14th Annual
Science Symposium
Volume I
May 8, 2008
Paradise Valley College
Foreword

The 14th Annual Science Symposium was held on May 8, 2008. Students enrolled in Organic Chemistry, Biology and Physics from Paradise Valley Community College (PVCC) participated in the event. I want to acknowledge Dr. Casey Durandet and Dr. Jim Doyle for their participation.

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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White Death

Joseph Blackburn CPhT

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April 18, 2008
Abstract

The number of tuberculosis patients is continuously increasing on a pandemic level and this is especially true in countries rich with HIV positive patients. Medical procedures and vaccines for this debilitating disease have not changed in years. The only diagnostic tools are archaic and do not even allow for efficient detection. Tuberculosis is a treatable disease with acute symptoms, an extensive and arduous treatment process, caused by an entity that cannot be seen with the naked eye, and has the capability of becoming drug resistant very easily.

Tuberculosis

Tuberculosis, a deadly and infectious killer plaguing one in every three people around the world, most notably the HIV/AIDS weighed down continent of Africa. [8] Abbreviated TB for tuberculosis and the scientific name of *tubercle bacillus*, it is an increasing and major pandemic problem that is caused by mycobacterium, mainly *Mycobacterium tuberculosis*. [12] This bacterium attacks the lungs, known as pulmonary TB, but other strands can also affect the bones, joints, skin, central nervous system, lymphatic system, circulatory system, and genito urinary system. New infections occur at a rate of one per second, how ever not everyone develops the symptomatic TB, but the latent TB. [3] An even bigger problem has been the rapid rise of multi-drug resistant Tuberculosis that is becoming ever more difficult to cure. It is estimated that nearly one billion people will become infected, 150 million will become sick, and 36 million will die from this disease worldwide between now and 2020. [3] Tuberculosis has plagued mankind for thousands of years and despite advances in medical treatment over those years, TB is still a global pandemic and leader in treatable deaths. Fueled by HIV/AIDS, lack of health services, poverty, and the emergence of drug resistant strains; tuberculosis is making an unwelcomed comeback. [6]

History/Other names

Tuberculosis has been around since the ancient times. TB has gone by several names, but the most common before the disease was classified was consumption, because it seemed that the people were consuming themselves from the inside with a bloody cough, fever, and pallor. Other names include phthisis, scrofula, lupus vulgaris, Potts disease, White Plague and the White Death. [12] The earliest known detection of tuberculosis was in bison remains dated 18,000 years ago. The earliest known human case was identified in Egyptian mummy remains dating to 4,000 B.C. The first physician to identify TB was Ibn Sina, in 1020 A.D. when it was written thoroughly about in The Cannon of Medicine. He diagnosed it as a contagious disease and used the method of quarantine in order to limit the spread of tuberculosis. This deadly disease was not dubbed ‘tuberculosis’ until 1839 by J.L. Schonlein. [12] *Mycobacterium tuberculosis* was identified and described by German Physician Dr. Robert Koch on March 24, 1882. He later received the Nobel Prize for his work in the field of physiology or medicine. [10] Every one in four deaths in England in 1815 and one in six deaths in France in 1918 were attributed to tuberculosis. It has been estimated that this deadly disease murdered 100 million people in the 20th
century. In 1916 tuberculosis patients in England were urged to go to sanitary institutes for their clean air and environment. Fifty percent of those who entered were dead within five years. After the introduction of the antibiotics it appeared that Tuberculosis was a thing of the past and could possibly be eradicated worldwide, until the evolution of HIV/AIDS came to be in the 1980's. The resurgence of tuberculosis resulted in the declaration of a global health emergency by the World Health Organization (WHO) in 1993 and the crisis is getting steadily worse. \[12\]

**Mycobacterium Tuberculosis**

*Mycobacterium tuberculosis* yields from the Kingdom Bacteria, Phylum Actinobacteria, Order Actinomycetales, Family Mycobacteriaceae, Genus Mycobacterium, and Species *M. Tuberculosis*. MTB is an obligate aerobe, which is why it thrives in tissues with high oxygen content, such as the lungs. \[11\] In order to see the bacteria under the microscope, MTB requires the acid-fast stain. MTB is classified as an acid-fast gram-positive bacillus bacterium primarily due to their lack of phospholipids on the outer membrane. The reason the gram stain is weak on the bacteria is because of the high lipid and mycolic acid content of its cell wall making them impermeable to the Gram stain. The acid-fast stain dye contains phenol, which allows for the bacteria to be stained and the bacteria is a bright red color on a blue background. \[12\] MTB divides very slowly at a rate of once every 16 to 20 hours. Compare this to Escherichia Coli, which divides at a rate of once every 20 minutes. This is the primary reason why patients must take antibiotics for almost a year in order to kill all the bacteria. This bacterium is very hearty in that it is resistant to weak disinfectants and can survive in the dry state for weeks. *Mycobacterium* is a non-motile, rod shaped bacteria that are found in habitats rich in water and soil. It is believed, but not proven that MTB jumped from animals to humans when cattle were domesticated and drinking their unpasteurized milk between 8000-4000 B.C. \[10\]

**Transmission**

Tuberculosis is a contagious disease that is transmitted when a person suffering from active pulmonary TB coughs, sneezes, speaks, sings, or spits. \[3\] For example a sneeze can expel an infectious aerosol of 40,000 droplets that are each 5 micrometers in diameter and hold the pathogenic bacterium known as *Mycobacterium tuberculosis*. \[12\] The inhalation of just one droplet can cause a respiratory infection and yield either active or latent tuberculosis. The sputum can linger in the air for hours, depending on the environment. Several factors go into the transmission of TB, such as the virulence of the strain, effectiveness of ventilation, duration of exposure, and the amount of sputum dispersed by the carrier. Tuberculosis is not spread through shaking hands, sharing food or drink, touching bed linens, sharing toothbrushes, or kissing. \[12\] Just because a person inhales the bacterium does not mean that it will cause disease. The immune system walls off the bacilli, which provide for a thick waxy coat, and then can lie dormant for years. Prolonged, intense, or frequent contact with someone who has TB increases his or her rate of contracting the disease. An average person with active and untreated tuberculosis typically infects ten to fifteen people a year. Risk areas that make someone susceptible to contracting Tuberculosis are: people who use illicit drugs, low income populations,
places where clinics and treatment are not available, health care workers, ethnic minority populations, and people suffering from immunocompromised conditions. After two weeks of isolation and treatment of the non-resistant TB with antibiotics, the patients tend to cease to be contagious.

Pathogenesis

The tuberculosis infection begins when the *Mycobacterium tuberculosis* reach the alveoli in the lungs, where they invade and replicate within alveolar macrophages yielding pneumonia also known as a local lung infection. Macrophages begin to surround the tuberculosis in the lungs and form scar tissue (fibrosis) over the wound. The bacteria may remain alive encapsulated in the macrophage for years and be in the latent phase, but the patient will not feel any symptoms or be contagious. The scar tissue and lymph nodes may harden due to the process of calcification of the scars. Sometimes immune defenses fail and the TB bacteria will begin to attack the macrophages and replicate inside the macrophages known as secondary tuberculosis or reactivation TB. Over time the centers will liquify and break through the granulomatous wall. The breakthrough of bacteria can result in pneumonia and spread to other organ systems of the body. In many patients the infection is an ebb and flow process. Necrosis and tissue destruction are offset by healing and fibrosis. When the tuberculosis has become active, some of the bronchi and cavities are joined giving rise to the material being coughed up. This is how the living bacteria are spread to others and become able to create an infection. Treatment with antibiotics kills the bacteria and then healing of the lung tissue can take place. After the treatment, the affected areas are then replaced with scar tissue.

Signs/Symptoms

When the body is infected with MTB, the immune system can often prevent a patient from developing symptomatic tuberculosis. A doctor is able to make the distinction between Active TB and Latent TB. Latent TB is when a patient has a positive test and is infected with the tuberculosis bacteria, but has no symptoms and is not contagious. Active tuberculosis is pathogenic and makes the patient very ill. The signs and symptoms of an active pulmonary tuberculosis patient are a cough lasting three or more weeks that may produce thick, cloudy, and sometimes bloody sputum from the lungs. Systemic symptoms include unintended weight loss, chills, night sweats, fever, rapid heartbeat, swelling in the lymph nodes of the neck, pallor, fatigue, malaise, loss of appetite, and pain when breathing or coughing. When the disease becomes active, 75 percent of cases are pulmonary TB. In the other 25 percent, the infection moves from the lungs to other sites of the body including the central nervous system called meningitis, the lymphatic system called scrofula of the neck, the genitourinary system called urogenital tuberculosis, bone and joints called Potts disease of the spine resulting in back pain and joint destruction, and tuberculosis of the kidneys which yield blood in the urine. These kinds of infections tend to occur in children and the immunosuppressed. An especially serious form is miliary tuberculosis, which can also be known as disseminated TB. Miliary tuberculosis causes lesions in the lungs and is almost always fatal unless treated and even then it still has a 25 percent rate of causing death.
When a patient has developed the aforementioned symptoms then a medical doctor, preferably a Pulmonologist or infectious disease specialist needs to run tests and diagnose the patient. The diagnosis can be done in several ways, including a complete medical evaluation, a physical examination, skin tests, chest x-rays, and analysis of the sputum. Tuberculosis is a very difficult disease to diagnose and needs several tools to confirm the active infection primarily due to the fact that it is a very slow growing bacterium. The most common diagnostic tool to test whether a patient is infected with *Mycobacterium tuberculosis* is called the Mantoux tuberculin skin test. A 0.1 ml of tuberculin purified protein derivative, PPD, is injected into the hyperdermic layer of the inner surface of the forearm. The injection is to be done with a tuberculin syringe with the bevel of the needle facing upward. When done correctly the injection produces a pale elevation of the skin that is six to ten millimeters in diameter to see the results. The patient must return within 48 to 72 hours after administration of the PPD.\textsuperscript{10} If the patient fails to return then the procedure must be repeated. The reaction is measured across the forearm in millimeters of the indurated area. A positive reaction would yield a palpable, hardened, and raised area at the injection site, but do not measure the erythema or redness of the skin. While no reaction at the injection site means a negative test for TB. The skin test is dependent on two factors of the measurement in millimeters of the induration and the patients' risk of being infected with tuberculosis. The classification of a positive Mantoux tuberculin skin test is divided up into three categories. The first is an induration five or more millimeters, which is considered positive in the following patients. HIV infected patients, patients with organ transplants, a recent contact with a person with active TB, and patients who are immunosuppressed from other diseases. The second is an induration of ten millimeters, which is considered positive in the following patients: injection drug users, recent immigrants from high prevalence areas, residents and employees of high risk settings, Mycobacteriology laboratory personnel, and children under four years of age especially with those exposed to high risk adults. The third is an induration of fifteen or more millimeters is considered positive in any person who holds no risk factors for tuberculosis.\textsuperscript{12} The unpleasant entity about the Mantoux test is that it is possible to have a false-positive or a false-negative test. A false-positive is when the patient reacts to the TST even when they are not infected with MTB. Some causes of false-positive reactions are a previous bacillus Calmette-Guerin vaccination, an infection with non-tuberculosis mycobacterium, incorrect test administration, incorrect interpretation of reaction, or incorrect bottle of antigen used. Even though the latter half of these are unlikely to happen in a medical setting the reality is that they do. A false-negative test typically yields from some people not reacting to the TST even though they are infected with MTB. Some reasons for this result would be a recent attenuated vaccine, a viral illness, very old tuberculosis infection, a recent tuberculosis infection that is within eight to ten weeks of exposure, or the possibility that the patient is infected with an overwhelming amount of tuberculosis that the body is not able to fight the injection enough to produce a positive test. If a patient seeks to get the Mantoux test they need to wait at least one month after a smallpox or any other attenuated vaccination. Another test that is making ground in developing countries is called microscopic-observation drug-
susceptibility (MODS). MODS is a very reliable and accurate method with results in as little as seven days. This test relies on the sputum sample of patients to detect the presence of *mycobacterium tuberculosis*. Another test to diagnose TB is called the Polymerase Chain Reaction, PCR, in which it detects the genetic material of the bacteria. The test is extremely sensitive and specific. Results can be obtained within a couple of days. The Mantoux tests only if a patient has been infected with the tuberculosis bacteria, but does not indicate on whether the infection is active or latent. If a patient tests positive for TB, then further tests are necessary to confirm the infection and see whether it is an the active stage. Tests include chest x-rays and culture tests. For an active TB, the x-ray will show white spots where the immune system has walled off the bacteria or it may show cavities in the lungs caused by the active TB. The chest x-rays can also reveal evidence of active tuberculosis pneumonia and may show fibrosis (scarring) or calcification (hardening) in the lungs. Culture tests are evaluated when the sputum is tested for the tuberculosis bacteria for 3 consecutive mornings. It is cultured on a selective medium, known as Lowenstein-Jensen medium or Middlebrook medium, that encourages the growth of the bacteria, where it is then tested on by antibiotics to see if they respond to the treatment. Depending on which antibiotics work the best will determine which medications are to be prescribed to the patient.

**Latent/Active TB**

Not everyone who becomes infected with *mycobacterium tuberculosis* becomes ill. Two conditions result from this circumstance. In Philosophy the law of excluded middle says that it must be either A or non-A; this law applies to a latent TB infection and an active TB disease as that it can only be one or the other, but not both at the same respect in time. A latent TB infection exists when Tuberculosis is in the body but does not make the patient sick. The latent TB patient has a skin test result of a positive TB infection, a normal chest x-ray, and a negative sputum test. The bacteria in the body are alive, but inactive and cannot be spread to others. A latent TB patient should still seek treatment to prevent the active TB disease from developing. A patient with active tuberculosis has a positive skin test indicating a tubercular infection, abnormal chest x-ray, and/or positive smear or culture. The patient is contagious and has the ability to spread the pathogen to others. The patient will show the signs and symptoms as previously mentioned and will need a rigorous course of antibiotics as treatment for up to a year.

