given as prophylaxis for coronary arteriosclerosis. The last common medication that is used is zoledronic acid which inhibits bone resorption and can suppress bone turnover for long periods of time; it is often used to treat osteopenia¹.

Research

Research is currently being used to explore the benefits of utilizing stem cell research as a treatment option for HGPS. The expression of A-type lamins is developmentally regulated, however they are absent in the early embryo including early embryonic stem cells. Since they are absent in the early embryonic stem cells it has no effect on the development of the fetus and explains why the child may appear normal at birth but as the cells start to deteriorate, premature aging becomes evident in the first two years of life due to the lack of A-type lamins to support the high cell turnover that occurs with growing and aging. One study suggests that lamin A mutations likely cause premature stem cell exhaustion that depletes certain tissues and result in the premature aging of those tissues⁹. It is debatable at this point whether stem cell therapy shows to be beneficial as treatment for this disease, further research is needed to support stem cell therapy as an effective therapy or cure.
As stated previously, research is also being conducted in FTI as an effective treatment option of HGPS. FTIs are currently showing promising results in treatment of HGPS. With the results of the clinical trials it will show whether it can be an effective treatment and possibly a cure for HGPS.

**Conclusion**

In conclusion, HGPS is an extremely rare, fatal genetic disorder that affects children. Children may often appear normal in infancy but then begin to experience profound characteristics of premature aging typically by age 2. HGPS appears only affect the tissues that have a high cell turnover such as skin, hair, adipose tissue, skeletal structures, and vasculature. The children may have an appearance of an elderly individual there no deficits in their cognitive ability or neurosenory functions. Cancer, cataracts and type 2 diabetes are not associated with the pathophysiology of HGPS.

There is no cure and limited treatment options for children diagnosed with HGPS, partly due to how rare this disease is and due to limited research available. With the advancement of technology, the development of other medications may significantly improve the quality of life and life span of children affected by this disease. FTIs, which are also used to treat cancer, are showing promising results in the treatment of HGPS and will hopefully be available as a treatment option for HGPS. At this point stem cell therapy does not seem like the best treatment option, further research is needed to further investigate the role stem cells play in the development and effect of A-type lamin and progerin to find a cure or make stem cell therapy a good treatment option.
References


Finally
A set of teeth you just can't lose

Dental Implants

Zaid Zaki
April 22, 2010
Abstract:

Dental implant is an artificial titanium fixture, placed surgically into the jaw bone which can be used to replace a single tooth, to support a bridge of two or more teeth, or to provide a secure anchor for an entire set of dentures. Dental implant is a restorative technique used to restore the function, esthetic, integrity and morphology of the mouth.

History of dental implants:
Dating back over 1350 years ago, the Mayan civilization was the first to adopt the idea of endosseous implants (implants embedded into bone). Whilst excavating Mayan burial sites in Honduras in 1931 archaeologists found a fragment of mandible of Mayan origin, dating from about 600 AD. This mandible, which is considered to be that of a woman in her twenties, had three tooth-shaped pieces of shell placed into the sockets of three missing lower incisor teeth. For forty years the archaeological world considered that these shells were placed under the nose in a manner also observed in the ancient Egyptians; however, in 1970 a Brazilian dental academic, Professor Amadeo Bobbio studied the mandibular specimen and took a series of radiographs. He noted compact bone formation around two of the implants which led him to conclude that the implants were placed during life (1).

Other civilizations were looking for ways to replace missing teeth, ancient Egyptians used tooth shaped shells and ivory and The Etruscans, living in what is now modern Italy, replaced missing teeth with artificial teeth carved from the bones of oxen.

Modern teeth implant started when professor Per-Ingvar Branemark was conducting a research on the healing pattern of bone tissue, he accidently discovered that when pure titanium comes into direct contact with the living bone tissue, the two literally grow together to form a permanent biological adhesion. He named this phenomenon "osseointegration" (2).
There are different types of dental implant

- **An artificial bone substitute:**
  This type of implant involves a synthetic bone substitute being fitted on top of the bone to help rebuild the shrinking ridge and provide sturdy support for dentures. Because it is made of the same type of mineral found in natural bone, this type of implant bonds to the existing jaw bone.

- **Endosteal implants:**
  This type of implant is inserted into the jaw bone to serve as the tooth’s root. This is the most common implant with very high success rates. We will discuss this type of implants in further details.

- **Subperiosteal implants**
  This type of implant, usually an option for persons who can no longer wear conventional dentures, involves a lightweight, specially-designed, metal implant that fits directly on the existing bone.[see fig.3]

- **Bioengineered tooth replacement (under study, concept)**
  It is a fully functional tooth replacement as an organ replacement therapy, which suggests the use of embryonic stem cell that is implanted in the jaw of the patient that will grow into space of the missing tooth. This implant is still under study and stem cell research but there has been a success in mice bioengineered tooth replacement(4).

**Health risks and dental implants:**

According to the American Academy of Implant Prosthodontists, implants are made of biologically compatible materials which have undergone extensive testing over a period of several years. Since these materials are largely metals, such as titanium, and have never been living tissue, there is no likelihood of causing an antigen-antibody response which could cause rejection similar to that which sometimes occurs with heart and kidney transplants.

**Endosteal implants**

This is the most common method and most successful implant within all different types of implants, the implanted tooth mimic the actual tooth as it is made of separate components; the implant itself which is threaded titanium screw (fixture) which represent the root which work as an anchor for the second component which is the prosthesis. The prosthesis represent the crown part of the actual tooth, Endosteal implant is a multi-step process which involves two dentists, oral surgeon which places the titanium root in the jaw and restorative dentist who creates the prosthesis.

Before the start of procedure, patients pass through different type of evaluations and clinical examinations to determine the suitability of the patient to the implant, this include radiographs (X-rays) of the patient teeth and jawbones and examination of the soft tissue of the mouth, it
must be free of any pathogens, healthy and the quantity and the quality of the gum tissue in the immediate area where the implant will be placed is adequate.

The radiograph (X-ray) and other examinations will help the dentist find that there is an adequate quantity of bone in the region of the planned tooth implant and that this bone is of sufficient quality. Making this determination involves evaluating the shape of the bone (both width and height). It also involves evaluating the density of the bone (both outer cortical and inner medullary bone). [see fig.4]

There can be situations where the treating dentist will find that the bone in the region of the planned implant is not adequate. This deficiency can be naturally occurring, such as that bone resorption (bone loss) that takes place in those regions where teeth have been extracted. This type of defect is most common in those cases where multiple teeth were extracted many years previously.

In other cases the bone deficiency can be attributed to dental disease, such as bone loss due to the effects of advanced periodontal disease (gum disease). Since the success of a dental implant will be greatly dependent upon the bone in which it is placed, the treating dentist may feel that it is necessary for them to perform a bone grafting procedure for their patient (such as a sinus lift) so to replace missing bone or add to existing bone(3).

As the dentist examines the patient and reviews their x-rays, they will search for other potential complications. The location of various anatomical structures, such as sinuses, nerves, blood vessels and the roots of adjacent teeth must be identified. This is important because tooth implants must be positioned in a fashion where they are suitably distant from these objects.

1. Surgical placement of the implant(s) into the bone. This is usually done right in the dentist’s office, with a local anesthetic. After surgery, there is a healing period of
approximately four months. During this time, the implants fuse to the bone by a process known as 'osseointegration'. [See fig.5].

2. Next, there is a minor surgical exposure of the top of the implant, whereby the dentist will attach the post to the implant. The function of the post is to become the support for either one tooth or a set of teeth. This is a short procedure that usually requires only local anesthesia. [see fig.6]

3. The last phase is the restorative phase. The dentist will take impressions and then make a prosthesis that will attach to the implants. This will require several visits. Once completed, the mouth will be restored to natural looking, strong teeth

![Figure 6](image)

![Figure 7](image)

Materials used in making the implants

Titanium is the metal of choice when it comes to implants; its rigidity and strength are comparable to those of high noble alloys commonly used in dentistry. ASTM International (the American Society for Testing and Materials) recognizes four grades of commercially pure titanium, or Ti, and three titanium alloys (Ti-6Al-4V, Ti-6Al-4V Extra Low Interstitial [low components] and Ti-Al-Nb).5 Titanium is a highly reactive metal that readily passivates to form a protective oxide layer, which accounts for its high corrosion resistance. The low density of
titanium provides for high-strength, lightweight prostheses. Additionally, dental porcelain can be fused and bonded to titanium to produce an esthetic, lifelike restoration.

Titanium and its alloys form passivating oxides on the implant surface that permit close apposition to the physiological fluids, proteins, soft and hard tissues, in this process where implant structurally and functionally connected is called osseointegration, because of osseointegration, titanium is considered biocompatible implant material to the point that the human body act as titanium is part of its own.

**Conclusion:**
Many individuals suffer from the loss of one of more of their teeth and end up suffering the rest of their from either dentures or dental devices now they don’t have to suffer anymore with dental implants they get almost actual teeth as it last long almost 20 years, low maintenance and pain free, the only disadvantage of the dental implant is the cost as it range from 1000-20000s for the set of teeth but if we looked at it from the point that don’t decay and don’t will not have any cavities it would be worth it on the long run.
Bibliography


Are you a Caffeine head?

An investigation of the worlds most widely used and abused psychoactive stimulant

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CHM 236
4.8.2010.
Abstract

Caffeine is a naturally occurring psychoactive stimulant that is present in, but not limited to: coffee beans, tea leaves, chocolate, and kola nuts. Coffee, which contains Caffeine, is the world's second most consumed liquid. Water is the first. Approximately 400 million cups of coffee is consumed in the United States everyday. Caffeine may also be synthesized in research laboratories and has several uses in the medical world. The negative effects of caffeine abuse may be detrimental a person's overall health. Caffeine has several chemical, neurological, anatomical, and physiological effects on the human body (Matissek 2002).

Caffeine And Its History

Caffeine has always been present in the natural world. The first successful extraction of Caffeine (C₈H₁₀N₄O₂) was accomplished by Friedrich Runge in 1821. It was later synthesized in the laboratory by Emil Fischer in 1895. Caffeine is an alkaloid which means it is a heterocyclic compound containing Nitrogen. Other common alkaloids that are also psychoactive stimulants include Nicotine (C₁₀H₁₄N₂) and Cocaine (C₁₇H₂₁NO₄).

![Nicotine molecule](image1)

![Cocaine molecule](image2)

![Caffeine molecule](image3)

A Nicotine (C₁₀H₁₄N₂) molecule  A Cocaine (C₁₇H₂₁NO₄) molecule  A Caffeine (C₈H₁₀N₄O₂) molecule

When Caffeine is in a pure state it is has the appearance of a crystalline white powder. Caffeine is odorless and has a bitter taste. Caffeine is so common throughout the world and several cultures that people often forget it is in fact a psychoactive stimulant. A psychoactive stimulant may be classified as a substance that affects a person's mood and perception while increasing alertness and cognition. Caffeine is also is a diuretic. A diuretic is any chemical that
increases the excretion of urine from the body. This then may lead to dehydration if consumption of Caffeine is at a high level and not properly replenishing water in the body (Weinberg 2001). 