**Treatment**

Once the pulmonary tuberculosis has been diagnosed then the doctor will prescribe a series of medications. It is essential that all the medication be taken over the course of the treatment. Before medications, patients in the 20th century were sent to sanitariums where there was cold, clean air, enforced rest, and copious amounts of food that were believed to cure the disease. This process helped minimally, but it was not until the correct antibiotics came around that the *Mycobacterium tuberculosis* was on its heels. Typically patients take medications for six to twelve months to completely destroy the bacteria. The length of treatment and exact drugs depend on if the patient has active or latent TB, age, overall health, and results from the tests completed by the doctor.
are four main types of medications that are prescribed as the first line of defense for pulmonary tuberculosis patients: Rifampin, Isoniazid, Ethambutol, and Pyrazinamide. \[6\] In the initial treatment and in any retreatment of pulmonary tuberculosis, Rifampin must be used in conjunction with at least one other tuberculosis drug. Rifampin capsules a semi-synthetic antibiotic derivative of rifamycin B that comes in 300-milligram capsules for oral administration. \[2\] It inhibits DNA dependent RNA polymerase activity in susceptible cells. This is the mechanism of action by which Rifampin exerts its therapeutic effect. The biological half-life in the blood is approximately 3 hours. Elimination occurs mainly through the bile and to a lesser extent, urine. Peak blood levels in normal adults typically occur between two and four hours following the oral administration of a 600-milligram dose. Rifampin should be administered once daily, either one hour before or two hours after a meal. Adults are recommended to take 600 mg (2 capsules) in a single daily administration. Children five years and older the prescribed dosage is 10-20 milligrams per kilogram. Data is not available for children under five years of age and is not recommended. Rifampin has alcohol, methyl, and amine groups, carbonyls, benzene rings, chiral carbons and enantiomers in its extremely large molecule. Rifampin has a scientific chemical name of 3-[[4-methyl-1-piperazinyl]imino]methyl] rifamicin. The drug is slightly soluble in water, freely soluble in chloroform, and soluble in ethyl acetate and methanol. Its molecular weight is 822.95 g/mol. \[2\]

The other major medication in the first line defense that is used to treat tuberculosis is Isoniazid (INH). Isoniazid is used to treat or prevent a TB infection. The mechanism of action occurs when INH inhibits the synthesis of mycolic acids, an essential component of the bacterial cell wall. In therapeutic levels Isoniazid is a bactericidal agent against active growing intracellular and extracellular Mycobacterium tuberculosis organisms. INH is chemically known as isonicotinyl hydrazine or isonicotonic acid hydrazine. It has an empirical formula of C<sub>6</sub>H<sub>5</sub>N<sub>3</sub>O and has a molecular weight of 137.14 grams per mole. This molecule has two amine groups and a carbonyl group as substituents. Isoniazid peaks in the blood one to two hours after consumption and its half-life is six hours. Typical dosage for adults is 5 mg/kg up to 300mg daily in a single dose. Children are able to take 10-15mg/kg and also up to 300 mg daily in a single dose. \[9\]

In cases of the latent tuberculosis patients, doctors recommend a preventative drug therapy to destroy dormant bacteria that may become active in the future. Treatment typically is a daily dosage of Isoniazid for six to nine months. Active tuberculosis
patients typically will receive a cocktail of medications. The previously four stated medications of Isoniazid, Rifampin, Ethambutol, and Pyrazinamide are used in different combinations according to the results of the lab tests. One drug called Rifaxil contains Rifampin, Isoniazid, and Pyrazinamide making it easier for patients to take their medication and is less confusing. Side effects of tuberculosis are not common, but when they do happen can result in grave illness. Treatment using Rifampin and Pyrazinamide are not risk free and the Center for Disease Control notified health professionals against this medication combination because of the high rates of hospitalization and death from liver injury during treatment with these medications. Liver damage from Isoniazid is rare and in older adults, INH hepatitis can even be fatal. Patients should also be advised against the use of Acetaminophen as it will cause further liver damage, even life threatening liver disease hepatitis. Doctors need to be sure to monitor blood tests, called liver function tests, during the course of Isoniazid therapy. Side effects from tuberculosis prescribed medications include: fever, chills, loss of appetite, jaundice, blurred vision, colorblindness, nausea, vomiting, malaise, rash, and muscle pain among others. Some patients will feel numbness and tingling in their extremities referred to as peripheral neuropathy from the medications and therefore Vitamin B6, pyridoxine, is commonly prescribed. Taking INH is not advised in pregnant patients or those suffering from liver disease or alcoholism. Mycobacterium tuberculosis replicates at a very slow rate of once every twelve to sixteen hours, therefore treatment of an active inflection is lengthy, typically six to twelve months, but sometime can be years. After a few weeks of antibiotic treatment the bacteria is no longer pathogenic and the patient should start to feel better. As with all antibiotics it is essential that the full course of therapy and medications be completed, especially with tuberculosis. If a patient stops taking the medication early or skips doses then this will create drug resistant strains that are often quickly fatal and not easily treatable. Efforts to help people stick to their regimen have been made and in some states it is mandatory that care provider’s check with the patients on a daily basis. Some doctors and clinics have used a program called direct observed therapy short course, or DOTS for short. In DOTS a nurse or other health care professional administers the medication on a daily basis to make sure the patient completes the full course of treatment. The main four drugs are taken for the first two months of therapy to kill any TB bacteria then the regimen is usually reduced to two medications based on what the doctor recommends. Undergoing treatment for such a long time, some patients can become discouraged, angered, and go into denial that they could be dealt with this disease. Doctors often refer patients to therapists or behavioral psychologists to help them deal with this long and arduous process in their lives. As a last possible resort surgery on the lungs may be appropriate when medication has failed, but this practice is very rare. Treatment with appropriate antibiotics will typically cure patients of their disease as long as they stick to the daily regimen.

Complications

If not diagnosed and treated early then pulmonary tuberculosis can cause permanent lung damage. The active disease can also travel to other systems of the body and cause life threatening complications. Meningeal tuberculosis occurs the mycobacterium
tuberculosis infects the brain and central nervous system. As stated previously, miliary TB occurs when the Tuberculosis bacteria spreads throughout the entire body in which children are extremely susceptible and almost always results in death if not diagnosed and treated rigorously. The most dangerous form of the disease is the recurrence of Tuberculosis after the initial infection, due primarily to the patient not finishing the full course treatment, and therefore yielding to the development of drug resistant strains of the disease. Those who do survive and did not seek medical attention typically develop chronic, debilitating symptoms, such as chest pain and a cough with bloody sputum.

Drug Resistant TB

The emergence of drug resistant tuberculosis has become an ever-increasing problem in the last three decades primarily due to poor patient compliance and HIV patients. Drug resistance is caused by inconsistent or partial treatment, when patients do not take all of their medications because they feel better, or doctors prescribe the wrong treatments. Multi-drug resistant, MDR, TB is referred to as organisms that are resistant to at least two of the first line drugs, Isoniazid and Rifampin. MDR TB is generally treatable, but requires extensive chemotherapy for up to two years and second line antibiotics, which are more expensive and have harsher side effects than the first line antibiotics do. MDR TB also is estimated to cost as much as 1.5 million in direct medical expenses and productivity losses. Extensively-drug resistant tuberculosis (XDR) is a strain of TB that is extensively resistant to first and second line drugs. XDR is resistant to Isoniazid, Rifampin, any Fluoroquinolone, and at least one of the three injectable second line drugs in kanamycin, capreomycin, and amikacin. XDR is twice as expensive as MDR TB, have more side effects, and the patient is most likely to die. XDR is rare in the world and is primarily seen in Southeast Asia, Sub-Saharan Africa, and the Soviet Union. Successful outcome depends on the extent of the drug resistance, severity of the tuberculosis, and whether the patient’s immune system is already under distress. The emergence of XDR TB has led to concerns that there may be one day an extreme pandemic in which patients contract a virtually untreatable tuberculosis disease.

Vaccine

Bacille Calmette-Guerin, BCG, is an attenuated vaccine that is given to patients around the world, especially in developing countries, in order to try and prevent TB. Developed in the Pasteur Institute in France in the early 20th century the vaccine was not used for mass vaccination until post World War II. BCG has been widely disputed as an effective vaccine in many countries, none more than the United States. BCG often causes confusion among test administrators as showing false-positive results for tuberculosis. BCG is not recommended in the United States unless patients meet certain criteria, for example AIDS patients.

Epidemiology

Tuberculosis is the leading infection disease cause of death and represents more than a quarter of the world's preventable diseases. According to the Center for Disease Control
and Prevention, CDC, nearly one in every three people in the world is infected with *Mycobacterium tuberculosis*. About two million people die from tuberculosis around the world every year and another eight million are infected with this deadly bacterium. The World Health Organization, WHO, reports that the largest number of new cases in 2005 occurred in the South-East Asia region, which accounted for 34 percent of incident cases globally. Sub-Saharan Africa has been hit the hardest by the disease, occurring at a rate of 350 cases per 100,000 persons. Africa also holds the highest number of deaths and mortality rate per capita, primarily due to lack of resources; i.e. medical facilities, medications, and medical personnel. In the United States ten to fifteen million people are infected with tuberculosis and there are 22,000 new cases each year.

![Global Incidence of TB](image)

The annual incidence rate ranges from 350 per 100,000 in Africa to 41 per 100,00 in the Americas. In 2005, the country with the highest incidence of TB was Swaziland with 1,262 cases per 100,000. India had the largest number of new infections with over 1.8 million. The United States has a TB case rate of 5 patients per 100,000. Tuberculosis is the greatest infectious killer of women of reproductive age and the leading cause of death among people with HIV/AIDS. The following global picture shows the TB incidence rate per 100,00 persons in 2005. Red indicates greater than 300, orange is 200 to 300, yellow is 100 to 200, green is 50 to 100, blue is less than 50, grey is not applicable for reasons undefined.

HIV and TB

Treating patients who are co-infected with tuberculosis and HIV in a world where 30 percent of the 40 million AIDS patients are infected is a particular challenge. HIV positive patients are more likely to develop the resistant strains of Tuberculosis and TB is the leading cause of death in HIV/AIDS patients. HIV is the single most factor on the resurgence of tuberculosis, especially drug resistant tuberculosis, in the last 25 years. Without immediate treatment most people co-infected will cease to exist in a matter of months. Tuberculosis is an opportunistic infection that thrives in AIDS patients. The most powerful AIDS medications, called protease inhibitors, interact with the tuberculosis medications reducing the effectiveness of both the medications. To avoid
the interactions patients have been known to stop taking their protease inhibitors in order to complete a short treatment of TB antibiotics.

Prevention and Elimination

The prevention and elimination of tuberculosis is crucial in maintaining the wellness of the world's future. Doctors, health professionals, and community leaders need to maintain control, educate the community about TB, accelerate the decline of the disease, develop new tools for diagnosis, treatment, and prevention. Also they need to engage in global TB prevention and control, monitoring progress of patients' treatments, and reach leaders of high-risk groups especially in other countries. Providers should also ensure the implementation of infection control procedures to prevent exposure to TB in their clinics, offices, and hospitals. Patients need to keep their immune system healthy, get tested regularly especially if they are at risk of becoming infected, consider preventative drug therapy, stay home, ensure adequate ventilation, cover their mouth, and most importantly finish the entire course of medication.

Conclusion

*Mycobacterium tuberculosis* does not care about race, creed, religion, sex, color, marital status, or how much money you make. MTB will infect one in three people and chances are that you have or will contract the bacterium. Whether the infection becomes active or is walled off and goes into a latent phase is yet to be determined. Tuberculosis is a very serious disease that kills millions every year and unfortunately is making a comeback in the form of drug resistant TB. Patients, Doctors, and community officials need to be aware of the consequence of this deadly disease and take proactive action. The spread of tuberculosis can be controlled, but it is up to the infected patient and their doctor on whether they will take immediate action and see the treatment to the end.
   http://lungdiseases.about.com/od/choosingtreat4/a/TB_drug_treat.htm


   http://www.lungusa.org

   http://www.cdc.gov/tb/pubs/nowisthetime/default.htm

   http://doctorswithoutborders.org/news/issue.cfm?id=2404

   http://www.mayoclinic.com/health/tuberculosis/DS00372

   http://www.nlm.nih.gov/medlineplus/tuberculosis.html#cat22


    http://www.nmhct.nhs.uk/pharmacy/inoa-proc.htm

    http://www.webmd.com/a-to-z-guides/tuberculosis-tb-topic-overview

    http://en.wikipedia.org/wiki/Tuberculosis
Trichloroethylene: The chemical & physical properties, uses, health concerns, exposure and regulations.

Devon Boyne
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Abstract

Throughout the industrial age many contaminants have been released into the environment that propose certain health risks to the general population. It is difficult to determine what effects these chemicals have had on human beings. Vigorous studies of specific contaminants have led to inconclusive results. Several factors can be attributed to this lack of definition; one being the comparison of humans to “lab rats”. It is also difficult to attribute one single cause to disease and carcinogens in human beings. A chemical exposure may not even be considered due to the fact that there is no easily accessible way for current health systems to receive data on exposure outcomes (1). This is an in depth report of one of these chemicals, trichloroethylene (TCE).

Trichloroethylene: The chemical & physical properties, uses, health concerns, exposure and regulations

Additional Names for Trichloroethylene (TCE):
acetylene trichloride, ethylene trichloride, ethyl trichloride and 1,1,2-Trichloroethylene (2).

Chemical and Physical Properties

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<tr>
<td>Molecular Weight</td>
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<tr>
<td>Density</td>
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Boiling Point 87.2 degrees Celsius
Melting Point -84.7 degrees Celsius
Vapor Pressure 77 torr @ 25 degrees Celsius
Vapor Density 4.5 (air=1)
Solubility Soluble in alcohol, ethers, petroleum distillates and other halogenated solvents
Conversion Factor 1 ppm = 5.37 mg/m^3 @ 25 degrees Celsius

(retrieved from Chronic Toxicity Summary (3))

**Intro**

Trichloroethylene is an organic volatile liquid (4). That is, it can evaporate at a normal temperature and pressure. This colorless liquid has a sweet odor that is comparable to chloroform (4). This chemical is mostly insoluble in water but soluble in many organic substances (2). There are two techniques that can successfully produce this haloalkene. The first process involves reacting ethylene dichloride with chloride which produces two products, trichloroethylene and tetrachloroethylene (5). These products would then require additional treatment in order to be separated. The more favorable way to produce trichloroethylene is a one step process called oxychlorination of ethylene dichloride (5). This produces the desired product and water molecules; which forms two layers and are easily separated. Other forms of synthesizing this chemical exist but are less commonly used (2).

Oxychlorination of ethylene dichloride:

\[
\text{Cl}_2\text{CCH}_2\text{Cl} + \text{HCL} + \text{O}_2 \rightarrow \text{ClHCCCl}_2 + 2\text{H}_2\text{O}
\]

Today, trichloroethylene has many uses in the industrial economy due to its chemical and physical properties. It has been in use for over a century. There are many health concerns associated with TCE and several ways that a person can become exposed. The Environmental Protection Agency currently regulates and controls this substance’s release into the environment and atmosphere. Per year, it is estimated that over 291,000 lbs of TCE are used within the United States (2).

**Uses**

Use of the chemical, TCE, began in 1864 (2). Presently the majority of the
trichloroethylene used in the United States is employed in the industrial field. In the early 90's the use of TCE fell but since then has been steadily increasing (5). There are six grades of Trichloroethylene sold in the United States; neutral inhibited vapor–degreasing, alkaline amine-inhibited, extraction grade, formulation grade, paint application grade and high-purity, low-residue grade (2). Trichloroethylene is primarily used during metal cleaning and degreasing operations, both in the liquid and vapor phase (5). It has low flammability, high stability, low specific heat and is non-corrosive (5). These properties make it an excellent solvent for degreasing during the preparation of metal parts (5). Another, secondary use of trichloroethylene is during the production of polyvinyl chloride, insecticides and pharmaceuticals (5). During this process it is used as a chemical intermediate, that is, it is present during the reaction but not in the final product. Trichloroethylene’s chemical properties make it a more ideal solvent during these processes than other chemicals.

To a lesser extent, trichloroethylene is also present in commercial products. It can be found in household items such as paint removers, adhesives, lubricants, varnishes and household cleaners (6). Trichloroethylene can also be used as an effective insecticide and disinfectant (2). Just as it can be used in industrial field, TCE can also be used commercially for metal cleaning.

There have been several different uses for trichloroethylene in the past that are now discontinued. Before 1970, trichloroethylene was used in food processing as an extractant (2). TCE will extract such things as caffeine from coffee, oils from olive, soybeans and maize among others (2). At certain exposures, trichloroethylene can cause a person to become unconscious and at one time was used as an anesthetic (6). These applications of trichloroethylene are no longer an acceptable means to obtain the desired outcomes.

**Human Health Concerns due to exposure**

There are several health concerns associated with the chemical Trichloroethylene. When this haloalkene is metabolized in the body it can form several compounds found to be toxic to humans; such as, chloral hydrate, trichloroacetic acid, dichloroacetic acid and trichloroethanol (8). However, because experimenting on human beings is unethical most studies have been conducted on animals. There have been some studies involving humans, but the exposure amount has been significantly less on humans than on lab animals. There are three main areas in the body that have shown negative effects due to exposure and been extensively studied: the central nervous system, the liver and the kidneys (6). Exposure to this chemical may also impair fetal development during pregnancy and have subtle to severe effects on the lungs (7). There is very little information available concerning these specific effects. Lack of exposure data on this chemical leads to inconclusive results. But, dependant on the amount a person or animal is exposed to TCE, there is undoubtedly a concern.

**Effects on the Central Nervous System:**

It is shown through human and animal studies that acute exposure to trichloroethylene has mild to severe effects on the central nervous system; at high levels of exposure even causing death (8). The effects of chronic exposure at low levels include dizziness, headache, drowsiness, nausea, confusion, exhaustion, and blurred vision (8). One study on human subjects involved a group of people who were voluntarily and purposely exposed to the chemical at 110 ppm (6).
The group experienced two four hour periods of exposure separated by a one hour and a half period of non-exposure (6). The subjects of the experiment were reported to have a reduced performance on tests of perception, memory, reaction time, and dexterity (6). Another study observed that humans who were exposed to 27 ppm in a four hour time period experienced drowsiness (6). It was then reported that increasing the exposure to 81 ppm caused the subjects to acquire a headache (6).

Occupational studies of people exposed to trichloroethylene have yielded similar and more severe results. One study conducted in 1955 involved workers at an industrial company that had been exposed to the chemical for approximately 3.75 years (6). The workers who were exposed to trichloroethylene at about 85 ppm experienced vertigo, headaches and short term memory loss (6). When compared to those who had been exposed at a lower part per million, it was found that the symptoms occurred more often with the people experiencing a higher rate of exposure (6). Still another study, in 1973, where workers were exposed to a vapor emission of TCE at about 32 - 78 ppm recorded effects ranging from eye irritation and drowsiness to heart palpitations and dizziness (3).

Studies done on animals closely mirror the effects experienced in human subjects. Exposure has been shown to cause disturbed sleep cycles in rats (6). Like in humans trichloroethylene force fed to rats at higher concentrations has effects on the central nervous system similar to that of an anesthetic (6). The short term effects of trichloroethylene at a low exposure have the most conclusive results because there is the availability to study subjects who have been occupationally exposed.

Effects on the liver and kidneys and carcinogenetic Effects:

Currently, the major concern with trichloroethylene is the possibility of it causing cancer in human beings. Animal testing has shown that this concern can be localized specifically to the liver and kidneys. There are a few biomarkers which associate this chemical with cancer; however they are not specific to TCE (1). It is theorized that it is not the actual chemical that causes cancer but the pathways it follows as it is metabolized through the body (1). As with other toxins, age, eating habits, respiratory ventilator rates along with other factors may have a role in human susceptibility (6).

The inhalation or oral consumption of trichloroethylene can lead to the formation of tumors in the liver. A 30 day study involving rats in 1983 found that as the exposure to the chemical increased there was a significant increase in the liver weights of the animals (3). This indicates the possible presence of some sort of tumor growth. However, following a rehabilitation phase, the liver weights decreased and returned to a size comparable to that of an unexposed control group (3). There have been several other studies that have observed similar increases in liver weight. One in particular, which again progressed for 30 days, found through interpretation of a concentration-effect curve that even at a lower concentration the liver was still effected (3). It has been observed that force feeding the animals trichloroethylene has more severe effects on the liver than exposure through inhalation (8).

Though limited, human subject studies have found there may be a link to liver problems and TCE. Liver function tests administered on a group of people occupationally exposed in 1984 showed abnormal results (3). One specific case in this test group experienced liver failure among other effects associated with TCE (3). Tests show that TCE does have effects on the human
liver, but is not yet directly linked with liver cancer.

Nephrotoxicity is also a major concern with trichloroethylene. Nephrotoxicity is the poisonous effect a substance, either medication or chemical toxin, has on the kidneys (9). It is possible that exposure to TCE may cause tubular degeneration in the kidneys, even going as far as to cause cancer (1). One method of determining danger to tubules is testing urine for an excess of serum proteins (1). A high concentration of proteins in the urine, called proteinuria is a proven sign of kidney damage. A six month study in which rats were exposed to the chemical by inhalation detected proteinuria (1). Other studies followed which found similar results.

Another possibility associated with nephrotoxicity and TCE is the appearance of formic acid. This again is tested through urine samples (1). This chemical is not the direct cause of formic acid. TCE actually causes a depletion of B(12) which in turn causes depletion of folate and allows for the formation of formic acid (1). A one year study in which the substance was administered to rats via drinking water found that the formic acid, at 40 weeks, caused tubular degeneration (1). At 52 weeks the tubular degeneration was not present but there was increased tubular pigmentations (1).

As with the liver there is no direct link with TCE and cancer. In a two years study on rats and mice, though the subjects experienced lesions to the kidneys the animals did not develop cancer (1). There have been cases in humans who were exposed to TCE inadvertently that developed kidney cancer (1). But, it is not clear if this chemical was the actual cause. More research and longer studies are required to determine if TCE is indeed carcinogenic.

**Exposure to chemical and Sources of Release**

It is important to understand how a person can become exposed to this volatile chemical in order to accumulate data on the effects it has in the human body. A person can become exposed to trichloroethylene either by inhalation or consumption. Inhalation can occur because a person works directly with the chemical or lives near a company that manufactures or uses trichloroethylene. The chemical may be present for up to 5 days after it is released into the air (2). It is also likely for TCE to react with pollutants in the air forming compounds such as phosgene, dichloroacetyl chloride and formyl chloride (2). Of course, precautions are taken to avoid these outcomes. All commercial grades are of TCE are equipped with stabilizers to prevent auto-oxidation (2).

Over 90 percent of all emissions into the atmosphere are due to degreasing operations (6). More minor sources of the emission of this haloalkene include disposal sites, landfills, losses from paints, adhesives etc. (7). Contaminated drinking water can also be a source of emission. Water in a person’s home may be tainted with TCE and activities such as showers may cause emissions into the air (7). In 1988, it was estimated that 49 million pounds of trichloroethylene is released into the atmosphere per year by manufacturing and industrial companies from the United States (6).

Ingestion of trichloroethylene occurs through drinking water. Today, TCE is in fact the most common source of contaminant in the groundwater (7). Due to improper disposal methods by industrial companies in the past, TCE has polluted many water supply systems. It affects over 60 percent of the drinking water in the United States (4). TCE will evaporate quickly from surface water but it may remain in ground water for a long period of time (7). This occurs because
the chemical will stick to particles in the water (7). For the same reason, if trichloroethylene is spilled on soil it is much more difficult to evaporate and eventually will leach into the groundwater (7). Any contact with the soil may cause a person to become exposed. It is very easy for a person to become exposed to trichloroethylene in their everyday lives.

EPA Regulations and removal from water supply

It is required by the Safe Water Drinking Act, set forth in 1974 for the Environmental Protection Agency (EPA) to determine the safe amounts of health hazardous contaminants allowable in the drinking water (4). The EPA determines MCLGs, maximum contaminant level goals, depending on the behavior of the chemical and how severe of health risk the contaminant proposes. For trichloroethylene, the MCLG has been set at zero (4). This goal, like most is not possible to enforce, therefore the EPA has set the maximum contaminant level (MCL) for TCE at 5 ppm (4). This standard was determined by measuring how much TCE could be removed from the water supply using approved methods (4).

The EPA requires that the water suppliers check the water to ensure that it is not above the maximum contaminant level (4). If tests show contamination above the MCL then immediate steps must be taken so the water remains consistently at or below this level (4). The EPA approved method for removal of TCE is using granular activated carbon in combination with packed tower aeration (packed tower aeration is a reverse osmosis distillation device) (4). Regulations are enforced by the Environmental Protection Agency to ensure the population experiences the least amount of exposure possible.

Conclusion

Trichloroethylene is an extremely useful chemical in many industrial operations. Its use will continue in years to come because of the unique properties that make it an ideal solvent and a successful chemical intermediate. It is apparent that there are health concerns regarding exposure to this chemical especially to the central nervous system. There is not yet enough information available to determine whether or not TCE is a carcinogen. There are several ways a person can be exposed to TCE. A person may even become exposed in their own home through drinking water and air emissions from nearby companies. Regulations enforced by the Environmental Protection agency are put in place to protect the health of the general population.

Based on the research available, I have concluded that TCE is not a direct cause of cancer; but is a factor that can lead to the development of cancer. If a person is chronically exposed to TCE it can make them more susceptible to this disease, especially if they have a predisposition. In the future, the greater concern with chronic exposure to TCE will be liver and kidney failure. Over a long period of time even low exposure will be shown to cause serious health problems in the general public. It is difficult to avoid the emission of this chemical into the atmosphere. There needs to be better filtration systems.

It is imperative that as much TCE as possible is removed from drinking water. As more
exposure outcome information is gathered, removal efforts will be increased. More focus will be put on developing ways to cut down the release of trichloroethylene into the environment. TCE is a chemical that has contaminated the environment, risking the health of millions of people. But, this chemical does not stand alone. Over the years the consequences of economic advances have been prominent in the environment. It is only left to determine which toxins propose the most danger and if the chemicals are worth the risk.
References


2. UN Water Assessment. Trichloroethylene Data Site. 


7. Agency for Toxic Substances & Disease Registry. ToxFAQs for Trichloroethylene (TCE). 


Chemical Explosives

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Abstract

There are many compounds defined as explosive that vary greatly in explosive power. Chemical explosives are classified as either high or low. High explosives are further broken down into primary and secondary explosives. On a molecular level, explosives have many similar functional groups that contain the elements carbon, nitrogen, and oxygen. Blending existing explosives compounds creates many of the explosives used by the military.

Explosive definition and classification

There are three types of explosions mechanical, atomic, and chemical. An explosive is a material that can be initiated to undergo very rapid, self-propagating decomposition that results in the formation of more stable material, the liberation of heat, or the development of a sudden pressure effect through the action of heat on produced or adjacent gases. Chemical explosives are generally separated into high and low power. Velocity of detonation determines whether a compound will deflagrate or detonate. If a compound has a detonation velocity above 3500m/s it usually detonates. Velocity of detonation refers to the rate that the combustion wave travels through the explosive and is one of the most important factor is rating explosive. Brisance refers to the rate of an explosion to reach its maximum pressure. Many explosives are also given a relative effectiveness factor, which compares an explosive's detonation velocity to TNT. Most low explosives have a pushing force while high explosives have a shattering force.

Low power chemical explosives

Low explosives have detonation rates under 1000m/s and will usually deflagrate instead of detonate. Deflagration is a rapid subsonic combustion. Most low explosives are mechanical mixtures of compounds. Common uses for low explosives are flares, gunpowder, and internal gas combustion engines.

Gun Powder

Gunpowder is a low explosive that consists of a mixture of potassium nitrate, charcoal, and sulfur. The nitrate provides the oxygen. The sulfur lowers the ignition temperature and increases combustion speeds. The reaction for the combustion of gunpowder is $10\text{KNO}_3 + 3\text{S} + 8\text{C} \rightarrow 2\text{K}_2\text{CO}_3 + 3\text{K}_2\text{SO}_4 + 6\text{CO}_2 + 5\text{N}_2$. It is resistance to shock and friction and must be ignite by heat or flame must be used. It has been in existence since the 10th century when the Chinese used it to propel rocks through bamboo stalks. Gunpowder in a bullet generates enough pressure to propel the projectile without destroying the outer case.

Road flares

Road flares are low explosives and their composition varies along with the manufacturer. One compound that is consists in almost all flares strontium nitrate (Sr(NO$_3$_2)) is responsible the red-orange flame color. Strontium nitrate is not a good oxidizer so it often mixed with a better oxidizer or an energetic fuel.
Internal combustion engines

In America alone there are well over 200 million automobiles that operate with internal combustion engines. The combustion of the gas and air mixture is classified as a low explosive, making it one of the most frequently occurring explosive reactions in the world. Inside the engine the pressure of the hot gasses does the work of moving the solid internal parts of the engine.

High power chemical explosives

High power explosives have a detonation rates between 1200 m/s and 9000 m/s. The high explosive category is further divided into primary and secondary explosives. Primary explosive are extremely susceptible to detonation and are sensitive to heat, shock, friction, impact, flame, and spark. Two common primary explosives are lead azide and lead stynphate. Secondary explosives are more stable than primary and often need a detonator. RDX, HMX, and TNT are common secondary explosives.

Primary explosives

Lead Azide – Pb2(N3)2

![Lead Azide molecule diagram]

Lead Azide is one of the most commonly used primary explosive and has a detonation velocity of approximately 5300 m/s and a molecular weight of 291.24 g/mol. Due to its rapid detonation, lead azide can facilitate the ignition of secondary explosives. It is extremely susceptible to heat, shock, and friction and is less sensitive to impact, in comparison to other primary explosives. It must be stored in aluminum, as it will react with all other common metals. Lead azide is synthesized by adding lead acetate to a solution of sodium or ammonium azide and was first made, by Quintus Curtius Rufus, in 1891. During the decomposition of lead azide N2 gas is formed.
Lead styphnate – C6H3N3O8Pb

\[
\begin{array}{c}
\text{O} \\
\text{O}_2\text{N} \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{O} \quad \text{Pb}^{2+} \\
\end{array}
\]

Lead styphnate has a detonation velocity of 5200 m/s and has a molar mass of 450.29g. It is resistant from detonation from impact, but not heat or static and doesn’t react with metals. It ignites easily, but is not a good initiator of secondary explosives, so it is commonly mixed with more powerful primary explosives that don’t ignite as easily. Common uses include airbags, detonators and bullet priming caps. The formula for the formation of lead styphnate is \(\text{C}_6\text{H}_3\text{N}_3\text{O}_8\text{(s)} + \text{PbO}\text{(s)} \rightarrow \text{PbC}_6\text{H}_2\text{N}_3\text{O}_8\text{(s)}\) and was first made in Germany by Von Hertz.¹

Mercury fulminate – Hg(ONC)_2

\[
\begin{array}{c}
\text{O} \\
\text{N} \equiv \text{C} \quad \text{Hg} \\
\text{C} \equiv \text{N} \\
\text{O} \\
\end{array}
\]

Mercury fulminate is an extremely unstable primary explosive that is especially sensitive to shock and friction. It has a molecular weight of 284.62g/mol and a detonation velocity of 4300m/s. Blasting and percussion caps are its primary uses. Mercury fulminate was discovered in 1799 by the British chemist Edward Charles Howard. Synthesis of mercury fulminate is a two-step process. First reaction involves nitrating mercury, \(\text{OHNO}_2 \rightarrow \text{HgNO}_3 + \text{OHNO}_2 + \text{NO}_2\). The second step involves adding ethanol to the mercury nitrate in the presence of excess nitric acid, \(\text{HgNO}_3 + \text{HNO}_3 + \text{C}_2\text{H}_6\text{O} \rightarrow \text{Hg(ONC)}_2\)

Secondary explosives

Trinitrotoluene (TNT) – C7H5N3O6

\[
\begin{array}{c}
\text{O}_2\text{N} \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{NO}_2 \\
\end{array}
\]

Trinitrotoluene is one of the most stable high explosives. It can be stored for long periods of time and melts before it reach its ignition temperature. TNT is synthesized by performing a triple nitration of toluene and has a molecular weight of 227.13g/mol. It has
a detonation velocity of 6900m/s and has an R.E. factor of 1, because it is the reference point for comparison. The reaction for the denotation of TNT is 2 C7H5N3O6 → 3 N2 + 5 H2O + 7 CO + 7 C. Joseph Wilbrand invented trinitrotoluene in 1863 and because of its low cost, safety in handling, compatibility with other explosives, low melting point, moderate toxicity, and low sensitivity TNT was the most used military explosive of the 20th century.¹

Cyclotrimethylenetrintritramine (RDX) – C3H6N6O6

RDX is a very powerful and brisant high explosive with a detonation velocity of 8,750m/s. RDX has an average R.E. factor of 1.6 (chart), which means that RDX releases 1.6 times the energy of an equal molar amount of TNT. RDX has a molar mass of 222.11g and is prepared by combining hexamine with nitric acid, (CH2)6N4 + 4HNO3 → (CH2-N-NO2)3 + 3HCHO + NH4+ + NO3-. G. C. V. Herz began producing RDX in the 1920's, after discovering in explosive properties. Many military explosives are mixtures of different explosives. RDX used in making many types of explosives including the first plastic explosive.