**Synthesis Of Caffeine In Nature**

![Chemical Structure](Image)

Xanthosine is a naturally occurring Nucleoside found in plant cells. A Nucleoside may be defined as a organic molecule present in plant cells is consisting of glycosylamines that are bonded to Ribose. Ribose is a simple monosaccharide which is found in all living cells. Essentially, Ribose is a simple sugar. The Xanthosine reacts with $S$-adenosyl methionine. $S$-adenosyl methionine is co-enzyme that has a positively charged sulfur atom which allows it to transfer or add a methyl group (CH$_3$). The process which the methyl groups is transferred using $S$-adenosyl methionine is known as a SAM cycle. Next, the enzyme known as 7-methylxanthosine removes Ribose from the Xanthosine molecule (Nehlig 2001). Once the Ribose is removed from the Xanthosine, a second SAM cycle occurs. This time the SAM cycle is working with different co-enzyme called 7-methylxanthine. At the end of the second SAM cycle Theobromine is formed. Theobromine is an alkaloid that has a very similar structure to Caffeine. Theobromine is a molecule that is abundant in chocolate and Cocoa leaves. Finally, a third SAM cycle occurs in order to add an extra methyl group (CH$_3$) to the molecule in order to produce our product, Caffeine (C$_9$H$_{10}$N$_4$O$_2$) (Nehlig 2001).
Metabolism Of Caffeine In The Body

Caffeine is taken into the body via the oral route. It will travel down the gastrointestinal tract and be absorbed via the lower intestines. The cytochrome 450 found in the liver is the main enzyme that metabolizes caffeine once it enters the system. Caffeine takes approximately forty five minutes to enter the blood stream. The effects such as altered mood, increased cognition, and increased energy are felt after this point in time. Increased heart rate and alertness may follow. The half life of the caffeine felt in the body varies from person to person depending on different variables such as weight, age, and health. The half life of a chemical simply means the amount of time needed for half of it to be used and metabolized. Once the caffeine is absorbed it will pass through the blood brain barrier. The blood brain barrier is your bodies natural safety mechanism that prevents harmful things, that may make a person sick, from entering the brain. Caffeine makes its way through the blood brain barrier because its chemical structure resembles that of Adenosine. Adenosine plays an important role in the body for several reasons. When Adenosine is in the form of Adenosine Triphosphate (ATP) it is a coenzyme that assists in energy transfer within the body. Adenosine is also a neurotransmitter found in the brain which helps regulate several actions in the body. Among other things, Adenosine helps regulate energy levels within the body (Nehlig 2001).

Caffeine has a similar chemical structure to Adenosine. The similar structure allows the Caffeine to bond to the receptors that Adenosine usually bonds to. When the caffeine does this it is known as an antagonist. An antagonist is any chemical that may be introduced into the body in order to reduce the effects of another. When caffeine then attaches to the receptors originally meant for Adenosine, the brain will release another neurotransmitter called Dopamine. Dopamine is a very important neurotransmitter that is involved with several things in the body. Dopamine helps regulate things like cognition, pleasure, motivation, mood, and sleep. Once completely metabolized the diuretic properties of caffeine will then make the body excrete it in the form of urine (Uretsky 2006).

This picture shows the structure similarities between Caffeine and Adenosine.
Medicinal Uses Of Caffeine

Caffeine is a widely used in the medical world for the treatment of several conditions. The most prominent use for medicinal caffeine is in the treatment of headaches. Caffeine is combined with several over-the-counter medications such as Tylenol (Acetaminophen) and NSAIDs (Non-steroidal anti-inflammatory drugs) to enhance their overall effect. Caffeine is coupled with pain-killers because it acts as a vasoconstrictor. The vasoconstriction effects of the caffeine allow the veins in the brain to shrink therefore alleviating pressure and tension in the skull. For this reason caffeine may be found in medications such as: Midol, Excedrin, and Darvocet (Weinberg 2001).

Another important use of caffeine is the treatment of apnea and bronchopulmonary irregularities in infants. In order to do this, caffeine is slightly changed to the caffeine citrate form. The caffeine citrate is a liquid and it metabolizes into the body and a higher rate, this is the main reason it is used in infants. The caffeine citrate solution works by stimulating the breathing centers in the brain and widening certain parts of the lungs in babies. Caffeine citrate may be used in adults, but only for severe migraines.

Negative Side Effects or Health Problems Related To Caffeine Consumption

Caffeine may affect the body in several different ways if it consumed at high levels for an extended period of time. Psychiatric disorders that may arise from caffeine consumption may include are: schizophrenia, anxiety, sleep disorder, and caffeine intoxication. Schizophrenia is a term used to describe a state of mind when a person is experiencing hallucinations, bipolarity, and mood disorders. The psychiatric disorders don’t usually arise in people until the consumption of caffeine exceeds 300mg a day for an extended period of time. Many people forget that it is a habit forming substance. Just like any other substance introduced into the body, the dosage must be increased over time to feel the same effect. Tolerance for caffeine builds in the body very quickly. This leads to physical and psychological dependence. The dependence leads to addiction (Cherniske 1998).

Research has been done to study the cognitive effects of animals after testing them will certain of levels of caffeine over a certain period of time. Over time some animals actually lose the ability to focus due to the over excitement the caffeine induces into their body.
This picture illustrates the effects of caffeine on a spider before and after introduction.

Many people may be surprised to know that withdrawal symptoms can and will exist as a result of caffeine use. Withdrawal symptoms may last anywhere from twenty four hours to ninety six hours. The time period of the withdrawal symptoms will last depend on the persons things like age, weight, and heath. During withdrawal a person may experience nausea, headache, irritability, and stomach pain.

Caffeine consumption during pregnancy has been a debated topic for several years. According to the United Kingdom Food Standards Agency, pregnant women who drink 200 mgs of caffeine daily have double the risk of having a miscarriage. 1 cup of coffee contains about 100 mg of caffeine. If a mother drinks two cups of coffee or more during pregnancy it may increase the chance of infant death (Cherniske 1998).

Excessive caffeine intake has been linked to other conditions such as hypertension and memory loss. When caffeine is ingested into our bodies it makes use more alert. A byproduct of the alertness is an increase in heart rate. After time heart arrhythmia may develop. Memory loss may be another surprising side effect of caffeine consumption. Caffeine affects the hippocampus of the brain. The hippocampus is the part of the brain associated with long term memory. This happens because neurogenesis is the hippocampus is reduced and therefore synapses that part of the brain decrease as well (Nehlig 2001).
Caffeine and Religion

Several religious circles find the consumption of caffeine goes against their beliefs and ideals. Mormons, under the Church of Latter-day Saints, feel that consumption of caffeine may be habit forming. Other religious organizations in Islam and Seven-Day Adventist also feel that caffeine consumption is bad for the soul. It is also looked down upon due to the fact that it is a mind-altering stimulant (Bruan 2003).

Caffeine and You

How is your consumption? Caffeine is all around us every day. When we drive down the road, every other business complex has a Starbucks waiting to greet you. Studying for a big test? Better drink a Red Bull. How do you feel when you don’t have coffee in the morning? These are important questions that need to be asked. However caffeine has made it into your life; remember everything is best in moderation.

Conclusion

Caffeine consumption has been commonplace for thousands of years. From early cultivation in the fields of Ethiopia, to the ancient Chinese dynasties that traded coffee beans along the Silk Road, to the Starbucks down the street, caffeine has been a part of human existence for a very long time. Caffeine when used medicinally has been proven to alleviate pulmonary and breathing irregularities for infants. Caffeine also helps adults deal with migraines. There are many benefits of caffeine consumption such as: increased cognition, alertness, motivation, increase energy, and lowered levels of fatigue. Just as there are two sides to every coin, the negative side effects that may result from excessive caffeine consumption are: hypertension, nausea, miscarriage, caffeine induced psychosis, and addiction. Caffeine is a highly marketable, highly accessible substance. Many people forget that it is actually the world’s most highly used psychoactive stimulant. With a healthy diet, exercise, and moderation caffeine may be a helpful tool.
Bibliography


Company Greed Dictatorship, the Difference between Name Brand and Generic Medication

Fineas Zirbo
22 Apr. 2010
Abstract:

Every visit to the pharmacy leads to a discussion between buying a brand or generic name medication. Many consumers are forced into buying the generic version of the medication even though they prefer the brand simply due to the high price of the brand. This paper will analyze the difference between two commonly bought over the counter medications; ibuprofen, acetaminophen and their brand names of Motrin and Tylenol. It will also compare these two drugs to their brand names sold overseas and how that system should be adopted in the United States.

Brand vs. Generic Medication:

It seems that in today’s economy people take a second look at the way they spend their money. More and more people are looking to save money in any way possible by scouting for sales, coupons or possibly buying an off brand name item. This way of thinking might work when buying common household cleaners or clothing that does not come from a high end retailer, but where should the line be drawn? Should this mentality be applied to things that we ingest in our bodies such as medication? It seems that every drug store offers two choices when buying both over the counter medication, medication that does not need a prescription, and medication that requires a prescription. One can choose between buying the more expensive brand name medication or the cost saving generic equivalent. A generic medication is a type of medication that is produced and distributed without any type of patent protection where as the brand name is protected by a patent. Through a detailed study of the difference between a generic formulary and a brand formulary, a case study on Motrin, Tylenol and their generic equivalence and a comparison between the United States and France this paper will argue for brand name drugs and why they should always be placed in one’s shopping cart.

The U.S. Food and Drug Administration set rigid standards for the manufacturing of and distribution of all types of medication that are sold throughout the United States. In order for a generic drug to meet FDA approval it must; contain the same active ingredients as the innovator drug (inactive ingredients may vary), be identical in strength, dosage form, and route of administration, have the same use indications, be manufactured under the same strict standards of FDA’s good manufacturing practice regulations required for innovator products and be bioequivalent. Although these factors might make it seem that a generic drug is identical to the brand name, a problem arises within two of the factors set by the FDA; the fact that the inactive ingredients might vary and their bioequivalence factor.

The two case study medications involve the brand name Motrin with its generic ibuprofen and Tylenol with its generic acetaminophen. Brand name medication take the name set by the company that manufactures the drug while generic medications take the name of the active ingredient, for example ibuprofen and acetaminophen. The active ingredient in the brand name drugs Motrin and Tylenol are ibuprofen and acetaminophen respectively. The difference arises in the different binders and coatings the brand name drugs and generics are held together with. This is what leads into the bioequivalence. The FDA defines bioequivalence as “the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study”. This bioequivalence only refers to the active ingredient and its interaction site
but it skews over the method that the active ingredient is taken to that binding site via the binders and coatings that hold it together.

Every company has its own version of the brand medication available for purchase on their shelves right next to their brand name equivalent. Since the FDA states that the generic and brand medication need to have a ninety percent bioequivalence, “The average difference in absorption into the body between the generic and the brand name was only 3.5 percent”. Although these numbers might seem low, it still indicates a difference between the two and leads to the assumption that the generic medication from one store can differ from that of another store while the brand name is all the same no matter where it is bought.