Cyclotetramethylene-tetranitriname (HMX) - C4H8N8O8

HMX has a molecular weight of 296.20g/mol, which helps make it one of the most powerful chemical explosives available. It has a detonation velocity of 9,100m/s and a R.E. factor of 1.7. Common uses of HMX range from nuclear weapon detonation to propelling solids. W. E. Bachmann discovered HMX as a byproduct of RDX synthesis in 1940. HMX is primarily a military explosive because in is expense and difficult to produce, however it is a very a very stable explosive. Upon detonation HMX decomposes into N2 and CO2.
Functional groups

There are no set criteria for determining whether a compound will be explosive or not. Explosive molecules are often associated with having functional groups that are highly reactive or unstable. A list of these functional groups follows:

Compounds Containing Carbon

C=C=C=C dienes
C=C=allenenes
triple bonded carbons alkynenes, alkynes, haloalkynes, polyalkynes

Compounds Containing Carbon and Nitrogen

C=N=N-C azo compounds
C linking N rings triazoles, aziridines, nitriles, diaziridines
CN$_2$ diazo compounds
C-N$_3$ alkyl, aryl azides
C=N=N-N triazenes
C triple bond N dicyanogen

Compounds Containing Carbon and Oxygen

C linking O rings oxiranes
C-O-OH alkyl hydroperoxides
(-CMe$_2$O-O-)$_3$ trimeric acetone peroxide
C-O-O-C dialkyl peroxides

Compounds Containing Carbon, Nitrogen and Oxygen

C=N=O nitroso compounds
C-NO$_2$ nitro compounds
C-O-NO$_2$ alkyl nitrates
C-O-NO$_2$ alkyl nitrates
C=NOH oximes
C-N=N-O- arenediazoates, bis(arenediazo) oxides
C(NO$_2$)$_2$ gem-polynitroalkyl compounds
CO O-N=O acyl nitrates
CO O-NO$_2$ acyl nitrates
C triple bond N—O nitrile oxides

Compounds Containing Nitrogen and Oxygen

NO nitro oxide
NO$_2$ or N$_2$O$_4$ dinitrogen tetroxide
H$_2$NOH hydroxylamine and salts
N$_2$O dinitrogen oxide
N$_2$O$_5$ dinitrogen pentoxide

Compounds Containing Nitrogen and Other Elements

N-X N-halogen compounds
N-metal N-heavy metal compounds
NF$_2$ difluoroamino compounds
Compounds Containing Halogens, Oxygen, and Other Elements
O-X hypohalites
O-X-O₂ halates
N-Cl-O₃ perchlorylamide salts
O-X-O halites, halogen oxides
O-X-O₃ perhalates, halogen oxides

Government explosive blends
Amatol- a mixture of TNT and ammonium nitrate
Baratol- a mixture of TNT and barium sulfate
Composition A- a blend of RDX and wax
Composition B- Blend TNT, RDX, and Wax
Composition C-4- majority of composition is RDX
Octol- part TNT and part HMX

Conclusion
There are many types of chemical explosives on the market the majority a limited
to the use of demolitions, mining, and military. Chemical explosives range from low to
high power. With detonation velocities from a few inches per minute to over 9000m/s.
high power explosives are categorized into primary and secondary. Primary charges are
very unstable and detonate easily. A primary explosive can be used to ignite secondary
explosives, which are more stable and can be more powerful than primary explosives.
Explosiveness can be related to different highly reactive or unstable functional groups


Cloud Chambers and their Implications to the Physical Sciences
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Abstract
Cloud chambers have played an integral part in the beginnings of high energy particle physics. The history of cloud chambers and important discoveries are discussed. In addition, the physical concepts in relation to cloud chambers are addressed.

In the night skies of the Northern and Southern regions of our planet and beyond, one could see a multitude of spectacular phenomena. Auroras (North/South polar lights) inspire with their colorful hues of reds, greens, and blues. Centuries past folklore of different cultures attempts to explain phenomena such as this. In middle age Europe for example, the lights were the reminders of warriors that had died in battle. The colorful light emanating from the heavens were the warriors that had the privilege to resume their fight in the great beyond. Another culture; the Inuit around the Hudson Bay, believed that there was a passage to the heavens through the North Polar Lights and the light was spirits guiding the dead through this passage.\textsuperscript{31} It was not until the advent of modern particle physics that we were able to describe atmospheric phenomena such as the North/South polar lights.

Charles Thompson Reese Wilson was working as a meteorological observer in 1894. Atop the mountain of Ben Nevis (the highest mountain in Great Britain), Wilson became intrigued with coronas and glories and desired to recreate them in the laboratory.\textsuperscript{26} It was this inspiration from the physical world that initiated the development of the cloud chamber.

When CTR Wilson first set out to produce clouds in the laboratory, he experimented with a method of the Scottish engineer, John Aitken. In short, Aitken found he could form a cloud by injecting an airtight jar with water vapor. He determined that clouds were forming by the condensation of water molecules around dust. Through experimentation, he deduced that if there was dust present, a cloud would form. Aitken was not successful in producing clouds in dust free air. Wilson found that by expanding the chamber by 25% (a ratio of 1.25 the original size), he was able to form the condensation even in dust free air.\textsuperscript{32}

Wilson hypothesized that the droplets in the dust free air were forming around invisible nuclei. The role of electric field was crucial in validating Wilson’s hypothesis. When Wilson applied electric field to the cloud chamber, he saw that the droplets forming were quickly swept away. It was because the particles allowing for condensation carried a charge, that they were able to be affected by the electric field Wilson applied.\textsuperscript{32}

The properties of electric field allowed Charles Wilson to make the important observation that charged ‘nuclei’ were inducing condensation. It was Michael Faraday (1791-1867) who proposed the definition of electric field we accept today. Faraday explained that the electric field exists in the vicinity of a charged object. The electric field also exerts a force on other charged objects within that field. The equation for electric field is as such:

\[ E = \frac{F_e}{q} \]
where the vector (having magnitude and direction) \(E\) is the electric field (with units of Newton/Coulomb), and vector \(F\) is the electrostatic force measured in Newtons, exerted on a minuscule test charge \(q_0\) by some other larger charge \(Q\), for example.\(^{6}\) As an illustration of how this can be used to solve for a variable, consider this data: An electric field of 100 N/C is applied to a cloud chamber, what is the \(F_e\) (electrostatic force) exerted on an Alpha particle (Helium nuclei)?

Solving for \(F_e\) ... \(F_e = q_0 \times E\) . This yields: \(F_e = 2(1.6 \times 10^17(-19) C)(200 N/C) = 6.4 \times 10^{17}\) Newtons of force exerted on the Alpha particle. Because an alpha particle consists of 2 neutrons that have no charge, and two protons that each have a charge of \(1.6 \times 10^{-19} C\), we multiply the charge of the proton by two to find \(q_0\).

We can also determine the value of \(F_e\) using Coulomb’s Law:

\[
F_e = \frac{k_e Q q_1}{r^2},
\]

where \(k_e\) is a constant \((8.9875 \times 10^9 \text{ Nm}^2/\text{C}^2)\), \(Q\) is a charged particle exerting a force on \(q_1\), and \(r\) is the distance between \(Q\) and \(q_1\). The standard units for electrostatic force are Newtons. The standard unit for charge is Coulomb and the standard unit for \(r\) is meters. A useful application of these two equations is that we can equate them (set \(F_e=F_o\)), and solve for the different variables.\(^{6}\)

\[
F_e=F_o
\]

\[
q_1E = \frac{k_e Q (q_1)}{(r^2)},
\]

which simplifies to

\[
E = \frac{k_e Q}{r^2}.
\]

The electric field is represented graphically by the illustration of field lines. A general rule is that for a positively charged atom, the field lines will emanate from it. Consequently, field lines will terminate at an atom with a negative charge. Also, it is important to note that the electrostatic force of like charges will deter one another. For example, if you place two electrons next to each other, they will repel one another. Therefore, there will be an attractive electrostatic force of dissimilar charges \((+,-)\). Electric field is crucial in understanding how charged particles will interact with each other, and within a cloud chamber exposed to an electric field.

In addition to the role of electric field, electromagnetic radiation also played a role in Wilson’s discoveries. Wilson, in fact, was able to further verify his hypothesis by exposing his cloud chamber to X-rays, a type of electromagnetic wave/radiation.\(^{25}\)

All electromagnetic waves are the product of accelerating charges.\(^{6}\) This equation

\[
c=\lambda f
\]

is a common tool used to solve problems related to electromagnetic waves. The variable \(c\) is a constant: the speed of light \((3 \times 10^8 \text{ m/s})\), with units of meters/second. Lambda \(\lambda\) is the frequency of the wave and is measured in meters. The variable \(f\) is a frequency, with units of Hertz (revolutions/sec). Because the speed of light is a constant, this equation could be used to
find an unknown frequency or wavelength. Using the equation, we could determine the frequency of a gamma wave with a measured wavelength of 1 pm.
Solving for the unknown frequency yields:

\[ f = \frac{c}{\lambda} \]

\[ f = \frac{3 \times 10^8 \text{ m}}{1 \times 10^{-12} \text{ m}} = 3 \times 10^{20} \text{s}^{-1} \]

Compare this to \( 5 \times 10^6 \text{s}^{-1} \) (5 MHz [mega hertz]): A typical frequency of an AM radio wave. Conceptually, it makes sense that the gamma wave

It was not until the “miracle year” of 1905,\(^1\) when an equation relating the wave and particle properties of light allowed for physicists to efficiently solve for the energy of a photon of light.\(^2\) That year, Einstein both provided a clear explanation of the photoelectric effect, and unveiled his famous theory of special relativity. Einstein hypothesized that light was composed of packets, of which we now call photons. He proposed that the energy of one of these photons would be product of the waves frequency and Planck’s constant. (E=hf) Einstein’s work with light was critical because it helped to illustrate the “dual nature” of light. The dual nature refers to the fact that light has both characteristics of waves and particles. Einstein’s theories provided understanding has to why certain experiments would suggest light was a particle, but yet others would suggest light was a wave phenomena.

The amount of energy a photon has is a function of its wavelength and its energy is measured in electron-volts. The electron-Volt is a unit of energy defined as “the kinetic energy that an electron gains when accelerated through a potential difference of one Volt.”.\(^3\) The value of 1 electron-Volt is \(1.6 \times 10^{-19} \text{ Joules}. \) This is derived from the fact that 1 Volt = 1 Joule/Coulomb and that the charge of a single electron is \(-1.6 \times 10^{19} \text{ Coulombs} \). The electron-Volt is a common unit of measurement used to describe a single molecule, such as photons in electromagnetic radiation. Commenting on the electron-Volt, Richard Feynman stated in a 1997 lecture “...instead of taking a definite unit in the same system (like \(10^{20} \text{ J}\)) they have unfortunately chosen, arbitrarily, a funny unit called an electron-Volt....I am sorry that we do that, but that’s the way is for physicists.”\(^4\)

The equation Einstein developed relating waves and particles to light was

\[ E= hf. \]

The variable \( h \) is Planck’s constant, and has a value of \(6.63 \times 10^{-34} \text{ Joules}. \) Frequency is represented by \( f \) and has units of revolution per second (Hertz).\(^5\) As an illustration, let’s use this equation to determine the energy of an AM radio wave and a gamma wave. Radio waves have the lowest energy of the electromagnetic spectrum, and have a frequency of \(10^6 \text{ Hertz}. \) Gamma waves have very high energies. An example gamma wave will have a frequency of \(10^{21} \text{ Hertz}. \) Using the equation \( E=hf \), the energy in Joules for the radio wave is

\[ \frac{(6.63 \times 10^{-34} \text{ J sec})(10^6 \text{ rev})}{\text{sec}} = \frac{1 \text{ eV}}{1.6 \times 10^{-19} \text{ J}} = 4.14 \times 10^9 \text{ eV}. \]
Let’s compare this to the energy of the photon of a gamma ray, which should theoretically be many magnitudes greater than that of the radio wave.

\[
E = \frac{(6.63 \times 10^{-34} \text{Jsec})(10^{21} \text{ rev})}{1.6 \times 10^{-19} \text{f}} (1 \text{ eV}) = 4.14 \times 10^6 \text{ eV (or } 4.14 \text{ Mega-electron volts)}.
\]

There are types of electromagnetic radiation and particle radiation that are classified as ionizing radiation. For a type of radiation to be identified as ionizing, it must be capable of producing ion pairs by interacting with other substances.\(^8\) There are four general types of ionizing radiation: Alpha and beta radiation, which are particle radiation, and Gamma and X-ray radiation which are electromagnetic. To explain for the varying levels of penetration exhibited by different types of radiation, one must account for how much the radiation will interact with its environment. Attenuation will occur when a particulate or photon is highly interactive. In general, the greater the range a particular radiation has, the less it interacts with what it collides with.

Alpha particles (the Helium nuclei) have a comparatively large mass. Although they have a short range (60 micrometers in tissue), they have a potential to be very damaging within that range, with energy at around 6 MeV.\(^6\) This explains why they are not able to penetrate human skin, but they pose serious danger when inhaled or ingested. Alpha particles have such a short range that they are easily shielded by paper or tissue, for example.

Beta particles are electrons traveling at extremely high speeds. They have a mass of \(9.11 \times 10^{-31}\)\(^1\). They have energies that can range from many KeV to 5MeV,\(^6\) and therefore are also an internal hazard. For practical purpose, X-rays are produced for clinical application by smashing beta particles into metal targets.\(^1\)

X-rays are a type of electromagnetic radiation. As previously alluded, the X-ray is produced from beta particles. The X-ray is emitted as a photon when rearrangement of atomic electrons occurs, after an inner orbital electron is displaced. The X-rays were discovered in 1895.\(^2\) The X-ray is a perfect example of how we utilize potentially radiation to our benefit. If you were to break your foot after a cycling accident, for example, you would have an X-ray taken of your foot. The way this is achieved is by Bremsstrahlung; a mechanism that produces X-rays from excited electrons (beta particles).\(^1\) When a wound filament in the cathode of the X-ray tube is heated, electrons are produced in a flow toward the anode, which is made of tungsten (the target material).\(^2\) These electrons will be approaching relativistic speed as they react with the tungsten. When the electron circumnavigates around the large tungsten atom, its velocity decreases. As the velocity of the beta particle changes, it releases energy in the form of X-rays.\(^2\) Through this method, both the amount of electrons being emitted from the anode, and the intensity of the X-ray could be controlled. Increasing the current (units of Amperes) being delivered to the cathode will increase the heat of the filament, which will generate more electrons. The increase in the amount of beta particles reaching the anode will in turn, increase the amount of radiation being delivered. Generally, there is an Ammeter in place that is used to monitor the amount of current being delivered. If you increase the voltage (potential difference) being distributed to the circuit, this will increase the velocity of the beta particles approaching the tungsten anode. This increase in velocity gives the beta particles more energy, and thus the intensity of the X-rays themselves will be greater. After the beta particle emits X-rays, the X-ray
recoils off of the focal spot of the anode and imposes an image on the film of the object (your broken foot) in question. We could determine the kinetic energy of a beta particle in this system with the equation:

\[ KE = \frac{1}{2} MV^2 \]

Gamma radiations are most commonly emitted from elements undergoing radioactive decay, and can be very damaging to biological systems if not properly shielded.

Electromagnetic radiation and particle radiation alike, have varying levels of penetrating capabilities. Here, I put forth a table summarizing the penetrating capabilities and energies of the alpha, beta, and gamma constituents. The term Quality Factor (QF), refers to the amount of biological damage that can occur due to the radiation. The Alpha particle has the highest QF, and therefore has the highest potential for damage. Compare this to the small QF for the gamma and beta radiation. Beta radiation can cause external damage if exposed to large amount, while gamma rays are an external hazard, even in small amounts.

<table>
<thead>
<tr>
<th>Penetration Distance</th>
<th>Energy</th>
<th>QF</th>
<th>Shielding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha Particle</td>
<td>60 micrometer in tissue</td>
<td>4-8 MeV</td>
<td>20</td>
</tr>
<tr>
<td>Beta Particle (electron)</td>
<td>~3 millimeter in tissue</td>
<td>KeV-5 MeV</td>
<td>1</td>
</tr>
<tr>
<td>Gamma Photon</td>
<td>1 meter in tissue</td>
<td>MeV +</td>
<td>1</td>
</tr>
</tbody>
</table>

In relation to the cloud chamber, we could detect the presence of all of these kinds of radiation. However, because all of these particulates and waves exist at the subatomic level, we are not detecting the unit itself. For example, to support his hypothesis, Wilson exposed his cloud chamber to X-rays. The X-rays induced condensation of the water droplets in Wilson’s chamber. Wilson did not “see” a photon in his chamber, but he witnessed the effect of that photon on the surrounding environment.

Wilson was able to further verify his hypothesis of ions in air by exposing his cloud chamber to other forms of radiation, such as X-rays. X-rays are a type of electromagnetic wave/radiation. X-rays have wavelengths between 10 nanometers (nano= $10^{-9}$) and 10 picometers (pico= $10^{-12}$). They can have energies ranging from 10 keV and a few hundred keV.

It was later determined that the ions Wilson proved were allowing for condensation in dust-free air were actually cosmic rays. Cosmic rays were discovered by Victor Hess in 1912. Cosmic rays are a type of particle radiation produced by sources in outer space. The sun is the Earth’s most abundant source of cosmic rays. Solar cosmic rays also have relatively lower energies, of around $10^{10}$ electron-volts per photon. The Earth is also subject to galactic cosmic rays, with energies of approximately $10^{15}$ electron-Volts, and extragalactic cosmic rays with even higher energies than that of the galactic cosmic rays.

Cosmic rays are primarily made of protons (around 90%). Alpha particles consist of around 9% of cosmic rays. The rest consists of electrons and a very small fraction (.1%) is made up of the photons of gamma rays. When primary cosmic rays enter the atmosphere, it can react and collide with particles in the air. This will break the cosmic ray into subsequent particles (secondary cosmic rays), such as pions. If the said pion were to collide with another air molecule, it would then break into a neutrino and a muon. Because of this decay, a small amount of primary cosmic rays reach the Earth.
Because of their high energies, cosmic rays can be potentially harmful to humans. There are mechanisms, however, that protect us from a majority of the higher energy cosmic rays. Both the earth and the sun’s magnetic field deflect the electrically charged particles, thusly significantly reducing the amount of galactic and extragalactic cosmic rays reaching the earth’s atmosphere.\(^2\) Circulating electric currents within the earth’s core are theorized to be the source for the magnetic field.\(^1\) The Earth’s magnetic field mimics that of a bar magnet, with the field exiting the north pole and entering at the south pole. A magnetic field could be applied to a cloud chamber. When doing so, deductions can be made about particles in the chamber, based on how they are affected by magnetic field. We use the equation

\[F_B = qvB\]

to describe the magnetic force \((F_B)\) experienced by a charge \(q\), with a velocity \(v\) in a magnetic field \((B)\). The standard units for \(F_B\) are Newtons. For velocity, the standard units are meters/second. The standard unit for magnetic field \((B)\) are Tesla.\(^6\)

Along with discovering ions in dust free air, one of the first contributions facilitated by the cloud chamber was the confirmation of Compton recoil electrons and the Compton Effect.\(^2\) Compton’s work was significant because it led to the acceptance of the photon’s behavior as a particle. He showed mathematically that when an X-ray photon collided with a stationary electron, the photon transferred energy and momentum to the electron.\(^3\) For his work, Arthur Compton shared the Nobel Prize with CTR Wilson in 1927.

Another scientist, Dmitri V. Skobeltsyn also did a substantial amount of work with the cloud chamber in the 1920’s. In 1927, when he was studying the Compton Effect, he observed tracks of relativistic particles (particles approaching the speed of light) in the cloud chamber. The fact that these particles appeared as a group of particles had implied that this was the first observation of the cosmic rain shower phenomena.\(^5\)

One of the most significant discoveries made with the cloud chamber was made by Carl Anderson in 1932. Anderson was studying cosmic rays when he observed a type of track that curved in a magnetic field identical to that of the electron, but in the opposite direction. With this observation, Anderson deduced that this particle must have the same mass as an electron, but an equivalent and opposite charge of 1.6 x 10\(^{-19}\). This particle was named the positron, and was the first of many antiparticles (particles with the same mass and opposite charge) to be discovered. The detection of the positron made the invention of PET (Positron Emission Tomography) possible.\(^3\) Due to the fact that the PET scan is a common tool used in diagnostic imaging, the initial detection of the positron with the cloud chamber had a significant impact in nuclear medicine and biophysics. For the detection of the positron, Anderson was awarded the Nobel Prize in 1936.

In 1932 Patrick M.S. Blackett designed an optimized cloud chamber. The cloud chamber design allowed for particles to induce the camera to take a photograph. This was obviously more efficient than manually taking photographs of tracks. Blackett was able to achieve this by placing a Geiger-Muller tube above and below the original cloud chamber. When the Geiger-Muller tubes detected the particle, it was then that a photograph was taken. After this modification, Blackett made multiple contributions, including verifying Anderson’s discovery of the positron. Blackett was awarded the Nobel Prize in 1948.\(^2\)

During the 1950’s, new and improved particle detectors were developed, making the Wilson Cloud chamber virtually obsolete. The bubble chamber was invented in 1953 by Donald Glaser.\(^2\) The bubble chamber could detect subatomic particles more efficiently. Instead of using
the supersaturated vapor, as the cloud chamber did, the bubble chamber used a super heated liquid as a medium and target for the particles to pass through. An accelerator was used to deliver high energy particles to the bubble chamber. When the charged particles ionized the hot liquid, this would induce boiling and a track of bubbles would form. 36 This produced increasingly more complex tracks than one could visualize with the cloud chamber. Also, more data could be collected in a quicker amount of time using the bubble chamber method. For around twenty years, bubble chambers made many contributions to physics as the predominant particle detector. 12

Although cloud chambers are no longer very useful for collecting data, they still have function in the modern world of physics. Cloud chambers are still used as displays at universities and museums, for example. Furthermore, a cloud chamber can be built as a part of a physics lab experiment for high school or college students. Cloud chambers are successful at making the subatomic world of physics a part of the visual world. This is something I think could make even the non-physicist excited about the world of particle physics. A diffusion cloud chamber is a relatively inexpensive and simple devise to build. For this project, I chose to build a cloud chamber to present to my peers. Here I itemize the supplies and cost of the materials used to build our cloud chamber.

<table>
<thead>
<tr>
<th>Supplies</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure alcohol (99% Isoproyl)</td>
<td>Free (Physics Dept.)</td>
</tr>
<tr>
<td>Radioactive Sample</td>
<td>Free (Physics Dept.)</td>
</tr>
<tr>
<td>A clear box with an open top</td>
<td>$6.50 (Petsmart)</td>
</tr>
<tr>
<td>Metal plate</td>
<td>$1.00 (Home Depot)</td>
</tr>
<tr>
<td>Styrofoam</td>
<td>$2.50 (Home Depot)</td>
</tr>
<tr>
<td>Felt</td>
<td>$2.00 (Craft Store)</td>
</tr>
<tr>
<td>Superglue</td>
<td></td>
</tr>
<tr>
<td>Dry Ice</td>
<td>$5.00 (Grocery Store)</td>
</tr>
</tbody>
</table>

To operate the cloud chamber, we theorized that we were to build a Styrofoam box as vessel for the dry ice. The dry ice would then be packed in this box. Then, the metal plate would be laid on top of the dry ice. We would then place the clear box (open top face down) over the metal plate. On the inside of the box, we would have glued felt to the top of the box. This felt is to be soaked in the alcohol before it is placed on the metal plate. After placing the box onto the metal plate, a fog-like mist should appear almost immediately. However, online sources stated it should take around 15-20 minutes before tracks could be seen in the cloud chamber. 5

For the first attempt at building the chamber, we attempted to build our own clear box. With this, we used a sheet of Lexan plastic and corresponding silicone based glue. We used a table saw to cut the pieces for the box. We glued the box together and reinforced with electrical tape. After letting the glue dry for 24 hours, we glued a 2" strip of felt to the perimeter of the top of the box. After letting this dry, we soaked the felt with the pure alcohol and placed the box on the
metal plate. It was observed that very little alcohol was falling from the top of the chamber, where we glued the felt. After waiting 20 minutes and not seeing any activity, we re-soaked the felt and tried one more time. Soon thereafter, it became apparent that the box was becoming increasingly flimsy. Upon further inspection, it was determined that the glue was being broken down by the alcohol.

After this attempt, we thought of how we could modify our initial design that would be conducive of cloud formation. But first, I wanted to be sure that this goal was attainable. I took an empty pickle jar and placed an alcohol-soaked felt in the bottom of the jar. After closing the jar, I placed it with its metal lid down on the metal plate. To my somewhat surprise, we observed a cloud of alcohol vapor form as the felt produced a rain like mist. This observation had a few implications we had to consider when thinking about how we would optimize our cloud chamber design.

We wondered why the original design was not successful. More than one aspect of our design could have made the cloud chamber inoperable. Here, I will put forth a table explaining possible flaws and tentative solutions.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Reasoning</th>
<th>Tentative solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not efficient amount of dry ice</td>
<td>The chamber must be extremely cold at the base. If there was not an efficient amount of dry ice, the chamber would not be cold enough to cause an effective temperature gradient.</td>
<td>To pack the Styrofoam vessel with as much dry ice as possible. Also, to make sure the metal plate has direct and is in maximum contact with the dry ice.</td>
</tr>
<tr>
<td>The box was too large for the amount of dry ice we used.</td>
<td>If the chamber was too large to cool with the amount of dry ice we used, we would not effectively induce the required temperature gradient.</td>
<td>To build or purchase a smaller box that will be able to run with less amount of alcohol and dry ice.</td>
</tr>
<tr>
<td>The felt did not produce effective evaporation of the alcohol.</td>
<td>We did not visualize the initial rain like mist we had expected. This could either be due to the surface area of the felt, or the ability of the felt to evaporate the alcohol</td>
<td>Apply more felt to the top of the chamber or experiment with other materials, such as sponges.</td>
</tr>
</tbody>
</table>
The chamber was not air tight.

Clearly, the glue was unreliable; as it began to break down as we ran the experiment.

1. Attempt to build another box with a different kind of material (Lucite). Then, instead of sealing the box with glue, we would use a solvent to in effect, weld the plastic together. Thusly, creating a gas tight, more reliable structure.

2. Purchase a box that suits our needs, so we could focus our efforts on other aspects of the experiment.

In place of the tedious measurements taken from photographs of cloud chambers, physicist now use a tools referred to as Data Acquisition Systems to collect and analyze data. Data acquisition systems consist of a type of software that sync up with a computer and the experimental apparatus. Computer Automated Measurement and Control data systems are common data management systems used today. An example of the data management is illustrated in the operation of the HERA-B Muon detector. There are many facets to this system. However, in general, a computer is enabled to control an experiment through a specific interface. Through data transmitted to the computer, a curve can be graphed by the software.

Whereas cloud chambers have their current place in physics Americana, the field of high energy physics has taken off since they first used an accelerator to generate particles for the bubble chamber. There are some notable chambers that have an important role in the current study of subatomic particles in the atmosphere and beyond. For example, CERN began conducting an experiment in 2006 investigating cosmic rays and their effect on out environment. For this experiment, the Proton Synchrotron will be delivering the high energy cosmic rays into the chamber for reaction. The Proton Synchrotron is one small accelerator that is part of the network of accelerators at CERN. The faster that a particle can go; the more kinetic energy it will have. The more energy in the particle at the time of collision, the more data that experiment will yield. The technology used in these accelerating systems are increasingly more intricate and advanced than the detection devices of the past. Nevertheless it was predecessors such as the cloud chamber and bubble chamber, which brought the study of high energy particle physics to the forefront of scientific exploration.
References


10.) *Four Primary Types of Ionizing Radiation* (n.d.). Retrieved April 14, 2008, from www.unt.edu/research/eh/ppt/Four%20Primary%20Types%20of%20Ionizing%20Radiation.ppt


http://www.srl.caltech.edu/personnel/dick/cos_encyc.html

http://www.fnrf.science.cmu.ac.th/theory/radiation/xray-basics.html


http://hyperphysics.phy-astr.gsu.edu/hbase/magnetic/magearth.html#c

http://hyperphysics.phy-astr.gsu.edu/hbase/nuclear/radact.html#c2


http://www.windows.ucar.edu/tour/link=/physical_science/physics/atom_particle/
cosmic_rays.html&edu=high

http://www.windows.ucar.edu/tour/link=/physical_science/physics/atom_particle/particl
e_radiation.html&edu=high

http://www.windows.ucar.edu/tour/link=/physical_science/magnetism/em_xray.ht
ml&edu=high

http://www outreach.phy.cam.ac.uk/camphy/cloudchamber/cloudchamber1_1.htm


<http://www.ast.leeds.ac.uk/haverah/cosrays.shtml>


http://www.imv.uit.no/english/science/publicat/waynorth/wn1/part02.htm


http://www.mpi-hd.mpg.de/hfm/CosmicRay/Showers.html

http://physics.bu.edu/~duffy/semester2/c35_compton.html


Hereditary Breast Cancer
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Prepared for:
Dr. Hank Mancini
Chemistry 236
Abstract

Hereditary breast cancer with BRCA 1 or BRCA 2 mutation(s) account for 5%-10% of all breast cancer cases.\textsuperscript{1} An overview of pathology, treatment, and detection of BRCA1 and BRCA2 tumors is given. Although there is a well accepted role of these genes in breast cancer, minimal distinctions are made between the pathology and treatment of hereditary and non hereditary breast cancer.

Introduction

The American Cancer Society predicted an estimated 178,480 new cases of invasive breast cancer would be diagnosed in 2007.\textsuperscript{2} As much as 20% of those diagnosed with breast cancer, will have, in their lifetime, at least one relative afflicted with the same disease.\textsuperscript{3} As one of the most frequent type of cancer for women in the United States, this sector of oncology is a growing field. Whereas there has been many advances in oncology in the past decades, cancer still remains an enigma in a number of respects. Among breast cancer susceptibility genes that have been identified, two key genes, labeled BRCA1 and BRCA2 are being thoroughly researched. Determining the mechanisms of genetics and breast cancer may prove to positively impact other oncology research. However, there are also social implications to consider in the increasingly advanced field of genetics.