As the old saying goes, money makes the world go round and round and it appears that money dictates which type of medication people buy and use every day. “Today, 7 in 10 prescriptions filled in the United States are for generic drugs”. Insurance companies prefer the generic version of the medication because of their tremendously lower prices. “On average, the cost of a generic drug is 80 to 85% lower than the brand name product”. This directly affects patients that come to the pharmacy in terms of their co-pay. Depending on the type of insurance a prescription for a generic medication is usually lower than ten dollars for a thirty day supply while its brand name equivalent can cost over three times as much. This price is also reflected in over the counter medication as well. The following prices were taken on the 31 of March 2010 from a nearby CVS Pharmacy. Thirty tablets of brand name Motrin 600mg sell for $14.99 and the generic ibuprofen 600mg sell for $10.99. Thirty tablets of Tylenol 325mg sell for $2.89 and generic CVS-acetaminophen 325mg sell for $1.95. Brand name medication tends to have a higher price tag associated with them.

The lower price tag may be a direct affect of the methods that companies use to manufacture their generic medication. This study is limited to two different medications such as ibuprofen and acetaminophen. This focus is on these two medications because they have been around for a long amount of time, and the companies that first produced them do not hold any patents on the active ingredient. Once the patent on a brand name medication expires, other companies are allowed to manufacture the drug. In this case of over the counter versions of the medication many different retail pharmacies have their own versions of Motrin and Tylenol like CVS brand ibuprofen, CVS brand acetaminophen or Walgreens brand ibuprofen and Walgreens brand acetaminophen. Many of these companies prefer to sell their generic versions because the profit margin is extremely higher, about sixty to eighty percent higher. In the study of prescription medication, the pharmacy deals with their supplier that has contracts with different companies that vend the brand names or generic versions. A pharmacy usually tends to stock more of the generic product because they are dispensed at a much higher ratio due to insurance companies having a lower co-pay for generic medication.

There are two ways that a patient can request to be dispensed a brand name medication when filling a prescription. They can ask the pharmacy to dispense the brand or the doctor must write dispense as written or DAW. Pharmacies tend to revert to the generic medication in their fills unless the patient or the doctor has stated otherwise. The problem arises that the insurance companies are unlikely to pay for the medication if the patient simply asks for it. The usually cover brand medication with the DAW code written on it but at a much higher co-pay. The patient is forced to take the generic medication by the insurance company due to the lower price tag of the generic medication.

When it comes to prescription that can be purchased over the counter, without a prescription, the purchase simply depends on the preference of the consumer. Brand medication
costs a little higher but to some people the higher charge is worth it because they are buying the name brand. To other people the generic is just as good because it works the same and they ask themselves why should I pay more when I get the same affect. The same affect might be achieved, but is that extra fee worth it when it is taken in regard that this medication is entering our bodies.

The following is a survey that was taken at a local CVS pharmacy. People that purchased over the counter medication where asked why they choose the brand over the generic or why they choose generic over brand name. The same people were also asked if the prices for the two were to be the same would they change their choice. The people were surveyed on two shifts from two in the afternoon till ten at night on two separate nights. All of the people that purchased over the counter medication during the two shifts were asked the same questions and were informed of the survey after the questions were asked. A total of fifty-five people were surveyed on day one and a total of seventy three people were surveyed on day two. The following charts on the left side represent the people that purchased brand over the counter versus generic over the counter medication. The charts on the right side represent the number of people that would purchase brand medication versus generic medication if the price was the same.

Day 1: 55 people surveyed

Day 2: 73 people surveyed

The most important piece of knowledge that can be gained from the above charts is that price plays an important factor in the way people choose between brand and generic over the counter medication. On regular everyday purchases people tend to by the generic version of the
medication because of the lower price tag it bears. To the average consumer the brand medication would appear to be better because it has a better overall appearance, it is highly advertised and it is usually available in multiple flavors and not just the standard cherry flavors many generic medications might be limited to. The people that purchased the brand medication stated that they believe it simply works better for them. Out of the twenty seven percent that purchased the brand version, the majority of them claimed that they have always bought the brand version and that it always worked. Once the price barrier was lifted, the majority of the people would switch over to buying the brand. This indicates that the brand version is the preferred version for many consumers.

When buying any type of medication, whether it is brand or generic, the active ingredient is the determination of how the tablet or capsule will work. The brand name of the medication is Motrin with its active ingredient being ibuprofen. Ibuprofen has a chemical structure of C$_{13}$H$_{18}$O$_2$ (See figure 1.1 for molecular structure of ibuprofen). The standard I.U.P.A.C. name of the molecule is iso-butyl-propanoic-phenolic acid or (±)-2-(p-isobutylphenyl) propionic acid. Ibuprofen is a NSAID or non-steroidal anti-inflammatory drug. “It is used for relief of symptoms of arthritis, primary dysmenorrhea, fever, and as an analgesic, especially where there is an inflammatory component. Ibuprofen is known to have an antiplatelet (blood-thinning) effect, though it is relatively mild and short-lived when compared to or other more well-known antiplatelet drugs.” Usually people that pick up a bottle of ibuprofen from the pharmacy use it in order to relieve pain, fever, inflammation and/or swelling. It is a very common drug that is available in both over the counter doses and doses that require a prescription. Strengths of 400 mg and up require a prescription, with the most common being the 600 mg and 800 mg tablets.

**Figure 1.1**

![Molecular structure of ibuprofen](image)

The general structure of ibuprofen is a di-substituted benzene ring that contains the substitutions in the para position. The number one position carbon on the benzene ring is attached to a chiral carbon that is bound to a carboxylic acid, a hydrogen molecule and a methyl group. The number four position carbon is attached to an ethyl group with the second carbon being attached to two terminal methyl groups and a hydrogen molecule. The molecule is composed of both a non-polar and polar side with the carboxylic acid dictating the polar side. The presence of the chiral carbon creates the existence of the molecule to have two different enantiomers. This makes it possible that “two forms of the molecule can exist and can each have a potential for different biological effects and metabolism. Indeed it was found that (S)-(+) ibuprofen (dextibuprofen) was the active form both in vitro and in vivo.” The manufactures of the drug considered a logical move to advertise the drug as a single-enantiomer product until more testing was done on the molecule discovering the existence of a specific isomerase that converted the (R) enantiomer to the (S) enantiomer. Based on the high expense of manufacturing
a tablet of ibuprofen as a pure-enantiomer, the common formulation of ibuprofen is a racemic mixture.\textsuperscript{7}

Ibuprofen works by inhibiting the prostaglandin synthesis by decreasing the activity of the enzyme, cyclooxygenase, which results in decreased formation of prostaglandin precursors.\textsuperscript{2} This specific cyclooxygenase enzyme or COX for short is present in the body in three different types COX 1, 2 and 3. The action of this enzyme is to create prostanoids which regulate inflammatory and immune responses of the body. The chemical structure of ibuprofen and other NSAID drugs allows the blocking of these enzymes creating anti-inflammatory action. The classical COX inhibitors such as ibuprofen are not selective and tend to block all of the COX enzymes with no selectivity for the one, two or three.\textsuperscript{10}

In the manufacturing of the ibuprofen tablet certain ingredients are added as binders that hold the tablet together. The ingredients include; colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, pregelatinized starch, talc, stearic acid and titanium dioxide. The above inactive ingredients were copied from a package insert for ibuprofen 600 mg and 800 mg. These are the inactive ingredients that compose the generic form of the tablet currently being vended in many pharmacies.

In the United States, the FDA approved forms of the ibuprofen comes in both generic and brand name while in France it is only sold under the brand name of Nurofen. A comparison between the United States and France shows that French pharmacies are not tied into retail stores but are separate facilities. These pharmacies around France distribute Nurofen brand name without the availability of any generic form. A bottle of thirty tablets of Nurofen sells for around 1.74 Euros (approximately $2.34) which is equivalent to the price of a bottle of generic ibuprofen. The French pharmacies offer a brand name medication for a generic price.

The brand name medication is Tylenol with its active ingredient being acetaminophen. Acetaminophen has a chemical structure of $C_8H_9NO_2$ (see figure 1.2 molecular structure of acetaminophen). The molecular structure contains a benzene ring that is di-substituted at the para position. The number one position carbon molecule on the benzene ring has a nitrogen group attached to it that is bonded to a hydrogen molecule and a ketone. The number four carbon molecule on the benzene ring is bonded to an oxygen molecule that is bonded to a hydrogen molecule. The correct IUPAC name for acetaminophen is 4-(acetylamino)phenol. This molecular structure of acetaminophen causes it to be polar due to both oxygen molecules on either side. Acetaminophen has a standard IUPAC name of N-(4-hydroxyphenyl)acetamide.

Figure 1.2

![Acetaminophen structure](image)

acetaminophen
Acetaminophen has similar properties to that of ibuprofen but it differs in the fact that it does not have any anti-inflammatory properties. It works by "inhibiting the synthesis of prostaglandins in the central nervous system and peripherally nervous system. It blocks pain impulses generation and produces antipyresis from inhibition of hypothalamic heat-regulating center". The difference between the two drugs is that acetaminophen works through an indirect route of blocking the COX inhibitors. This affect is more significant in terms of blocking the central nervous system. Once the drug enters the body it is primarily metabolized in the liver. The liver converts the drug to inactive compounds through conjugation with sulfate and glucuronide. The characteristics of this drug allow it to be used as a pain reliever and a fever reducer.

Similar to the FDA approval of the generic form of ibuprofen, acetaminophen is also sold in the United States as both generic and brand. In France acetaminophen is only available as brand under the name of Doliprane. A box of thirty tablets of Doliprane holds a retail value of 1.74 Euros which is equivalent to $2.32. The price that brand name acetaminophen is sold under in France is similar to the average price the generic version is sold in the United States.

The competition between brand and generic medication is one that influences us all. Generic medication are much cheaper to produce and as a result more widely available to the public because of their lower costs. "Financial incentives to use generic prescription drugs may be successful, even for consumers who perceive generic drugs to be riskier than brand name prescription drugs. As the perceived level of risk increases, larger cost savings are required". In conclusion it seems that people are influenced by money. People desire to use brand name medication but the strong influence in savings dictates what people really buy. In my opinion there are two major factors that play into the decisions people make or are simply forced to make when buying generic over brand, the lower price of over the counter generics and the insurance company policy to cover generic medication at a lower co-pay or covering brand name but at higher co-pays.

Many retail pharmacy companies that produce generic over the counter medication acquire great profits from their sales. Their profits are acquired from producing the generic medication at an extremely low cost. Although the active ingredient is one the same with the actual brand, the binders that hold it together can differ. In my opinion, the quality is not the same between brand name medication and their generic equivalence. From a physical aspect, many of the generic medication that I have personally handled while working as a pharmacy technician seem to degrade causing the powdery over-coat to come off leaving a trail of dust behind. The brand medication just seems to be held to a higher standard that makes the overall physical appearance better. If the generic version of the medication degrades even before entering the body, what does this say about the method of absorption into the body? Would a person prefer a medication that stays in tack while entering the body and being delivered through the correct method or a medication that degrades before entering the body?

People prefer to buy brand medication and would choose to buy brand because it works better than the generic version. The following survey interviewed people in regards to consumer perceptions of risk and required cost savings for generic prescription drugs, "The response rate was 71.4%. The percentage of respondents who perceived that generic prescription drugs were riskier than brand name products varied from 14.2% to 53.8%, depending on the medical condition being treated". It seems that people desire to purchase brand name but simply cannot afford to. France has developed a system that sells the brand name of the drugs at our generic prices. The simple excuse that brand costs too much in the United States can be ruled out. It
appears that many companies in the United States are just in it for the money. If the FDA would impose rules for companies to only vend the brand name and set a price ceiling on how much they would be allowed to charge, the consumer would be guaranteed access to the best medication available on the market. People would have access to the best medication on the market. I believe that such a system would allow people to buy the brand name and as a result take medication that was formulated at the best of standards. The lower prices would give everyone access to the brand medication.
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Putting a Spin on the Physics of Sports

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Abstract

The world of sports is full of rich history and holds many worldly ties. The fundamentals of physics are widely used in almost every application of life. The paper goes into details on how the works of Sir Isaac Newton apply to the world of sports, specifically baseball. The application of the Force exerted on a ball, the Inertia and conservation of momentum as well as the forces that act on a ball in flight will be discussed in detail. The paper also goes into depth of the history of baseball to how the game looks today.