The term carcinogenesis refers to the development of cancer. Breast cancer carcinogenesis, is considered to be multifactorial, meaning that there is generally multiple factors that will determine if someone will develop cancer.\textsuperscript{4} Genetic susceptibility, environmental, and lifestyle factors are all accepted as having the capability of making a cell more prone to cancer.\textsuperscript{5} The discovery of breast cancer genes in the 1990’s have brought genetics to the forefront of breast cancer research.

Genetics

In the nucleus of every cell in one’s body (except for red blood cells which do not have nuclei) lies one’s genetic material. In normal human body cells (somatic cells), there lies 23 pairs of chromosomes, making a total of 46 chromosomes. In normal germ cells (sex cells), there are 23 chromosomes total. When a male and female germ cell produce a zygote, which will in turn have 46 chromosomes, 23 from the mother and 23 from the father. Within every chromosome there are many specific genes. Because our chromosomes occur in pairs, there are a pair of genes that correspond to the same trait(s). If a mutation is inherited by either the germ cell from one’s mother or father, this is called a germline mutation. Because it occurred in the very first cell (the zygote), it is therefore duplicated into all autosomal cells. If a mutation was not inherited via a germ cell, the mutation is termed as somatic. Somatic cell mutations will be duplicated in those cells that originate from the somatic cell with the initial mutation. Because they do not occur in the germ cell, they cannot be inherited.\textsuperscript{6}

As an illustration, consider the case of the BRCA 1 or BRCA 2 gene. If one of these BRCA genes carries a mutation, which could lead to breast cancer, and the corresponding gene on the other chromosome does not have a mutation, how does genetics determine if one will develop breast cancer? Because the mutations of BRCA1 and BRCA2 are germline mutations, there will always be one defective gene in somatic cell. However, BRCA1 or 2 related breast
cancers will not occur unless there is a mutation on both genes on both chromosomes. Therefore, another variable mutation in the second gene must occur in order for carcinogenesis to occur.

http://medicine2.creighton.edu/EDRNRegistry/pedigree.html

Here is an example of a pedigree used to assess a patient’s risk of inheriting breast cancer. It is also important to note that there has been limited availability to genetic testing, until recently. Furthermore, testing is still quite costly, depending on the amount of chromosome material that is being analyzed. Even with the advent of genetic testing, extensive family histories such as this prove to be an invaluable tool to the clinician and genetic clinic.

A single gene mutation in either BRCA 1 or BRCA 2 are accountable for 5%-10% of all breast cancer cases. There are four major Hereditary Breast Cancer Syndromes associated with mutations. Mutations of either BRCA1 or BRCA2 account for 80%-90% of hereditary breast cancer cases.

Diagnosis

To be diagnosed with Hereditary Breast Cancer Syndrome (BRCA1/BRCA2), certain criterion must be identified. For example, in a family with a mutation in one of these genes, an early onset of breast or ovarian cancer is typical (diagnosed before age of 50). A family history of both breast and ovarian cancer is also a sign of one of these mutations. Because these mutations are autosomal dominant, this pattern of transmittance is a characteristic of having a BRCA mutation. For a mutation to be autosomal dominant means that one only needs one copy of that gene, for the gene to be expressed.
Carcinogenesis

The mechanism that initially causes hereditary cancer is still under investigation. However, we do know that BRCA1 and BRCA2 are both tumor suppressor genes. Concerning BRCA1, studies are showing another gene, PTEN, plays a substantial role in cancer initiation. The PTEN gene's role in BRCA 1 is hypothesized to account for 50% of BRCA1 cases. Clinical trials for a PTEN targeted therapy are currently underway. While promising for those affected, there is still a significant percentage of hereditary breast cancer with no confirmed mechanism for carcinogenesis.

Pathology

When a tumor (overgrowth of cells) develops in any part of the body, it must be determined that it is cancerous. If the tissue is determined to be cancerous, it can either have remained where it developed (non-invasive), or have spread to surrounding tissue (invasive). On-invasive breast cancer cells are also referred to as being in situ. In breast cancer, in situ breast cancers will stay within the milk ducts or milk lobules of the breast, whereas invasive breast cancer may metastasize to other tissues via the blood or lymph system.

Cancer will be identified as being of a certain grade. Grade refers to the appearance of the cancer cells with microscopy. For breast cancer (including hereditary), the grade is based on a number system, ranging from 1-3; with 1 being the lowest grade, and 3 the highest. In general, cells of grade 1 are slow growing and still look very much like normal cells. These cells may be referred to as being low grade or well differentiated. Cancer cells of grade 2 are said to be of intermediate grade, or moderately differentiated. Cells of grade 2 no longer look like normal cells and generally faster growing than cells of grade 1. Grade 3 cancer cells are the most aggressive type of cancer cells. Cells of this grade are the fastest growing and do not even closely resemble normal cancer cells (poorly differentiated).

Along with having a certain grade, cancer is identified as being at a certain stage. The staging system will go from 0 to 4. Stage zero will refer to noninvasive breast cancer, such as ductal carcinoma in situ, which is confined completely within the breast ducts. Lobular carcinoma in situ is also noninvasive, but occurs in the lining of the lobules of the breast. Cancers that are of stages one through four are invasive:

- Stage 1: Measured to be less than 2 cm and has no signs of metastasis to the lymph nodes or any other tissue.
- Stage 2: Measured to be between 2 cm and 5 cm and/or has affected the lymph nodes.
- Stage 3: The tumor is larger than 5 cm and may be attached to surrounding structures such as the muscle or skin. However, there are no signs of the cancer spread beyond the lymph nodes.
- Stage 4: Cancer has spread beyond the breast/lymph nodes. This is referred to as secondary or metastatic breast cancer. The size of the tumor is irrelevant.
Treatment

Currently, there is minimal differentiation in the treatment of hereditary breast cancer and that of non-hereditary breast cancer. In considering distinctions between hereditary and nonhereditary cases, BRCA tumors are typically of a higher grade, and are estrogen-receptor negative. If a tumor is estrogen receptor positive, it will uptake an increased amount of the hormone estrogen, which will fuel tumor growth. The drug Tamoxifen is used to inhibit estrogen uptake. Due to the fact that BRCA tumors are estrogen receptor negative, the efficacy of this particular treatment is not substantiated. While new treatments have been developed per the PTEN study, these are still under clinical trials and have not yet been thoroughly researched. There are different treatment options based on the type of cancer determined through the diagnosis. In summary, classifications for treatment purposes are:

1. Ductal Carcinoma In Situ
   a. Lumpectomy followed by radiation therapy.
2. Lobular Carcinoma In Situ
   a. Lumpectomy
3. Stage I, II, IIIA, and Operable IIIC Breast Cancer
   Primary Therapies (to remove initial tumor)
   a. Breast conserving surgery with follow up radiation therapy OR
   b. Mastectomy (radiation therapy not obligatory)
      i. With both a and b, chemotherapy is recommended for supplemental therapy
   Note: survival is equivalent with both of these options

4. Stage III B, Inoperable IIIC, IV, Recurrent, and Metastatic Breast Cancer and others
   a. Mastectomy of breast conserving surgery with:
      i. Anthracycline-based chemotherapy and/or
      ii. Taxane based therapy

Drugs

Taxane based therapy differs from other chemotherapy because it interferes with the structural function cancer cells need to help them multiply. With the drug Docetaxel as an example, the structure of this taxane is as follows: Picture is courtesy of chemfinder.com. (Arrows indicate some of the chiral carbons in the molecule).

Prognosis

Prognosis for hereditary breast cancer is not differentiated from that of non-hereditary breast cancer. In the stage 4 Metastatic breast cancer, treatment is rarely curative. For operable cancer, survival rates vary, but is much higher than that of inoperable or systemic cancer. In situ non invasive cancers have a very low recurrence rate of between 2%-4%.
Prevention

The early detection of cancer in the context of Hereditary Breast Ovarian Cancer Syndrome is rooted in genetic testing to confirm the gene, increased diagnostic screening, and prophylactic procedures. When a patient is either confirmed of having a BRCA mutation, or are considered to have a high risk of developing breast cancer based on family history, there is a number of options they can consider. For carriers of BRCA mutations, there is a 20-fold increased risk of developing early onset breast cancer. In one particular study, many modalities of prevention were analyzed in 251 BRCA1 or BRCA2 carries. Of these, two-thirds were carriers of a mutation of BRCA1, and the remaining one-third were carriers of BRCA2. After a positive test result for either of the genes, it was advised that the patient receive annual mammography, monthly self-breast examination, and clinical breast examination (2-4 times per year). Prophylactic mastectomies were also discussed as an option. Within the study 29 women (14.9%) elected to have the prophylactic mastectomy. Of these women, 2 had carcinoma in situ in their tissue. Of those that did not undergo surgery, 12 of 165 were diagnosed with new primary breast cancer. Half of these were detected by radiographic means (5 by mammography and 1 by MRI). The other six cases were identified by physical examination (5 by self examination; one by clinical examination). While these methods have not been verified as a means of prevention per say, they have allowed for earlier detection. In addition, the study reported a higher percentage of women performing self examination after genetic counseling. This is surely a positive effect, given that 5 cases of cancer were detected by self examination.

Conclusion

In the context of hereditary breast cancer (BRCA1/BRCA2), I believe that current research will eventually lead to successful targeting strategies. However, I do not think it is unreasonable to assume that there are many people that will not have access to this testing due to insufficient income or their geographic location. Breast cancer genetics surely has made many discoveries in the past two decades. However, without targeted treatment for genetic susceptibility, this has minimal effect on clinical practice. Furthermore, the cause(s) of the majority of breast cancer cases is still unknown. It is my opinion that more genes and their mechanisms will be uncovered, but there will come a point where genetics alone cannot explain the mechanism of many cancers. In addition, because current technology does not allow for us to fix DNA, the knowledge of our predispositions may be waiting a long time for a cure for cancer.
References

The EpiPen®
Misty Curry
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Abstract

The EpiPen® is extremely effective in the treatment of anaphylactic reactions. The EpiPen® is a trademark of epinephrine. The EpiPen® is administered differently in adults and pediatric patients. Epinephrine can cause adverse side effects and aggravate existing medical conditions. Epinephrine is a hormone found in animals and it can be synthesized commercially and used as a reagent to produce other compounds.

The EpiPen® is a brand of epinephrine which is indicated for the prompt treatment of numerous conditions including: anaphylactic shock, bronchospasm, local vasoconstriction, premature labor, cardiopulmonary resuscitation, cardiac arrhythmias, and intra-cardiac injection during cardiac massage.¹ The EpiPen® is a spring-loaded syringe of epinephrine commonly used for the treatment of allergic reactions. This device is designed for quick and easy use during potentially life-threatening occurrences that can be used by pediatrics and adults. The EpiPen® is universally used for the treatment of severe anaphylactic reactions to insect stings—including bees or wasps—and certain foods. Normally, patients with allergic reactions who do not carry an EpiPen®, must seek emergency medical attention to prevent severe anaphylactic shock which can lead to death. “There are about 100,000 episodes [of anaphylaxis] each year in the USA, of which two-thirds are new cases, and almost 1% are fatal” according to David Golden, MD of John Hopkins Asthma and Allergy Center. The statistics are extreme and the cases of anaphylaxis usually go unseen by the public. Treatment of severe allergic reactions is often immediate with the usage of the EpiPen®. Epinephrine is administered by various dosages; however, the EpiPen® is distributed in pre-calculated dosages for adults and pediatric patients. There are side effects from the use of the EpiPen® as well as contraindications in the use of the medication. Epinephrine can be synthesized by various means; however, the stereochemistry is essential.

Epinephrine has the molecular formula C₁₉H₂₃NO₃ and has a combined molecular weight of 183.20 grams (Merck Index). Epinephrine may be known as one of its other six other names including: “(2)-3,4-dihydroxy-α-[(methylamino)methyl]benzyl alcohol, 1-1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol, 1-3,4-dihydroxy-1-[1-hydroxy-2-(methylamino)ethyl]benzene, 1-methylaminoethanolicatechol, adrenaline, and levorenin” (Merck Index). Lehmann noted various trade names of epinephrine such as: “Adrenalin ISM 1:1000 (Nuovo ISM), Anaehelp (Stallergenes), Anakit (Dome-Hollister-Stier), Dyspne-Inhal (Augot), and EPIFRI® (Allergan).” The Merck Index also lists trademarks of epinephrine including: “Anapen (Celltech), Primatene Mist (Wyeth), and Sus-phrine (Forest).” “Epinephrine is a hormone secreted by the adrenal medulla in response to stimulation of the sympathetic nervous system” as noted in Taber’s Cyclopedic Medical Dictionary. Epinephrine, otherwise known as adrenaline, is used in the (R)-form and it is an endogenous catecholamine which functions on alpha and beta adrenergic receptors (AHFS). According to the AHFS, the compound is used in the (R)-form because “the levorotatory isomer is 15 times more active than is the dextrorotatory isomer” and the

racemic form, racpinephrine, is approximately "one-half as reactive as the levorotatory isomer".

The EpiPen® is indicated for the treatment of hypersensitivity to foods, medications and insect stings that can potentially lead to anaphylactic shock. Epinephrine is a vasoconstrictor which works by "constricting the blood vessels..." (Taber’s 659). The constriction of the vessels delays the distribution and absorption of toxins in the blood stream. It is important to understand the concept of anaphylactic shock in so that proper treatment can be sought if needed. Anaphylaxis is a type of allergic or hypersensitive reaction to an allergen in which the allergen is absorbed into the blood or through the mucus membranes which triggers the body’s immune defense system, according to Taber’s Cyclopedia Medical Dictionary. Anaphylactic shock is a life-threatening reaction that needs to be treated immediately. Signs and symptoms of anaphylactic shock include: “acute respiratory distress, hypotension, edema, rash, tachycardia [rapid heart rate], pale cool skin, convulsions, and cyanosis [blue discoloration of the skin]” (Taber’s 92). Causes of anaphylactic shock include allergies to insect stings or bites, certain foods and medications. Many manufactures of snacks disclose information on the label that informs the consumers if the product was produced in a factory that may contain peanut products. Patients who have anaphylaxis to certain foods need to be cautious of the ingredients and the factory where the food is processed. Teachers and school nurses should be notified if a child has anaphylactic reactions and is required to carry an EpiPen®. Reactions to insect stings such as bees, wasps, yellow-jackets, and hornets are the most common forms of anaphylaxis. If a person is highly allergic to insect stings, one should do a few simple things such as “avoiding bright colored clothing, flowers, scented deodorants and shampoo, perfumes, and barefoot walks outdoors” (Goldfrank 1584). The individual should also be cautious when moving boxes, furniture, or working outdoors and wear protective clothing such as leather gloves. The American Journal of Nursing advises those patients who do not have severe allergic reactions to insect stings to rub aspirin on the affected area after moistening the site first. The article also recommends applying meat tenderizers to the site in order to diminish pain and itching associated with insect stings. In a study completed by David Golden, M.D., patients with anaphylactic reactions to stings were evaluated to determine if venom immunotherapy would help decrease the allergic reaction. Patients were observed who had a known history of an allergic reactions to insect stings and the results showed that “46% of patients had a systemic reaction” though “40% did not react to a live sting challenge” 2. Golden also noted that approximately ten years ago, “30-40% of patients” had reactions to a first sting with only “20%” of the patients having a reaction to a second sting. 1 Golden’s data is baffling when trying to predict the severity of a reaction or if an

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anaphylactic reaction will be present after a sting. Since it is impossible to determine if an allergic reaction will occur, those patients who have a history of allergic reactions need to be prepared. Pongracic and Kim’s study found that many people, who have a history of allergic reactions, do not seek treatment. In a study of primarily children, “89% of reactions” were caused by food. “Throat-mouth swelling as a symptom was reported in 44% of children and 68% of adults. An adrenaline kit was available at the time of the reaction in more than 75% but was administered only in 11% of children and 32% of adults.”3 The data stunningly shows that while treatment with epinephrine is available it is unused. Prescription of the EpiPen® is highly recommended to those patients who have a history of anaphylaxis to insect stings and foods.