Introduction

The passion that ignites a fan to sports or more specifically his team can undoubtedly be seen at any sporting event. As I sit here writing this very paper I have the NCAA college basketball tournament on and you can witness the true beauty in sports, the passion! And that’s just the college level. As for professional sports you can see the glory and pride in baseball parks all over America, it is no wonder it has been called “as American as apple pie” (13). Spring training is here once again coming to Arizona and Florida every year in March. Just take a trip on the freeway and you’re likely to see a license plate from just about every state full of Americans who just want to get the first peek of their team before the new season is to commence. But what makes Sports so fascinating? The rivalries? The walk-offs or game winning jumpers? The passion? It’s a combination of all of them with a twist of the dynamics of sports. And how they work has everything to do with physics; more importantly the father of physics Sir Isaac Newton. Ever wondered how much force linebacker Ray Lewis puts on a Quarterback as he comes around the blind side? Or how a ball can fly over 500 feet off a wooden bat? The truth is sports revolve around physics and Newton’s laws.

History of the Olympics

The first sports were talked about in Greek mythology as religious and political disputes were fought out. The first historical record of the ancient Olympics goes back as far as 776 BC (7). These games took place in Olympia and were dedications the Olympian gods. They continued this tradition for almost twelve centuries until 393 AD when the emperor at the time Theodosius declared them banned (7). They began as a one day event until 684 BC when they were lengthened to three days and to five days at the beginning of 500 BCs’ (8). The events of the first Olympics included running, jumping, discuss throwing, pentathlon and wrestling. Boxing soon added itself to list of Olympic events; this became an even more violent event as it progressed and boxers began using hard leather straps which left opponents with malformed faces (8). The winner of these events would have red ribbons tied around their hands and have flowers thrown at them from the crowd. The final day of the games would involve the herald announcing the Olympic winner followed by his father’s name and his homeland. The athlete would be crowned with an olive tree wreath upon their head as they were cheered (7).
The modern Olympic Games were started by a Frenchman by the name Pierre de Coubertin. Coubertin started the International Olympic Committee in 1894 in Paris, France. This committee set up the first modern Olympics which took place in 1896 in Athens, Greece. Many of the ideas were taken from the Olympics of old as a tribute. The Olympics were set up to help the world become more friendly and peaceful through sports. These first Olympics included participants from 14 different countries and were extended longer than the five days of the ancient Olympics. In the 1920’s they added the winter Olympics to the slate, due to rising popularity. The Olympics were a success and have grown into the largest sporting event in the entire world reaching hundreds of millions of spectators.

The History of Sports in North America

As the new country of the United States was being formed and searching for its new identity, sports were as well reforming to find new identities. In Mexico, on the other hand, Football or soccer as Americans know it has been and continues to be its National sport of choice. In Canada, a sport made by them, and by asking any Canadian, for them, in hockey has remained a pastime for a few hundred years. Since the late 19th century Canadians have picked up a second passion for an old Scottish sport which has been redefined into what is known as curling today. In America, in the early days sport was seen as a character builder. Football was first seen at colleges and universities in the late 19th century. There was however, barrier between social classes and sports. Most times it was rare and unknown for the middle and poor class to attend college and therefore see the sports played. The upper classes would participate in such sports as rowing, tennis, track and field and lacrosse while attending such universities. The working class seemed to be more into a developing sport called towne ball which was a ball and stick game. It was named after the frequent place it was played in the town common. In the south it was said to have been played as “a mark of maturity”. As the sport began to grow in popularity towards the start of the 20th century many factories and businesses had their own semi professional teams. Because of this many people began coming out to enjoy watching the game for entertainment.

The History and Evolution of Baseball

Ball and stick games have been played since ancient times as seen in Persia, Egypt and Greece. In early 12th century France games were played in courtyards with milk stools set up in similar formation to that of bases used in baseball. The British game cricket was first seen being played in Philadelphia in the 1750’s. In addition a game called rounder’s was also being played in the states that replicated the popular “towne ball” played in the south. The game was the basis for what we now call baseball. Many of the rules of rounder’s are still used today. The game was played with a wooden stick or an axe handle for a bat, remember this is a working class sport so money was hard to come by, and a ball was made of a bullet or slug wrapped in yards of string or yarn. One of the more traditional things still seen in baseball today known as the bench clearing brawl began in rounder’s; it was within the rules for a player to be called out by chucking the
ball at them after they hit the ball. The game went on for years as a community game that involved almost all the lower and middle classes, eventually changing its name to baseball in the early 1800’s (11).

The first official baseball club was started in 1842 call the Knickerbocker Baseball Club. Just three years later Alexander Cartwright, one of the founders of baseball, set up the first published set of rules. These were twenty rules outlining boundaries, fair and foul, the 90 feet spacing of the bases, strikes and balls and many other of the basic ground rules still used today. The game began to soar in popularity due to two key factors: the newspapers began coverage of the games and the rising attractiveness to gambling. The gambling was becoming the sole reason the games were even being played. However, it wasn’t only the spectators betting on the game it was players and even the umpires. In 1859, two amateur teams played before the first paid audience, over 2000 people paid fifty cents to get in, starting the minds of entrepreneurs. Soon after the civil war the National Association of Base Ball Players was formed and brought the notion of players getting paid to play. The first official baseball team was built a few years later in 1869 called the Cincinnati Red Stockings. The team went around the country playing all the local amateur teams and as would be expected finished an impressive 65-0. This incited others to believe that baseball could be a full time job. 1871 brought along the National Association of Professional Baseball Players (NAPBP) a very similar structure to the players association used today. Major League Baseball was official in 1876 when the birth of the National league was brought to life. The National league was a group of eight teams with all players on the team under contracts. The legitimacy of the game had to be reputable in order for the league to survive so gambling by all those involved had been strictly banned. Another small league gaining in popularity known as the western league changed its name the American league at the turn of the century. In 1903, they signed on a deal that would set up their champion being played against the National league champion in what would be the first world series (11). It had now become the time the National pastime, a business that entertained all of America.

The legends of the game

When looking over the history of Major League Baseball many players have stood out in there era as the player on top. But how is one to select the greatest player of all time? Clearly the game has evolved from generation to generation, so how can a player from 1910 be compared to a player in 1960, let alone 2010. As well it’s hard to compare a position player to a pitcher, the only thing the two have in common is they are both Major Leaguers, the intangibles are incomparable. There have been many amazing players throughout each era, but to define it, these are the greatest pitcher and position player of each of the four major eras, along with a few honorable mentions and historical icons.
The 1890's to 1930

The beginning days of baseball led to the development of many of baseball's original heroes. The greatest player of this generation has to be the most difficult of any generation to choose. There are two guys worthy of obtaining this title in Ty Cobb and George Herman "babe" Ruth. Ty Cobb played from 1905 to 1928 and was known as the "unconquerable king of baseball" (15). He had a lifetime batting average of .366, winning 12 batting titles both of which are still MLB records. He also set and held 90 other MLB records until recently. He was a first ballot Hall of Fame inductee which is a rare feat for any ball player (15). Babe Ruth started his career as a pitcher in 1914 but as most know turned out to be one of the best home run hitters of all time when he retired in 1935. Ruth ended his career with 714 home runs however he did strike out quite often. The style of play between the two players was vastly different as one swung for the fences as the other "played the right way" as Cobb quoted his style. The rivalry fueled baseball and was the catalyst for making baseball as popular as it became (15).

As far as pitchers go only one name stands out and that is Denton True "Cy" Young. Young made a name for himself in his time when pitchers were hardly noticed. He posted a win total of 511, a record that surly will never even be approached due to the five man rotations of today. He also struck out 2,802 batters while completing (pitching the entire game) 749 games over 7,356 innings all records for the time (12). The most prestigious award given to pitchers today the "Cy Young" was named after him for his dominance of his time (12). He played the game from 1890 to 1911 while he posted twenty wins or more in 15 seasons including a streak of five seasons over thirty wins. "The king of pitchers" still stands as one if not the greatest of all time (12).

The 1930's to the mid 1950's

This was a time when baseball had clearly been established and was standing high above the entertainment world. This is a generation that developed many superstars and saw the birth of ball players as celebrities. The greatest ball player of this generation was Ted Williams who by a very narrow margin beats out Lou Gehrig and Joe DiMaggio. Very strong argument can be made for all three players but Ted gets the nod in this argument (and NO! this isn't a Red Sox over Yankee bias). Ted is highly regarded for walking away from the game for five seasons during his prime, while still managing to put up 521 homers and 1839 RBIs. His greatest achievement is hitting .400 three times in his career (the last player to do so) with a lifetime batting average of .344 (4). DiMaggio, along with Hollywood persona, hit .325 lifetime with 1537 RBIs and 361 home runs (5). "Sweet" "iron man" Lou Gehrig was one of the hardest playing players ever as tribute to his 2130 consecutive games played. Gehrig also hit .340 lifetime with 493 homers and 1995 RBIs (2). It would be wrong not to mention Jackie Robinson who is widely known as the first African-American player to break into the majors. However, it is understated just how great he truly was and deserves the mention in the conversation as the greatest of all time.
This era also stands out with one truly deserving pitcher as the greatest ever that being Lefty Grove. Lefty won the MVP in 1931 when he posted miraculous 31-4 record. He posted a career win total of 300 while only pitching 17 seasons. He also led the league in strikeouts, seven straight years, wins four times and ERA nine times which is far and away more than any other player in history (6).

The late 1950's to the mid 1980's

This generation stands out as the most talented generation hosting a slew of players with arguments to be heard. Willie Mays wins the battle narrowly over Hank Aaron. Willie Mays hit an amazing 660 home runs while winning twelve gold gloves. And let us not forget he owns two MVP awards as well, Mays was simply the greatest all around player ever (18). "Hammerin" Hank Aaron makes a strong case for the honor as he hit 755 home runs and earned three gold gloves over his career. But don’t be fooled and label him as just a home run guy he also holds the records for RBIs (2297), extra base hits (1477) and total bases (6856) while making the all-star game every year he played (17). Pete Rose hit a career .303 in an era when the pitching was better than any other. He added 4256 hits a MLB record that will be hard to break, while adding 1340 RBI’s and 160 home runs (3). Despite what you think of his ethics after he stopped playing, this focus is on playing the game and nothing else. Other greats include Mickey Mantle notably hitting 536 home runs and Mike Schmitt was the greatest third baseman ever while adding 548 home runs.

As mentioned earlier this is when the pitchers really began making a name for themselves. This exceptionally talented group was lead by Nolan Ryan. Ryan was often known for throwing the ball over 100 miles per hour or to keep this physics related 160 km/hr. He holds the record for most strikeouts at 5,714, another record likely to stand awhile. His dominance over hitters is unparallel throwing seven no-hitters (record), twelve one-hitters (record), and eighteen two hitters while still posting an ERA of 3.19 (1,19). Sandy Koufax is the likely close runner-up with his four Cy Young awards. Koufax also added four no-hitters including a perfect game (1,20). Warren Spahn may be the greatest southpaw with his 366 wins. While Whitey Ford, Jim Palmer, Tom Seaver, Steve Carlton, and Rollie Fingers (a relief pitcher) all deserve mentioning (1).

The mid 1980’s to present

This generation takes more than numbers and awards to get you on the list due to recent findings. This era starting in the mid 1990’s has been tattooed with the labeling of the “steroid era”. For now we’ll ignore this notion and go in to detail with the greatest and come back to the reasoning behind this label. This generation was the coming out of speed into the game. While home runs were an increasing trend that fans craved to see. Overall this is a difficult choice as the top two happen to be favorites of mine but we’ll go Barry Bonds slightly over Rickey Henderson. Bonds the all-time home run king hit 762 bombers and won seven, yes seven most valuable player awards. He was also an excellent fielder winning eight gold gloves and invited to
fourteen all-star games. And did I mention he was quick? Barry stole 514 bases and was the first to hit forty home runs and steal forty bases in the same season (1). On the other hand Rickey was known for his “I am Ricky” speeches, the fact is Rickey was great and he knew it. Rickey was the quickest player to ever play the game and he knew how to steal a base, nabbing 1,406 bases and scoring 2,295 runs (1,16). Henderson was the greatest lead-off hitter of all-time; adding 3105 hits and 297 home runs (the most ever lead-off HRs). An episode of Sporscenter was once quoted saying, “if you split Rickey in two you’d have two Hall of Famers.” Since the era is not yet complete it may be premature to add three still active players for consideration but if they continue the same path there are no doubts; those players being Albert Pujols, Alex Rodriguez and Joe Mauer. Also worth mentioning are Kirby Puckett and Ken Griffey Jr.

As for pitchers the development of velocity caused by Nolan Ryan was something fans and scouts were drooling over. There have been many good pitchers this era with two absolute greats: Randy “the big unit” Johnson and Roger ‘rocket” Clemens. Both Randy and Clemens were strikeout artists who pitched at extremely high levels their entire careers. Randy is the closest to get to Nolan Ryan’s number of strikeouts with 4,875 while adding 303 wins (historic number for a pitcher in today’s game) and five Cy Young awards. Randy, also threw a no-hitter and a perfect game (when he was 40) with thirty-seven shutouts, while maintaining a low 3.27 ERA (1). The rocket has the most Cy Young awards of all-time with seven and added 4,672 strikeouts. He finished his career with a 3.12 ERA and an unsightly 354 wins (1).

**Performance Enhancing Drugs**

The information is still coming in and it reappears every season, yet another player has been accused or proven guilty of enhancing their performance with drugs. Before I spread some opinion around the facts and rules need to be established. Steroids were not against the rules until 1991 (10). However, baseball did not regulate, test or establish a disciplinary system until 2003 (13). Many have said that baseball knew much of what was going on and just turned a blind eye to the situation. Now why baseball did this is a judgment call some believe they didn’t feel it was a big deal while others including myself believe it was purely a money based decision. Baseball was on the fallout with the rise of the NFL and NBA and the strike in the mid 1990’s, people starting changing their feeling for the national pastime. In 1998, Mark McGwire hit 70 home runs and Sammy Sosa added 66 in a race that is said to have saved baseball. And in 2001 Barry Bonds hit 73 home runs despite being walked an average of almost two times per game. Keep in mind the previous record of 61 was hit nearly forty years earlier and it was broken five times in a five year period (3 times by Sosa) (10). Also important to note that ballparks are smaller, better bats were made, tighter balls were sewed and workout technology was far more advanced. Having said all that in 2003, due to pressure from congress, MLB randomly tested all players over the season. A list was created with 103 names of players who tested positive; the list was supposed to be confidential and taken just for the use of building a case identifying the problem (13). Baseball did feel this was a significant number and created a series of punishments (continually updated) that as of today suspends a player for 50 games (nearly 1/3 of the season)
for a first offense of any banned substance. A third offense leaves a player looking for a new career. The system works, however sometimes a player may take a supplement that unknowingly contains something on the banned list and be suspended for 50 games, a harsh penalty for picking a common GNC product. However, until the 2011 season players who use human growth hormones (HGH) cannot be proven guilty because the testing does not detect them.

With the stage set we can make room for opinions about asterisks, what should be done with those caught and is it fair to accuse without solid evidence. Baseball is widely known for its historic numbers and records and with most of them falling within this so called “steroid era” it’s easy to post a label. Now, clearly steroids and human growth hormones have been used more during this time than any other era by proof of the 2003 tests and the admission of such players as Alex Rodriguez, Mark McGwire, Jason Giambi and Andy Pettitte. Many of whom have found reasons to dance around using it such as Rodriguez say just to try it and McGwire saying it was to help with injuries. But wait a second, who are we to say they are lying? Maybe it is truth. The pressure to use the enhancers includes multi-millions, records and stardom. Is it right? No, but we have no idea how many players actually used the stuff, so maybe it was a level playing field. Mike Schmitt has been quoted as saying he doesn’t know if he would have taken them or not especially with all those pressures. Baseball should not label the era as the steroid era because it diminishes the works of so many players who didn’t use. As far as an asterisk goes I don’t believe that without factual evidence and an admission should be used to denote records. Listen, baseball people like myself will always know what Ruth and Aaron have done and we know what Bonds has done, it’s unfair to, in published form, lessen the significance of hard work. People can piece together their own stories and accept the truths they believe.

**Bryan “Moose” Haas**

I sat down with Moose and had a conversation about his playing days as well as the state of the Game today. Moose was born in Baltimore, Maryland where he began playing baseball at the age of six. Interestingly enough Moose is a south paw who throws with his right hand; he developed this from playing with his brother and only having a right hander’s glove. He got his nickname from his father when he was young because he felt he was always going to be a big kid. His best season was a sixteen win season with a losing team, his best winning percentage season he went 13-3. His first appearance in the majors was about two years after he was drafted thirtieth overall out of high school by the Milwaukee Brewers. We got to talking about the great players and what he thought of steroids in the game. He grew up a Brooks Robinson and Jim Palmer fan and as a pitcher he said the greatest player he played against was Rod Carew. As for steroids he said when they were not illegal he doesn’t know if he hadn’t retired that he wouldn’t have tried them to continue his career for the money players were making. I asked if he ever saw or heard anything when he was in Oakland with Jose Canseco, he replied I heard a lot of things but just kept to myself when it was brought up. When asked what is different about the game now from when he played he noted the speed and athleticism of the players. As we continued our
conversation we got to talking about the money players make now-a-days. He responded with the older player always told me I made to much, don’t blame the players for getting what’s out there. I tend to agree with him sure it’s a ridiculous amount of money to play a game but if you can get it who wouldn’t? He also told me a story how when he signed his last contract for 775,000 dollars, he was the highest paid player in baseball, that is for the few hours until Nolan Ryan became the first to make a million. We ended with what he missed about the game and what are his memorable moments. He told me he missed the clubhouse and hanging out with all the players while he didn’t miss the constant being on the road all the time. He finished his career with one hundred victories and won the ALCS with the Brewers. He noted the highlight of his career was being down 0 to 2 in the series and rallying back to win it 3-2 was his favorite time being a pro. He also pitched in the world series didn’t get the win but had a no decision. He also enjoyed his first game starting in his hometown where he pitched a shutout and in Yankee stadium when he threw a one-hitter (29).

Isaac Newton

Sir Isaac Newton was mathematician, chemist, astronomer, philosopher and most importantly the father of physics. Newton lived in the 17th century in England where he did most of his work. His first three laws of motion have become the basis and fundamentals of physics. His First law states that, “an object moves with a velocity that is constant in magnitude and direction, unless acted on by a nonzero force.” The second law reads, “The acceleration of an object is directly proportional to the net forces acting on it and inversely proportional to its mass.” And lastly the third states, “If object 1 and object 2 interact, the force exerted by object 1 on object 2 is equal in magnitude but opposite in direction to the force exerted by object 2 on object 1.” It’s important to understand that this is not all that Newton had accomplished. In fact it would take books to completely write about all the intelligence that Newton left on this earth, but for terms of this paper these first three laws will help understand how physics plays a role in baseball (14).

Baseballs and Baseball Bats

As baseball has grown the development of equipment has grown alongside it. As discussed earlier bats used in the early years could have been a range of long wooden sticks or axes. As professional baseball took off the baseball bat began to become more unified, in shape and length at least. Players of the day felt the heavier the bat the more distance and force they could extend into the ball. Babe Ruth for much of his early career used a 54oz bat until finishing his career with a 40oz bat; whereas players today use a bat about 31-35oz. According to physicists the optimum weight for a bat is 15-18oz; unfortunately wooden bats cannot be made this light. Bats must also be no longer than 42 inches and primarily made of maple or ash (25). So how can a baseball player and a physicist be so far apart on the optimal weight of a bat? And who’s right?
Figure A

<table>
<thead>
<tr>
<th>Bat Weight</th>
<th>Batted Ball Velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>20oz (0.57kg)</td>
<td>68.5mph (30.6m/s)</td>
</tr>
<tr>
<td>30oz (0.85kg)</td>
<td>76.2mph (34.0m/s)</td>
</tr>
<tr>
<td>40oz (1.14kg)</td>
<td>80.4mph (35.9m/s)</td>
</tr>
</tbody>
</table>

Well they both are, however, early baseball players neglected to factor in swing speed. It’s true that the more the bat weight the further the ball will travel however with a bat weight of 54oz the swing speed is dramatically lower then that of a 18oz bat. Physicist use this equation (Height/3 + 7) for the optimal bat weight for a MLB player (24). Today bats are made to output the best swing weight. Swing weight is the weight of the bat as it is swung, which is engineered to be lighter than the actual bat weight. They do this by distributing the mass throughout the bat as it is swung. As physicists we know this as the moment of Inertia. To examine the swing weight more the rotational aspect of the swing is broken down. Firstly, the rotation of the arm and bat together as a single system begin the swing about the pivot point of the shoulders. Secondly, the rotation of the bat itself about a pivot in the wrists (25).

Figure B

There are three parts to the swing, pull forward, wrist rotation and follow through. The pull forward as seen above is the rotation of the bat-arm system about the pivot of the shoulders, where no wrist rotation occurs. The wrist rotation shown below involves little arm movement and a torque is created by the players’ wrists which rotate 90° to the ball (25).
The follow through continues at the same angle through the ball at the original pivot of the shoulders. By studying the motion of inertia in the swing manufactures have used the equation to calculate just how much Inertia is exerted. \( I = T^2 m g / 4 \pi^2 \) where \( T \) is the time of the swing (7x10^-4) and \( d \) is the pivot to impact point (25).

\[ I = (7 \times 10^{-4})^2 (.145)(9.8)(.7112)/4\pi^2 = 1.25 \times 10^{-8} \text{ kg-m}^2 \]

* \( d \) is calculated from the pivot point to the sweet spot using a 39in bat (pivot at 6inches, the sweet spot at 5 inches in on the bat, so 28 inches= .7112m).