Administration of the EpiPen® is a fairly simple procedure. As with any pharmaceutical agent, one must carefully examine the instructions provided by the primary care physician or pharmacist. The EpiPen® medication comes with an easy-to-read instruction sheet with a practice auto-injector. It is a great idea to practice using the mock injector to avoid mistakes with the medicated injector when the time arrives. Sometimes patients can be overwhelmed or stricken with panic and fear when they are beginning to have an allergic reaction. Practicing the motion and application can help alleviate some of the nervousness associated with injecting oneself with a syringe. The EpiPen® can be used in four simple steps according to the package insert provided by Meridian Medical Technologies, Inc.

1. Step 1. Grasp unit by forming a fist around the unit with the black tip pointing downward.
2. Step 2. Pull off the gray safety release with your other hand and hold the black tip near your outer thigh.
3. Step 3. Swing and jab the black tip firmly into the thigh, by creating a 90° angle with the syringe.
4. Step 4. Hold the auto-injector firmly against the thigh for approximately ten seconds.

Strong pressure needs to be administered in order to activate the auto-injector. To avoid injecting one’s thumb with the medication, the hand should not be over the black tip at any time. The medicated device is good for one time use only; consequently, the cap should be replaced on the injector and discarded. To practice using the mock injector, the same steps should be followed; however, the mock injector does not contain a syringe or medication. Therefore, in step 3, the mock injector is jabbed into the thigh until a click sound is heard. This sound indicates that sufficient pressure was used to administer the injection. The mock injector does require less pressure in order to activate the sound and the gray safety release should be replaced so that the mock-injector can be used again. The EpiPen® comes in two dosages for adults and pediatrics; the EpiPen® and the EpiPen® Jr. respectively. As per Meridian Medical Technologies, Inc., the EpiPen® contains a dose of 0.3 mg epinephrine in a solution of 1.8 mg sodium chloride, 0.5 mg sodium metabisulfite, hydrochloric acid, and water. The EpiPen® Jr. delivers 0.15 mg epinephrine in a solution of 1.8 mg sodium chloride, 0.5 mg sodium metabisulfite, hydrochloric acid, and water. The hydrochloric acid is used to adjust the pH of the

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solution which will vary from 2.2-5.0.\textsuperscript{4} Many medications are administered to pediatric patients by body weight. Therefore, it is advised that the pediatrician or primary care provider evaluate the patient's weight in order to determine the appropriate dosage of epinephrine to be administered.

The EpiPen\textsuperscript{R} should be protected from light, due to deterioration and stored at a temperature of 25°C. Careful attention must be made to the expiration date of the medication. If the medication is past its expiration date, the medication should be immediately discarded and replaced.\textsuperscript{1} Side effects of epinephrine can be extensive depending on the individual. Side effects include: "fear, anxiety, tenseness, restlessness, headache, tremor, dizziness, lightheadedness, nervousness, sleeplessness, excitability, and weakness" according to the American Society of Heath-systems. Epinephrine can also aggravate pre-existing conditions such as: "psychomotor agitation, disorientation, impaired memory, assaultive behavior, panic, hallucinations, suicidal or homicidal tendencies, and psychosis characterized by clear consciousness with schizophrenic-like thought disorder and paranoid delusions" (AHFS). Some reports of necrosis at the injection site have been noted in repeated injections according to the AHFS. Clinical evaluation is advised for all patients who have existing health conditions or cardiac arrhythmias because the AHFS reports that epinephrine may cause potentially fatal cardiac arrhythmias. Possible contraindications in pregnancy are suspected although no sufficient studies have been completed in pregnant women as per the AHFS. As a result, epinephrine should only be used if the benefit compensates for the risks to the fetus and the primary care physician should be notified to discuss further options. According to Meridian Medical Technologies, Inc., "there are no absolute contraindications to the use of epinephrine in a life-threatening situation." Some may suspect that the size of the syringe in the auto-injector is not large enough for certain people. According to Pongracic and Kim's, the syringe may not be sufficient to penetrate the muscle in males or obese individuals. Though this topic is still under debate, the EpiPen\textsuperscript{R} should still be used to prevent further complications of a reaction. If symptoms of the reaction persist, further medical attention should be obtained.

According to the AHFS, epinephrine can be synthesized or extracted "from the adrenal glands of animals". One of the ways that epinephrine can be synthesized is by performing a Friedel-Craft reaction of catechol with chloroacetyl chloride. The chloroacetyl chloride converts the catechol to 2-chloro-3,4-dihydroxyacetophenone (Lehmann 66). The 2-chloro-3,4-dihydroxyacetophenone is reacted with methylamine to produce the final product of Dextrorotatory, Levorotatory-epinephrine (Lehmann).

\textsuperscript{4} Meridian Medical Technologies, Inc., subsidiary King Pharmaceuticals, Inc. Package Insert Data.
Another way to synthesize epinephrine is by performing an aldol addition and desilylation reaction (Singer 929). According to Singer’s study, veratraldehyde “undergoes [an] aldol addition by silyl ketene acetal in the presence of 1 mol% catalyst to give [the] adduct …” and the final product is R-(−)-epinephrine.

Epinephrine can be used as a reagent to synthesize other compounds such as dehydroadrenaline. Dehydroadrenaline is made by dissolving the epinephrine in hydrochloric acid and then adding water to the solution (Mitchell 270).

The reaction can be continued from the o-quinone formation from epinephrine to yield 3-[[4,5-Dihydroxy-2-[1-hydroxy-2-(methylamino)ethyl]phenyl]thio]propanoic Acid (Mitchell 270). The dehydroadrenaline is reacted with 3-Mercaptopropionic acid which is diluted with hydrochloric acid and then added to the solution which is stirred for an additional 30 minutes (Mitchell 270).
In conclusion, the EpiPen® is the preferred medication for the rapid treatment of anaphylaxis. The EpiPen® is a trade name of epinephrine or otherwise known as adrenaline. Indications of the EpiPen® include anaphylaxis to insect stings such as bees, wasps, hornets and certain foods. The EpiPen® is an auto-injector that penetrates the muscle and injects a pre-determined dosage of epinephrine into the system. Patients who personally administer the EpiPen® can avoid further medical attention. Although there is no evidence that supports whether an allergic reaction will definitely occur in patients who have a history of allergic reactions to insect stings, it is crucial that the individual continues to carry an EpiPen® to prevent possible anaphylactic shock. There are two dosages of the EpiPen® for adults and children and a prescription for this medication is required. Parents of children who are prescribed an EpiPen® need to become familiar with the process of administering the injection. Parents also need to notify school officials such as the teacher or nurse in case an allergy is present while at school. Adverse side effects of epinephrine can be lengthy; therefore, the medication should be taken only as required. Epinephrine is also known to aggravate pre-existing medical conditions such as schizophrenia as well as inducing potentially life-threatening cardiac arrhythmias. Consultation with a doctor is extremely important when choosing whether the EpiPen® is the appropriate medication for an individual. Epinephrine can be obtained from animals but is also easily synthesized in one to two step processes. Products such as 3-[(4,5-Dihydroxy-2-[1-hydroxy-2-(methylamino)ethyl]phenyl]thio] propanoic Acid can be obtained by using epinephrine as a reagent. The EpiPen®, as well as all medications, needs to be handled appropriately to avoid potential complications with the effects of the pharmaceutical agent. The EpiPen® should be stored in cool temperatures of 25°C and protected from light since deterioration of epinephrine can occur. Utilization of the EpiPen® or EpiPen® Jr. is crucial to prevent potential death from anaphylactic reactions.


Diffraction Phenomena
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Abstract
This article is about diffraction, interference, light, optics, diffraction grating, and spectroscopy. The creator of the monograph was Joseph Fraunhofer, who is normally recognized as an inventor of diffraction grating. Fraunhofer mentioned the difficulties in actually inventing the diffraction grating. Reflection is an alteration in the direction of waves when they jump off an obstacle; where refraction of waves is an alternation in the direction of waves as they go from one medium to another, diffraction is a change in direction of waves as they go by an opening or pass a barrier in their pathway (Kleppner and Daniel, 2005).

Introduction
Early in the nineteenth century, experiments were suggested and made to show that light is a wave motion. A key figure in this endeavor was Thomas Young, one of the most intelligent and clever scientists ever to live. In 1803, Young studied diffraction and interference of light already with results that gave strong support to the wave theory of Christian Huygens, as opposed to the particle or corpuscular theory of Isaac Newton. Further contributions were made by many other researchers, among them Augustin Jean Fresnel, who showed that light, is a transverse wave (Ekspong, 1999). The creator of the monograph was Joseph Fraunhofer, who is normally recognized as an inventor of diffraction grating. Fraunhofer mentioned the difficulties in actually inventing the diffraction grating. Fraunhofer was credited by a number of advance science, and also, he has discovered the solar absorption spectrum and made the diffraction grating. He changed spectroscopy from a qualitative art into a quantitative science by viewing how to get exact value of the light wavelength. Also, Fraunhofer created the field of stellar spectroscopy (Kleppner and Daniel, 2005).

Reflection is an alteration in the direction of waves when they jump off an obstacle; where refraction of waves is an alternation in the direction of waves as they go from one medium to another, diffraction is a change in direction of waves as they go by an opening or pass a barrier in their pathway. Water waves can travel around the curves, around obstacles, and go by openings. The capacity of traveling water around corners is understandable for longer wavelengths of water waves. Diffraction can be established by inserting tiny barriers and obstacles in a flow tank and looking at the path of the water waves while encountering the obstacles. The total diffraction becomes greater with greater wavelength and less with fewer wavelengths. In reality, when the waves' wavelengths are lesser than the obstacle, no visible diffraction takes place (Henderson). When we want to divide different wavelength's light great resolution, then we can use device of diffraction grating. This is so useful in today's world. "The super prism aspect of the diffraction grating leads to application for measuring atomic spectra in both laboratory instrument and telescopes" (Diffraction Grating, n.d.). Springer (2006) wrote the following:

A diffraction grating is an optical surface on which a large number of grooves, N, are located. The grating has the property of diffracting light in a direction related to its wavelength. Hence an incident beam with several wavelengths is angularly separated into different directions. Conversely, several wavelengths, \( \lambda_1, \lambda_2, ..., \lambda_n \) coming from different directions can be combined into the same direction. The diffraction angle depends on the groove spacing and on the incidence angle. (p. 71)

Here is an example of diffraction on soap bubble; it works amazing. Light is all colors' mixture. No one can see a light beam from one side to another side and look at light waves, but
anyone can look at light when light waves are estimated on a white screen. The thought of interference of different colors at different angles involve that the light wavelength is related with its colors. A spectrum can be observed a lot on an aquarium edges, glass, mirrors, or other kind of glass. These colored edges proposed that different angles are deflected by different colors in the pattern of interference. When light waves are going through both slits, which are in phase there must be constructive interference and result will be vivid light. If the waves reach at a spot on the display out of phase, the interference will not be helpful, and the result will be a dark line. This clarified why bubbles of an almost colorless soap liquid are expanded bright colors before they break. When look at the white light, from red to violet, the complete visible light range will be in a bubble of soap. As the wavelengths to be different, the film of soap is not able to reinforce or cancel every color at one time. All colors of rainbow, an oil drop on water, and bubbles of soap are phenomena of light is the reason of all diffraction, refraction, and interference. Interference colors are seen in bubbles of soap and oil on water are able to see in the peacock feathers (Color-Diffraction and Interference, n.d.).

In physics, wave–particle duality is the thought that all matter displays both wave-like and particle-like properties. Nave (2001) states following:

   The evidence for the description of light as waves was well established at the turn of the century when the photoelectric effect introduced firm evidence of a particle nature as well. On the other hand, the particle properties of electrons were well documented when the DeBroglie hypothesis and the subsequent experiments by Davisson and Germer established the wave nature of the electron.

We are concerned about two types of nature of light: first is particle nature of light and wave nature of light. In particle nature of light, the electromagnetic wave theory of light came across severe problems in trying to explain the practical spectrum of radiation from warm objects, which are “black body radiation” by the end of the nineteenth century. Some challenged the reconciling theory, and the experiment had been unsuccessful until Max Planck planned in the beginning of the 19th century that vibrating atoms that release light do so in isolated amounts. That is the energy which was hypothesized to be quantized, given by the relation

\[ E = N \hbar \nu \]

Where \( \nu \) is the frequency of vibration, \( N \) is an integer, and the constant \( \hbar \) is an empirical constant of nature required by dimensional analysis, and is called Planck's constant. Its mathematical value is given by \( \hbar = 6.62618 \times 10^{-34} \text{ Js} \). High frequency radiation like ultra-violet was guessed to make a huge contribution to the black body spectrum, in opposition to the experimental data.

“Planck's quantum postulate solved the problem because to emit even a single quantum of ultra-violet radiation would require a minimum energy much larger than the typical available thermal energy of order \( kT \): Hence very high frequencies would not be present in the radiated spectrum of a black-body” (Parwani, 2002). In 1905, Einstein bravely proposed that the light really consisted of and spread in isolated energy packets called photons (Parwani, 2002). In wave nature of light, Electromagnetic radiation takes energy from space. It contains visible light, dental x-rays, radio waves, and heat radiation from a fire. It shares some basic characteristics. These all move throughout a vacuum at speed of light, 3.00 x 10^8 m/s. It has "wave-like" characteristics. Electromagnetic radiation has equally electric and magnetic properties. Electromagnetic radiation's "wave-like" property is due to the cyclic oscillations of these components. We can give a frequency and a wavelength to electromagnetic radiation because every electromagnetic radiation shifts at the same speed. There will be fewer rotations passing a certain point per second if the wavelength is long; so, the frequency will be low. There
will be more rotations passing a certain point per second if the wavelength is short; so, the frequency will be high. Therefore, there is an inverse relationship between wavelength and frequency.

\[
\text{Speed of Wave} = (\text{Distance between peaks}) \times (\text{Frequency})
\]
\[
= (\text{Wavelength}) \times (\text{Frequency})
\]

\[
\text{Frequency} \times \text{wavelength} = \text{Speed of light}
\]

\[
\text{Frequency} = \frac{\text{Speed of light}}{\text{wavelength}}
\]

\[
\text{Frequency} = \left( \frac{1}{\text{wavelength}} \right) \times \text{speed of light}
\]

\[
\nu = \left( \frac{1}{\lambda} \right) \times c \quad \text{(Units of m/s)}
\]

\[
c = \nu \lambda \quad \text{(Units of m/s}^2\text{)} \quad \text{(Blaber, 1996)}.
\]

Here, we will see how water waves, sound waves, and light waves diffracted. Water waves diffracted when a wave is extended while comparing the slit size or minor than the wavelength. The water in the slit resonate such a point source when a narrow slit is reached waves. Thus, the secondary sources are launched by the waves the length of the slit is almost in-phase while some point was arriving in the forward direction. The diffracted wave looks like a circular wave with center on the slit. A wave walks instantly in a straight line whenever the slit size is a lot larger than the wavelength (Diffraction of water waves (opening), n.d.). The main parts of our knowledge with sound implied diffraction. In reality that you are able to hear sounds on sides of corners and around the wall included diffraction of sound and as well as reflection. In such cases, Diffraction is used for the sound to change direction around the obstacles. In reality, that diffraction is more evident with more extended wavelengths involved that we cannot hear high frequencies around obstacles better than low frequencies. For example, a marching band on the road. “You may perceive diffraction to have a dual nature, since the same phenomenon which causes waves to bend around obstacles causes them to spread out past small openings.” Being capable to listen to the sound when we are outdoor is also the example of the frequencies of sound, this dispersal of sound waves has effect when we are trying to soundproof a room. Also, the light is diffracted. Diffraction of light does not produce a clear dot as a picture is not produced when light from a specific spot going throughout a small circular hole; however, a disperse circular disc fairly recognized as Airy's disc bounded by fainter circular rings. This case is so importance of diffraction because the eye and many optical tools have spherical apertures. If this image cover of the spot is bigger than the created by the abnormality of the system, the imaging procedure is called diffraction-limited (Nave, 2001).