Baseballs have as well developed over the years. Since 1974, all balls must be made with cork or rubber wounded by yarn in a uniformed spherical shape. Cowhide is used to wrap around the sphere, before 1974 horsehide was used. Two stripes, usually red, are stitched tightly over the cowhide. It is written in the Major League rule book that the circumference must be between 9-9.25in and weigh 5-5.25oz. Before the Major leagues laid out ground rules in the early 1950’s balls sometimes were poorly stitched and at times were smaller than others leaving much inconstancies (21).

**A Baseballs Impact on a Bat**

A pitch is thrown with some velocity and the batter happens to be a home run or strike out guy, so we know there is only one thing on his mind, swing as hard as I can and make contact. So what happens to the bat when the ball strikes it? Or even what happens to the ball? How much force is generated when they meet? When a ball hits the bat the ball experiences deformation, the bat experiences some deformation but nowhere near the deformation of the ball. What happens is the energy from the ball is absorbed by the bat causing the “squishiness” of the ball to deform. An example can be seen by figure D. After the ball makes contact with the bat the ball looses speed, which is known as an elastic collision. We can determine the force exerted by using Newton’s second law of motion. The average pitcher in the major leagues throws with a velocity of 90mph or 40.2m/s. The average mass of a baseball is .145kg while the bats mass is 32
oz. A big leaguer swings the bat with a velocity of 48.1 m/s. The amount of contact time is 0.7 milliseconds (22,23) The average force can be determined by the equation:

\[ F = \frac{M_{bat}V_{bat} - M_{ball}V_{ball}}{\Delta t} \]

First the mass of the bat must be converted to the SI unit of Newton (N). 32oz=2lbs x .225N/lb = 0.45N. To fill in the equation we have

\( (0.45)(49.1)-(-0.145)(40.2) = 2327.14 \text{N} \) of average force when the ball make contact with the bat.

0.0007s

The Impulse (Something that changes the momentum of an object, a force acting over some time interval) can be calculated by \( I = F \times t = (2327.14)(0.0007) = 16.7 \text{ N} \)

Since we know we have a collision, we can now calculate the conservation of momentum the ball puts on the bat. The truth is that baseball happens in multiple dimensions but for this calculation well stay in one-dimension. Both the ball and bat have velocities before and after the collision the subscripts a and b will be used to represent these velocities.

\[ M_1V_{1a} + M_2V_{2b} = M_1V_{1b} + M_2V_{2a} \]

For purposes of this problem we will discount the force that the player is putting on the bat because it plays such a small role (22,23,24).

Figure D(22)

The purpose of the conservation is to determine the velocity of the ball after the collision. We need to understand that the ball and bat have both kinetic and potential energy. The kinetic energy can be determined by \( \frac{1}{2}MV^2 \) while the potential energy is a little more challenging to determine it can be represented by \( PE = mg-y \). However, we can assume we know that energy
plays a role in a collision and use the coefficient of restitution (e), which uses the elastic properties with the components of the respective velocities of the bat and ball. Baseballs are engineered to have a coefficient of restitution of 0.55 when the pitch is thrown at 90mph (24).

\[ e = \frac{V_{1e} - V_{2a}}{V_{1b} - V_{2b}} \]

By combining the two equations the velocity of the ball after the collision can be determined.

\[ V_{1a} = \frac{(M_1 - eM_2)V_{1b} + (M_2 + eM_1)V_{2b}}{M_1 + M_2} \]

\[ V_{1a} = 36.8 \text{ m/s} \]

Which tells us that momentum is not conserved after the ball leaves the bat. 40.2 - 36.8 = 3.4 m/s is lost from the ball about 8% of the momentum is lost (24).

**The Forces That Effect Spin and Nature**

There are three distinct forces that effect a ball in flight whether from pitcher to catcher or from batter over the left field wall that effects the ball. The first is well known, that being gravity acting downward at 9.8m/s², as it does on everything. The other two are aerodynamic forces of Drag and Magnus. When a ball is in flight air molecules are randomly bouncing off the ball evoking pressure (force) on different parts of the ball. Since the frictional force is applied to both sides of the ball equally there is no net force and why it is not accounted for. The Drag force, also known as air resistance, is applied as the air molecules collide with the surface of the ball, In effect pushing the ball in the opposite direction. For example, “A fly ball that carries 400ft would carry about 700ft if there were no drag.” For a pitched ball the effect is not as extreme but still an important role. The drag force takes about 10% of the velocity off a pitch from release point to catcher’s glove (27). This means when Ubaldo Jimenez throws his 100mph fastball to a batter it would be going 110mph if no drag force existed. The Magnus force on the other hand takes into account the spin on the baseball and what makes the ball curve. A pitcher like Barry Zito understands this force when he throws his curveball vs. when he throws his fastball. A fastball, because of the Magnus force, opposes the weight of gravity whereas the curveball drops so considerably with gravity. For a hitter, the more backspin they can impose on the ball the longer the ball will stay in flight as it opposes gravity. The Magnus and drag forces are proportional to the density of air. Density of air can be calculated by the equation \( \rho = \frac{p}{RT} \), where \( R \) is the dry air constant 287.05 J/kg-K. This form of the ideal gas law can be used because air molecules are a gas (27).
Altitude plays a direct role of the density of air. The higher the altitude the lower the density as well is the opposite. Humidity is another factor that affects density because it affects the air. Despite what most believe the humidity in the air actual makes the air less dense because a water molecule is less dense than an air molecule. Because the altitude plays a role on density pitches in high altitude will travel faster than at lower altitudes because it lowers the forces on the ball. It is because of this that pitchers must be aware of the Magnus force. Curveballs in altitude will not curve as much and fastballs will break from the strike zone more, making it much harder to command pitches at high elevation. For a ball in flight the altitude will reduce the drag and Magnus force. With a lower drag force applied the ball travels farther, while the reduced Magnus force opposing gravity leaves the ball in the air longer reducing the distance. So which force wins out, because they both can’t? Experiments have concluded that the drag force is greater than the Magnus force. Meaning the Force of the ball in altitude will stay in the air longer and travel farther (26, 28).

The Drag force can be calculated using the equation $F_D = \frac{1}{2} C_D \rho A V^2$ with $C_D$ being the drag coefficient. The Magnus force can be determined by the equation $F_M = \frac{1}{2} C_L \rho A V^2$ where $C_L$ is the lift coefficient. The lift coefficient is approximately the value of $S = R \omega / \nu$ and in many instances is used in place. However, it has been experimentally determined that the value of $S$ changes as velocity increases (28). Since baseball is played at relatively high speeds this causes a problem. As speeds ($\nu$) increase beyond 40mph the two values tend to drift farther apart. Even a Knuckleballer can toss a pitch faster than 60mph; $S$ tends to become an unreliable substitution. It was believed by certain physicists that the equation
\( CL = 2CD/(1 + (\nu/2CD)dCD/dv) \), however, this was later experimentally proven to not be accurate. For now research and experimentation are still searching for exactly how the \( C_L \) lift coefficient and in turn the Magnus force are determined mathematically \((26)\).

*The following calculations are for a 90° day in Phoenix for a ball hit with home run potential*

Drag force: \( F_D = 1/2C_D\rho AV^2 \)  
*drag coefficient constant is 0.3
\[
\rho = \frac{1.01 \times 10^5}{(287.050)(306)} = 1.15 \text{ and } r = 1.45 \text{in} = 0.0368 \text{m}
\]

\[
F_D = 1/2(0.3)(1.15)(4\pi r^2)(36.2)^2 = 3.874 \text{N}
\]

Magnus force: \( F_M = 1/2C_L\rho AV^2 \)  
*assuming that \( C_L = s = r\omega/v \)

\[
F_M = 1/2(0.015)(1.15)(4\pi r^2)(36.2)^2 = 0.193 \text{N}
\]

**Conclusion**

Baseball is a game of tradition and memorable moments and will forever remain America’s national pastime. Since the mid-1800’s baseball is a game neighborhoods and families have enjoyed playing as well as watching. The growth of baseball has not been without its “black eyes” like the black sox scandal to Pete Rose to the recent steroid issues. But like all great things baseball has stood the test of time and built themselves stronger despite setbacks. The Physics of baseball is one that can’t be easily broken down in one paper but the basic principles talked about lay the ground rules of just how important they are. The swing weight of a bat can help a player swing through with more force and more weight than once before. Such subtle differences can change the Inertia of a bat-ball collision to extreme variations. While even the difference of the humidity in Florida or the elevation in Colorado can change the way the ball moves through the air. Players must now have knowledge of all the forces acting on the ball; it could be the difference between the minors or the Pros.
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Satellites: Eye in the Sky
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Abstract

The physics of satellites is a topic that is not often looked upon, due to them being taken for granted. In this paper satellites will be discussed throughout with a strong emphasis on the physics it takes to keep them working. After a brief history of satellites, the paper will explain different types of satellites, orbits, and the how they work and are launched. The laws and equations used to get satellites into orbit and staying in orbit will also be discussed.

A satellite is anything that orbits another body in space. In fact, our moon is a satellite. The satellites we will be exploring in this paper are artificial satellites, or ones that are created and manufactured by man to serve specific purposes. Many of us do not realize that satellites are a fundamental technology that is crucial to the survival of our species. Satellites are one of the most advance pieces of technology in human history, invented in the course of the human exploration of space. The science that allows a satellite to function properly is based on the understanding the physics of motion and gravity. It is because of physics that we can use satellites; and, in turn, allow us to view over 1000 television channels, talk on our cell phones across the globe, get directions to places we have never been to, and support one of the best militaries on the planet. Satellites allow us to communicate and understand our world.

First, let us look back on the history of satellites, the types of satellites there are, and the types of orbits they can be configured to fly.

The first artificial satellite was launched into space by the Soviet Union during the cold war. It was named Sputnik I and was commissioned in 1957. Today, the United States, plus 40 other countries, have launched and operated satellites in space.

For the past 33 years, satellites have been launched into orbit and tracked by the United States Space Surveillance Network (USSSN). This network has monitored more than 26,000 objects in orbit around the Earth, all starting from the Sputnik I satellite and any object greater than 10 centimeters. There are about 3000 satellites in operation and 6000 useless ones in orbit; the latter, we refer to as space junk.

Satellites serve many purposes. They are used in weather forecasting, navigation, cell phone service, information gathering and reconnaissance, photography and scientific imaging, space exploration, and military applications. Most satellites are unmanned and controlled by computer or remotely by humans on the ground. A few satellites, like the International Space Station, the Russian station, Mir, and other space stations in the past are also considered satellites. In addition to these, there have also been a number of satellites placed into orbits around some of the planets and moons in our solar system.

Satellites are one of the most important pieces of technology the world has invented. One reason is, the use of cell phones and other important communication systems. Satellites are the reason we have cell phones. In a nutshell, when we make a call the signal is established with a cellular communications antenna, which routes the signal to a central station and sends the signal to a satellite. That satellite then shoots the signal back down to another central location and routes the signal to another cellular tower that sends the signal to the person you’re calling.

Satellites use a multitude of specialized instruments to accomplish their mission. These instruments, mainly composed of electronics and precision mechanical systems. Without the protection of Earth’s atmosphere, these instruments are exposed to extreme temperature changes, radiation, cosmic rays, and bombardment of particles ranging from dust-size material to larger pieces of space junk.

One of the most common and significant threats to satellite systems and their orbits is solar flares. A solar flare can produce a significant amount of atomic particles that bombard the satellites electronics causing systems to fail. These failures can interfere with satellite communications and
navigation systems causing a satellite to lose its orbital status. A failure to orbital controls can send a satellite spinning out of control and unable to correct its orbit or perform its task correctly. Combined with state-of-the-art technology, satellites can perform these tasks for several years orbiting the planet in the harsh environment of space.

Satellites are made up of a lot of parts; therefore, the more parts the less reliable the system is. When it is not easy to reach Earth's orbit, or send another spaceship and repair something that breaks, satellites have to be designed and made with the upmost precision and care. Mechanical and electrical tolerances must be high, programming of the onboard computers needs to be robust and as error free as possible. Everything must work, or else it is just a piece of scrap metal, falling around the Earth until the orbit decays and the expensive hardware burns up in our atmosphere.

Many satellites, especially communication satellites, are stabilized by using three axis. One axis is facing north, one is facing Earth, and the other points in the direction of the velocity vector, a location inline of the satellite's trajectory. There are three different ways a satellite can maintain its position and trajectory. Orbit is measured and maintained with Sun sensors, Earth sensors, or radio frequency sensors. If errors are found in altitude, they are fixed using wheels with rotational inertia. Of these wheels, there are gyroscopes, momentum wheels, and reaction wheels. Gyroscopes act as motion sensors, momentum wheels move in one direction, and reaction wheels move in both directions. The method these wheels use to move the satellite is by using thrusters on them to exert torque on the axis. Just as thrusters work with rotating wheels to help position the satellite, they also help keep the satellites in the correct altitude.

There being no gravity in space, the fuel for the thrusters may not always be 'floating' near the nozzle that sprays the fuel out of the thruster under pressure. For this, engineers use a bladder to make sure the fuel gets pushed out and not the access air around it. The fuel used is called hydrazine, and is two parts nitrogen and four parts hydrogen. This special fuel does not need to be mixed with oxygen and therefore it is called a monopropellant. The fuel can last relatively long in a satellite. This is because Newton's first law of motion states that a body stays in motion unless acted upon by an opposing force. There being no opposing forces in space, such as air resistance, very little thrust is needed to adjust the satellites position. Satellites are not required to stop in orbit, so while the same amount of thrust is needed to stop it from moving, satellites can get great mileage on a small amount of fuel.

Since there is no air resistance in space, satellites are anything but aerodynamic. Communication satellites are mostly square shaped. There are various instruments attached to the outside of the box-shaped vessel, such as antennae, thrusters, and solar arrays. When the satellite begins its orbit, the solar arrays, which look somewhat like shiny wings, fold out of the sides to face north and south. They rotate so that they are facing the sun as much as possible to charge the system's batteries.

The materials that make up satellites must be light yet strong. The lightness makes them easier to take up into space, but the strength keeps them from braking or bending under acceleration. It also keeps the antennae and arrays rigid and pointing in the correct directions. These materials may be aluminum, magnesium, or titanium. They can also be a mix, or composite, of materials designed to offer maximum strength, light weight, and resistance to the extreme and sudden temperature changes of space.

On top of being made from strong exotic materials, satellites have many other factors that make them reliable. One thing that insures the reliability of satellites are the series of test prior to launch. The launch reliability, including both the launch vehicle and initial operation of the satellite, may be 75% for early launch vehicles and new programs and as high as 95% for mature operations” (access science communication satellites).
There are five types of satellites in use today. Satellites are designed according to the mission they will be used in. There are six main types of satellites: weather, communications, navigation, scientific research, Earth observation, and military.

Weather satellites monitor the Earth’s atmosphere and weather patterns to assist meteorologist in predicting weather and storm forecasts by using sophisticated sensor and imaging systems. Many of these satellites are required to monitor the same location for long periods of time. These satellites are placed in geostationary orbits that allow the satellite to image the same area of land in order to produce a series of images that can show weather patterns and track storm systems. Without these satellites, meteorological studies and early warning systems would not be possible.

Another type of satellite is a communication satellite. These are the satellites that are most commonly used every day by people all around the world. Every time we make a call on our cell phone we are using a communication satellite. “By providing reliable communications among diverse and geographically distant populations, satellites have helped to make the world a global community. Communications satellites represent at least 40% of the total number of satellites and 30% in cost” (Gordon). Most communication satellites use geosynchronous orbits. The geosynchronous orbit means that the shape of the orbit is circular, not elliptical. Another very important part of geosynchronous orbits is that the satellites appear as if they are stationary, because they orbit at the same velocity as the Earth rotates. This makes them ideal for communications because we can trust that there is always a satellite somewhere over us that will pick up our signal. Communication satellites are probably the most useful to civilians. Only because they are the reason we can use our cell phones 24/7, 365 days a year. Communication satellites are also used for satellite TV and many military satellites are communication satellites. "The demands of military missiles and communications drove, and largely funded, the initial development of communication satellites" (Sterling).

Global Positioning Satellites, more commonly referred to as GPS satellites, are favored by many travelers and mapping organizations. One example of a GPS system is Global Navigation Satellite System (GLONASS). Like the United States’ GPS system, GLONASS was developed in the 1970’s. Now available to civilians, these systems were originally developed for military use. Although not the whole system available to civilians, in short, the military gets the better part of the system, which is understandable. “The activity centered on GPS-based products and services has grown rapidly. Development of GLONASS would accelerate the pace of growth of applications, which range from precision landing of aircraft to guiding a motorist in an unfamiliar city” (Misra).

The idea behind any global positioning satellite is that the GPS in your car or in your pocket can find its position by calculating the position of four or more satellite in the sky. The GPS unit measures its distance from the four satellites, and uses an equation to figure out its own position. GLONASS consist of twenty four orbiting satellites. These satellites travel in mid Earth orbits, specifically at an altitude of 25,510 kilometers above earth. They have twelve hour orbit periods. The twenty four satellites are arranged in three orbital planes, so that there are at least four satellites in the sky for ninety nine percent of the world. They are inclined at 64.8 percent. Each satellite transmits two different frequency signals, one for civilians and the other for the military.

Scientific research satellites are the most interesting of all the different types of satellites. Out of these satellites the most common one is the Hubble Space Telescope. Sitting at 569km above Earth, the Hubble telescope does not have to look through the blurry atmosphere, therefore being able to deliver much deeper and clearer pictures of space. The orbit this satellite uses is a low-Earth orbit. This has an orbit period of about 97 minutes. This orbit, especially for a telescope, must be very precise. The reason being is the telescope has to take long exposure pictures. To do this in orbit means to open the lens shutter at the right time at every orbit, to gather light. The orbit has to be the same as it was every
other time so the exposure is the same.

There have been a number of research satellites being put into space lately. Their mission is to search for Earth-like planets across the universe. The term, exo-planet, is used to describe them. Astronomers have different techniques for looking for these planets. Some examples of these techniques are looking for the change in brightness as the planet passes in front of the star, or looking for the tell-tale wobble caused by the orbit of the planet. Astronomers can calculate the mass and diameter of the exo-planet by using orbital calculations to determine this information.

Earth observation satellites perform a number of tasks, from geographical and ecological studies to Internet mapping programs. Earth observation satellites are involved in global warming research such as the National Aeronautics and Space Administration's (NASA) Earth Observing System (EOS). EOS is a coordinated group of polar-orbiting and low inclination satellites used to gather information on the Earth's land masses, atmosphere, oceans, and biosphere over a long-term period. EOS systems are just one of such Earth observation programs that depend on orbital mechanics.

I met with Dr. Ke Chiang Hsieh. He is a professor of physics at the University of Arizona. His research consists of using space probes to study cosmic rays. These cosmic rays he studies in particular are nuclei of Hydrogen atoms. They have had their electrons stripped. Dr. Hsieh uses satellites as tools for his research. This use of them requires knowledge of them to some degree. He must know what instruments he can attach to the satellite that will work in extreme temperatures, such as near the sun or far out in the solar system. Dr. Hsieh would design the instruments to put on the satellites to detect particles. Some satellites he has worked with are, SOHO, Cassini, and a Russian satellite (K. C. Hsieh, personal communication, April 26, 2010).

Ironically, the most commonly known type of satellites are military spy satellites. These are satellites that are used by the military to gather photographic information or intercept radio signals for reconnaissance analysis by various agencies. They are very effective because they are hard to block from gathering information since they are so high up.

There are two main types of spy satellites; ones that listen in on radio signals and some that see using sophisticated imaging systems. The satellites that listen to communications are known as signals intelligence (SIGINT) satellites. The satellites that take pictures are called image intelligence (IMINT) satellites.

Without satellites, nations around the world would not be able to function. Satellites have become a part of the nation’s critical infrastructure ("http://www.osd.dp.noaa.gov/ml/cip.html") and is now governed by policies that require operators and builders of government satellite technology to abide by the directives under the Critical Infrastructure Protection (CIP) program set forth by the United States Presidential Directive PDD-63 in May of 1998.

Satellites can orbit in several different ways. These orbital configurations allow the satellites to perform specialized missions and carry out their intended use high above the surface in outer space.

An orbit can be defined by three factors. The first factor is the shape of the orbit, either circular or elliptical. The second is the altitude of the orbit. Altitude is constant for a circular orbit and changes constantly for an elliptic orbit. The third factor is the angle of the orbit relative to the equator. An orbit that takes a satellite high over the north and south poles, or close to the poles, has a large angle. An orbit that brings a satellite close to the equator has a small angle.

To accommodate their missions, satellites can be launched into various orbits by large rocket engines designed to counteract the pull of Earth’s gravity. The rocket can place the satellite in one of six types of orbit:

1. Low Earth orbit (LEO)
2. Mid Earth orbit (MEO)  
3. Highly Elliptical orbit (HEO)  
4. Geosynchronous orbit (GSO)  
5. Sun Synchronous orbit (SSO)  
6. Polar orbit

The LEO places the satellite just above the Earth's atmosphere between 160-200 kilometers. At this altitude, satellites can experience atmospheric drag. Under 200 kilometers, a satellite can suffer rapid orbital decay from atmospheric gases in the Earth's thermosphere, between 100-500 kilometers. At 500 kilometers, and higher, the exosphere can produce drag on the satellite. The LEO requires the least amount of energy to launch and can be used for astronomical research satellites such as the Hubble Telescope. LEO satellites

Mid Earth Orbits (MEOs), are usually used for Global Positioning Satellites. A medium orbit has a orbital period of around twelve hours. The Global Positioning Satellites are placed in a way that people can use GPS's wherever they are on Earth. They orbit at twenty-thousand kilometers above Earth, in a close to circular orbit. In order for the GPS's to work, at least 4 satellites must be visible in the sky at any one time.

Highly Elliptical Orbits (HEOs) are above geosynchronous orbits. HEOs are not very common but they refer to orbits that have a high altitude apogee and a low altitude perigee. These orbits are relatively rare, but two examples of satellites that use these orbits are, Molniya 1-01 and Vela 1A. Molniya was a military satellite, launched by The Soviet Union, and Vela was launched by the United States.

Geosynchronous orbits, travel right above the equator at around thirty-five thousand, nine-hundred kilometers. If you were to look up at a satellite in a geosynchronous orbit, it would appear stationary because it orbits with the rotation of the earth. Because the satellites in geosynchronous orbits stay stationary relevant to Earth, they make for good weather/meteorological satellites and some communication satellites.

Sun synchronous orbits are great for mapping and scientific research as well as military surveillance. The reason being is, their inclination is ninety degrees. This means that their orbit plane is perpendicular to the plane of Earth's equator. Sun synchronous orbits require small changes every once in a while, with the help of thrusters. These orbits are also, good for carrying scientific research tools that require solar illumination at various angles.

Polar orbits change with the seasons. As the Earth orbits the Sun, polar orbit satellites have possible access to viewing every part of earth. It is almost as if the satellite went around Earth in a horizontal motion as well as a vertical motion. These orbits cross periapsis at the same local time every day, despite changes such as, day light savings.

Orbits can vary in altitudes from 250 kilometers to over 32,000 kilometers. The higher altitude a satellite is in, the longer the orbital period will be. Think of altitude as the radius of a ball, the bigger the radius, the more surface area a ball will have. A basketball has more surface area than a baseball does, so it would take an ant longer to travel around the surface of the basketball then it would a baseball.

Orbits can also travel in the same direction the planet rotates, which would be called direct or prograde orbit. A satellite can also travel opposite of the rotation of the planet, which would be called retrograde. These orbits allow a satellite to maintain its location over a specific target or travel in a specific direction in order to perform its mission.
(Orbital Mechanics)

A satellite's orbit is equally as important as the satellite itself. The orbit provides the platform on which the satellite carries out its mission. Orbital dynamics is the science and mathematics behind placing a satellite in orbit. There are fundamental concepts that are often misunderstood when discussing objects in orbit around a planet, or object of greater mass. Many people believe that an object in space is floating because of the absence of gravity. The fact is, gravity is still a major contributor to an object's orbit. A satellite in orbit is actually falling in a trajectory that is tangential to the planet. This combination of velocity and gravity work together in keeping the satellite from falling directly into the planet. The force of gravity curves the satellite's trajectory and the tangential velocity of the satellite counteracts the force of gravity, allowing the system to reach an equilibrium that allows the satellite to stay in orbit indefinitely.

Most Satellites follow an elliptical orbit. A good way of showing the difference of an elliptical orbit and a circular one is by using conics. A conic is a flat plane that cuts through a cone. For a perfect circular disc would fit somewhere in the cone perpendicular to the axis of height of the cone. Now, if you adjust the plane so it slices the cone at an angle but still follows the curvature of the cone, then that plane becomes an ellipse. If you tilt the plane even more it become a parabola and then a hyperbola.

To further understand the fundamentals of orbiting objects, there are a few things we need to discuss. There are at least six different factors in calculating an orbit mathematically. These factors are, semi-major axis, eccentricity, inclination, argument of periapsis, time of periapsis, and the celestial longitude of the ascending node. All of these factors sound more menacing than what they really represent.
(Orbital Mechanics)

The semi-major axis and eccentricity are the size and shape, respectively, of the orbit's ellipse. The inclination is the angular distance of the of the orbits plane from the equator plane. Argument of periapsis is the angle between the orbit's periapsis, the point where the satellite is closest to the center of the body being orbited and the ascending node, the point where the satellite transfers from north to south on the plane of reference.

The time of periapsis is the time it takes the satellite to travel through the periapsis. The celestial longitude of the ascending node is the angle between the origin of longitude and the ascending node, or point in which the satellite crosses the plane of reference going from south to north.

Although it may seem like there is a lot that goes into the orbit of satellites, many of these degree factors come out to be zero. One example is an inclination of zero degrees, meaning the satellite orbits the planet above the equator and at the same direction of rotation as the planet.

"The simplest and only exactly solvable problem in celestial mechanics is that of one particle moving about another. Since anybody with spherical symmetry looks gravitationally like a point mass from the outside, the results from this problem may be used to describe approximately the relative motion of two finite bodies, such as a planet around the Sun or a satellite around a planet" (Harrington). There are a few scientific concepts that should be defined to fully understand the physics of satellites. These are basic concepts of mechanics such as orbital period, orbital speed, energy, momentum, etc. The first concepts deal with the orbit in specific. They are altitude, orbital radius, orbital period, orbital momentum and orbital speed. Altitude is distance from the surface of the relatively stationary body, in this case Earth, to the satellites. Orbital radius is very similar to altitude. It is the distance from one body's center of mass to the other. In the case of a satellite orbiting Earth, the only difference is that altitude is measured from the surface of Earth, while orbital radius is measured from Earth's core to the satellite. The equation for orbital radius is

\[ r = \frac{mv^2}{F_C} \]

where \( F_C \) the centripetal force and \( m \) and \( v \) are mass and velocity, respectively. This equation only works if the orbit is circular.

Orbital period is next. That is the time period it takes a satellite to complete one orbit. This is represented as

\[ T = 2\pi \sqrt{\frac{a^3}{\mu}} \]

\( T \) is in seconds, \( a \) the length of the orbit's semi-major axis, \( \mu = GM \) the gravitational constant times the mass of the central body. Then the last orbital equation is orbital speed. This is simply the speed at
Running head: SATELLITES: EYE IN THE SKY

which the satellite travels around the mass. Mathematically it is expressed as

\[ v = \text{square root} \left( \frac{m_2 \cdot 2(G)}{(m_1 + m_2)r} \right) \].

The period that a satellite travels at, depends on its orbit. In the majority of cases a higher orbit would mean it takes a greater amount of time to orbit Earth. This is simple to understand because a circle that has a larger radius will also have a larger circumference. The radius would apply to the altitude while the circumference would apply to the path the satellite takes around the Earth. As for orbital speed, using the equation above we see that the higher the radius, or distance from the Earth, less velocity the satellite will have. This is because radius is being divided.

Next, let us discuss the mathematical laws established by Sir Isaac Newton. Not only are they important to satellites and space travel, they are core elements to understanding physics. Newton's laws are a bit more simple in their most basic form. The first law is mainly just an idea. It states that an object in motion or at rest will stay in motion or at rest unless acted upon by an outside force. Simply, if you throw a ball it will never stop, of course on Earth we have friction of the ground and the air putting a force on it that will slow it down.

Newton's second law is that force is a product of an objects mass and acceleration, or \( f = ma \). The third law is like the first law in that it is an idea. All forces have an equal and opposite force. For example, if you push on a wall with 20 Newtons of force, the wall is in fact pushing back at you with 20 Newtons of force. This law is also known as the action-reaction law. These three laws apply to almost all things related to space flight and satellites. The first law is why satellites always circle Earth, because of the second law we know how fast the rocket must be going to leave Earth's atmosphere.

Kepler's laws are also very important to the motion of orbits. With Keplarian motion we can find an equation for elliptical orbits.

\[ r = \frac{p}{1 + e \cos(v)} \]

This is also the mathematical form of Kepler's first law. If you have ever taken a calculus two class, this type of equation may be familiar to you. We can tell by the, \( r = f(v) \), style equation, as well as the \( \cos(v) \), that this is a polar equation. All polar equations are graphed as ellipses. So, to make things easier, think of a planet as orbiting vertically, like a Ferris wheel. Now mentally set the vertical axis of the center mass as the y-axis, or the axis of \( p/2 \), and the horizontal axis as x-axis, or the axis of \( 0 \), and the orbit you are looking at becomes the graph of a polar equation. In the above equation \( r \) = the radius from the orbiting object to the center mass, or the object it is orbiting, and \( p \) = the parameter of ellipse. (The Parameter of ellipse can be found with this equation,

\[ p = \frac{a(1-e^2)}{e}. \]

\( a = \text{the semi-major axis, and } e = \text{the eccentricity. These variables are the same for the elliptical, polar equation.) Finally, } v = \text{the true anomaly, or the degree that the orbiting mass has traveled from } 0. \text{ In a standard polar equation, } v = . \]

All satellites experience a centripetal force. Centripetal force is the force that makes object curve, instead of going straight. In a perfect circle the direction of centripetal force would point exactly toward the center of the circle. Even in an ellipse the direction of force will point towards the center of curvature. Using the idea from Newton's second law, that force equals mass multiplied by velocity, we can put the radius of the circle in the equation, and get

\[ F = \frac{m^2}{r}. \]

This is the basic equation for centripetal force.
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Using many of these calculations, such as thrust, energy, and Newton's laws, we are able to accurately launch a satellite into space. Satellites are launched into space using rockets, otherwise known as launch vehicles. Most commercial satellites ending up in a geosynchronous orbit are first put into a geostationary transfer orbit, or GTO. Unlike the geosynchronous orbit that is round a GTO is elliptical and is the same distance over the equator that it will be in when it is in its final Geosynchronous or GSO orbit. The satellite uses its own thrusters to "fix" its orbit making it more round than elliptical, and thus, a GSO.

What does it take to get into this position? What steps are involved from launching to releasing the satellite from the rocket? Launch vehicles are distinguished by their ISP, or Specific Impulse, measured in seconds. This ISP is used in Tsiolkovsky's rocket equation which determines the final velocity of the rocket as the payload is released into orbit. The equation is, The change in velocity is equal to the effective exhaust velocity times the natural log of the initial mass divided by the final mass, or

\[ \Delta v = v_e \log \left( \frac{m_0}{m_f} \right) \]

There are other variations of this equation. The other variations account for atmospheric friction and launches that have multiple stages of separation. Causing different forces of thrust are the propellants used. They can either be solid or liquid, yet most are liquid. Some liquids are storable liquids, which are exactly what they sound like, liquids that can be stored for long periods of time. These are usually kerosene or alcohol and can also be synthetically produced. They are usually mixed with liquid oxygen as the oxidizer. RP-1, or Rocket Propellant One is a kerosene fuel. It is a common rocket fuel because of its storability, increased safety compared to other fuels and low cost. Other fuels are cryogenic liquids, which are harder to keep stable but last longer because they can have more density in the same volume of storable liquids, and hypergolic liquids, which require no igniter because they ignite when in contact with the oxidizer. Igniting without an igniter makes them more reliable when that is an issue in the mission. There are also solids used as propellants. “The reliance on expendable launch vehicles to lift satellites into orbit will remain at the core of the industry for at least the next few decades” (Novotny).

Hutchinson's Dictionary of Space Exploration depicts launch window as “time span during which a spacecraft can be launched safely and best accomplish its mission trajectory.” (Helicon 412). Launch windows can be very different. They can be as little as an hour or two, or as big as a couple of weeks. If the window is missed, it can take a while for the next chance to take place. This amount of time varies with the mission as well. The launch window is set by various factors including, the weather and the position of the Earth's orbit and rotation. The destination of the mission must also be taken in to account. The other planets in the solar system, as well as our sun have a gravitational effect on Earth orbiting satellites. So, even in the case of launching satellites, that will ultimately just orbit Earth, the launch window must be accounted for. “Launch windows for missions to the planet Mars occur approximately only every 26 months” (Helicon 412).

Satellites are tools that people use every day. There importance to people is drastic and without them our society would not be able to do many of the things we take for granted. So instead of thanking “God" for the food at your table, or for helping you find your way out of a forest, thank the true heroes, the satellites and the ones who built them. It was satellites that researched the weather and the ocean currents that helped get that food on the table and the fish in the oven. And, it was the satellites that picked up your GPS signal.
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Works Consulted.