\textit{Interference} takes place when two or more than two waves of light to be related at a certain point. A constant interference pattern is seen if (a) the sources are kept up relationship of constant phase with one another, (b) the sources have equal wavelengths, and (c) the principle of superposition can be applied (Serway and Faughn, 2006, p. 811). There are two type of interference: Constructive and Destructive interference. In constructive interference, the value of path difference determines whether the two waves are in phase when they arrive at \( P \). If the path difference is either zero or some integral multiple of the wavelength, the two waves are in phase at \( P \) and constructive interference results. The condition give by for constructive interference is

\[
\text{Greek Delta, } d = d \sin \theta_{\text{bright}} = m \lambda
\]

Order number, \( m=0, \pm 1, \pm 2 \ldots \). The central bright fringe at \( \theta_{\text{bright}} = 0 \) in known as zeroth-order maximum. When \( d \) is an odd multiple of \( \lambda / 2 \), the two waves reaching at \( P \) are 180° out of phase and increase to destructive interference. Therefore, the condition for destructive interference at \( P \) is given by
Greek Delta, $d = d \sin \theta_{\text{dark}} = (m + 1/2) \lambda$ (Serway and Faughn, 2006, p. 811-812).

As soon as a photon has gone through the polarizer, it could not be difficult to tell whether it approached from slit 1 or slit 2. The photons start behaving more like waves after the particle-like information gone. Walborn (2003) states following:

"Similarly, if we place a linear vertical polarizer between the quarter-wave plates and the detector, we again erase the which-path information. However, in this case we observe a fringe pattern—commonly called anti-fringes—that is exactly out of phase with the pattern we saw through the horizontal polarizer. Anti-fringes exhibit a central minimum (dark stripe)" (Walborn, 2003).

There is other technique also to observe interference in light, which is Newton’s ring. From this method, we also can observe interference in light waves by another method, which is by putting a Planoconvex lens on top of surface of a flat glass. With this placement, the air image between surfaces of the glass varies in width from “0” at the contact point certain value $r$ at $P$. If the radius of the lens curve $R$ is much bigger than the distance $r$, and if the system is observed from above light of wavelength $\lambda$ (lambda), a light pattern and dark rings is seen. Newton has invented the circular fringes, which are known as Newton’s rings. We can get an example for the radii of the bright and dark bands in terms of the radius of curve $R$, and vacuum wavelength, $\lambda$.

For instance, the dark rings have radii of $r = \sqrt{(m \lambda R/n)}$ (Serway and Faughn, 2006, p. 793).

Certain functions require that some light rays should become less in size. This problem come across if a signal of light approaching as a wide, different mode beam at the recipient must become into a small spot according to detect it by a photodiode. The inner beam covers up some specific area and includes light rays all the way through a specific range of slopes. The area, which we had, determined the necessary density ratio. “The maximum ray slopes allowed at the detector may be determined either by the optical properties of the device used to compress the light beam or it may be limited by the fact that the ray angles can be no more than 900 if the beam is to reach the detector at all” (Marcuse, 1971).

Wave interference happens when two waves get together during travel along a similar medium. “The interference of waves causes the medium to take on a shape which results from the net effect of the two individual waves upon the particles of the medium.” To start the examination of wave interference, think about two pulses of the same amplitude shifting in unlike directions along the same medium (Henderson).

We have two type of diffraction is single-slit diffraction and double-slit diffraction. In single slit diffraction, diffraction takes place when waves pass through very small openings, around obstacles, or by sharp edges. The pattern of diffraction formed by a single slit on a far screen consists of a central bright maximum line by less bright fringes flashing with dark regions. The angle $\theta$ at which the pattern of diffraction has zero intensity which is given by

$$\sin \theta_{\text{dark}} = m \left( \frac{\lambda}{a} \right)$$

$m = \pm 1, \pm 2, \pm 3 \ldots$ is the width of the slit and $\lambda$ is the light wavelength incident on the slit (Serway and Faughn, 2006, p. 811).

In Young’s double-slit experiment, two slits taken apart by distance $d$ are enlightened by a wavelength of single light source. The pattern of interference is included in bright fringes and dark fringes are viewed on a screen a distance $L$ from the slits. The bright fringes given by

$$d = d \sin \theta_{\text{bright}} = m \lambda$$

Order number, $m = 0, \pm 1, \pm 2 \ldots$
For dark fringes known as destructive interference given by

\[ d = dsin\theta_{dark} = (m+1/2) \frac{\lambda}{2} \]

Order number, \( m = 0, \pm 1, \pm 2 \ldots \)
The bright fringes' position \( y_m \) on the display can be decided with use of the relation \( sin\theta = tan\theta = \frac{ym}{L} \), which is true for little angles.

\[ y_{bright} = \left( \frac{\lambda}{L/d} \right) m \]

Order number, \( m = 0, \pm 1, \pm 2 \ldots \) (Serway and Faughn, 2006, p. 811).

There is two other type of diffraction for laser system: the Fraunhofer diffraction and the Fresnel diffraction. As we said above, Fraunhofer is recognized an inventor of diffraction grating. The laser system is a basic of Fraunhofer diffraction, which is now generally used in most of the particle size studies, because it is easy to use, and to reproduce, as well as a quick process. In this technique, an intensity diffraction model from particles is measured by a concentric photo detector. Generally, a diffraction image model depends on the shape of a particle; whereas, the pattern size depends on the size of the particle. The latter data states only that the normal particle size analyzer is used for the particle size. Fraunhofer diffraction makes an arrangement with the limiting cases where the light is coming from the diffracting point is monochromatic and equivalent. Further, the picture plane is at a space huge balanced to the diffracting object size. In the particular case of Fraunhofer diffraction, the incoming light should be parallel, and the picture plane should be at a very long space compared to the diffracting object. The other type of diffraction is Fresnel diffraction. It is the more common case where these limitations are relaxed. This makes it mathematically more difficult. Several cases are able to be treated in a reasonable experimental and graphical method to give details of some observed phenomena. Fresnel diffraction was invented by a French physicist Augustin-Jean Fresnel who was the creator of wave optics theory (Nave, 2001).

Diffraction gratings are very helpful to measure accurately the light wavelength. For example, gases provide light of some specific colors. Every element contains its own unique configuration of emission lines. For example, astronomers are able to tell what elements are composed of by the stars by measuring the light wavelength when astronomers gaze at stars through diffraction gratings. Also, they can tell about the elements by measuring the light wavelength absent from the spectrum. This is recognized as spectroscopy (Nave, 2001).

We can read CD and DVDs by using diffraction and interference, and it shows you here how it works. A compact disc tracks work as a diffraction grating; making a part of the white light's colors. The formal track makes apart on a CD is 1.6x10^-6 meters, equivalent to about 625 tracks/millimeter. This is in the series of common laboratory diffraction gratings. The wavelength of the red light 600 nm, this would provide a primary order diffraction maximum at about 22° (Nave, 2001). In reality, light is an electromagnetic wave. All waves are bright and colored, and go back and forth at some specific angle, which known as polarization. This is also accurate for laser light; however, it is more similar than any other source of light. Since it is much similar, it is able to be focused as well to extremely small diameters where the light concentration energy turned out to be great that we are able to cut, drill or rotate with the beam. This is helpful in CD player and surgical machine. It can also be made very different shades of one color, so there will be wavelength of just one light. White light has each color in the spectrum; however, even a colorful light, such as a red LED (light emitting diode) have a nonstop interval of wavelengths of red color (What is Laser?, 2008).

In diffraction, refraction is the useful term and however, related to this topic. Refraction index is the definition of the light speed in vacuum divided by the light speed in the medium.
The refraction keys of some general substance are described below. "The values given are approximate and do not account for the small variation of index with light wavelength which is called dispersion" (Nave, 2001).

\[ N = cv \]

<table>
<thead>
<tr>
<th>Substance</th>
<th>Index of Refraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuum</td>
<td>1.000</td>
</tr>
<tr>
<td>Air</td>
<td>1.00277</td>
</tr>
<tr>
<td>Water</td>
<td>1.33</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>1.63</td>
</tr>
<tr>
<td>Methylene iodide</td>
<td>1.74</td>
</tr>
<tr>
<td>Diamond</td>
<td>2.417</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>1.362</td>
</tr>
<tr>
<td>Glycerine</td>
<td>1.473</td>
</tr>
<tr>
<td>Ice</td>
<td>1.31</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>1.59</td>
</tr>
<tr>
<td>Crown glass</td>
<td>1.50-1.62</td>
</tr>
<tr>
<td>Flint glass</td>
<td>1.57-1.75</td>
</tr>
</tbody>
</table>

Snell's Law speaks about the refraction index; the two media to the directions of transmission in terms of the normal angles. Snell's law can be derived by the Fresnel Equations.

\[ n_1 \sin \theta_1 = n_2 \sin \theta_2 \]

\[ \frac{n_1}{n_2} = \frac{\sin \theta_2}{\sin \theta_1} \] (Nave, 2001).

An interferometer is related to the interference. It is composed from more than or equal to two separate telescopes that their signals about to come together, so if they were approaching from a telescope's separate parts as how big the two telescopes are at a distance. An interferometer motion moves towards a telescope of diameter equivalent to the largest partition among its individual elements. On the other hand, as many photons are not collected through the interferometer as it should be by a huge telescope of its size (Nave, 2001). Another phenomenon of nature is the mirage which is created in the atmosphere by refraction. A mirage is able to be seen when the temperature of earth is extremely warm that the air straight above the land is hotter than the air at higher it is warmer than air at higher altitude. For example, sometimes you see flooded on road when it is high temperature, but in reality, the road is dry. This shows an example of mirage (Serway and Faughn, 2006, p. 768-769).

An electromagnetic wave goes underneath an alternation of phase of 180° on reflection from a medium with a refraction index greater than the medium in which the wave is shifting. There is not become any difference when the wave, shifting in a medium with greater index of refraction, reflects from a medium with greater index of refraction, reflects from a medium with a minor index of refraction. The light wavelength, \( \lambda \) in a medium with index of refraction \( n \) is

\[ \lambda \cdot n = \frac{\lambda}{n} \]

Where, \( \lambda \) is the light wavelength in open space, light is coming across a thin film of width \( t \) will be reflected the film's top and bottom side; every ray goes under a possible phase alternate as explained above. Both rays are combined again, and bright and dark fringes will be viewed, with the conditions of interference given by the following table,

<table>
<thead>
<tr>
<th>Equation ((m=0, 1, \ldots))</th>
<th>1 phase reversal</th>
<th>0 or 2 phase reversals</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 2nt = (m+1/2) \frac{\lambda}{\lambda} )</td>
<td>Constructive</td>
<td>Destructive</td>
</tr>
<tr>
<td>( 2nt = m \frac{\lambda}{\lambda} )</td>
<td>Destructive</td>
<td>Constructive</td>
</tr>
</tbody>
</table>

(Serway and Faughn, 2006, p. 811).

Selective absorption, reflection, or scattering can make unpolarized light to become polarized. Light can be polarized by an object if it passes waves containing electric field vectors going back and forth in directions vertical to that direction. When unpolarized light goes through a polarizing sheet, its intensity is lessened by half, and the light turns into polarized. When its following the polarizing sheet with transmission axis at \( \theta \) angle with respect to the transmission axis of the primary sheet, the transmitted intensity is given by

\[ I = Io \cos^2 \theta \]

Where \( Io \) is the intensity of the light after passing through the first polarizing sheet.
When the angle of incidence makes an angle of 90° between the reflected and refracted beams, reflected light is entirely polarized. This angle of incidence is called the polarizing angle \( \theta_p \), and satisfies Brewster’s law, given by

\[
n = \tan \theta_p
\]

Where \( n \) is the index of refraction of the reflecting medium (Serway and Faughn, 2006, p. 812). Polarization of light is the base for the polariscope. It uses observable facts, to find inner stresses in objects or to discover the power of refraction in gemstones. A polariscope is composed of two mirrors, by which reflection linearly polarizes light when Brewster’s angle or angle of polarization focused. The two mirrors are generally placed perpendicular to each other and placed with a very slight tester in between them. When the tester is seen, it will prove whether the tester is birefringent due to the property of polarized light (The Polariscope, n.d.).

The polariscope is an optical examination tool helpful to find inner stresses in glass and other see-through materials like plastics and synthetic resins. A polariscope is made up mainly from a light source and two across polarized lenses like Polaroid. The polariscope source of light is increased under a lens, and it’s power-driven by both independent batteries and an outer power source. Inspected material is located between the two lenses of polariscope and seen through the lens reverses the light source lens (ITG SUBJECT: POLARISCOPE, 1973). The non-quantum electromagnetic field explanation is referred as fresh monochromatic to the idealized case; a wave spreads in vacuum next to the positive z-axis of coordinate system of a right-handed. A complete wave description could be given either identifying its own electric field vector or, its own magnetic field vector, since the both quantities are related by the equation

\[
B(r, \theta) = n \times E(r, \theta).
\]

Where \( n \) is the vector of unit in the direction of propagation, and \( E \) and \( B \) are calculated in c.g.s. units. (Degli’Innocenti and Landi, 2004).

Generally, the kaleidoscope, which we make today, is made from three extended thin mirrors set in a circle, with changeable, see-through, colored objects at the end and an eyepiece on the other side end. In 1817, David Brewster has discovered the kaleidoscope. The fundamental kaleidoscope is composed of two mirrors leaning at an angle of 45 to 60° to each other. “When three rectangular mirrors of the same dimensions are arranged to form an equilateral triangle, rays of light from an object will form multiple images due to the reflections from the mirrors” (Cowens, 2004). It creates five images at every width of 60°, but in reality it is only one image (Cowens, 2004).

Color spectrum is the wonderful instrument; it includes seven colors and its own different wavelength. If sun rays going from a prism, a group of colors is formed such as a rainbow. It was invented by Isaac Newton, who has invented the universal theory of gravitation as well. Color spectrum is the group of colors. The light separating in this technique is known as dispersion. A rainbow is produced by a color spectrum as sunlight is going through prisms including of water droplets. In conditions of physics, light is a kind of electromagnetic wave. The space between two peaks of these waves is known as the wavelength. The colors, which we can see to be different, are determined on the light wavelength what we are observing. Human beings are not able to see the color spectrum because there is some particular light wavelengths act as stimulus the retinas of our eyes, causing us to recognize colors. The colors are already arranged in the spectrum; the sequence red, orange, yellow, green, blue, indigo, violet. Every color has actually its different wavelength. The light is recognized by the highest wavelengths as red and that with the lowest wavelengths as violet. The distance of wavelengths the human eye is able to see is recognized as visible light.
Red 780 to 622 nm
Orange 622 to 597 nm
Yellow 597 to 577 nm
Green 577 to 492 nm
Blue 492 to 455 nm
Violet 455 to 390 nm
1 nm (nanometer) = 10^{-9} m (The Color Spectrum, n.d.).

The mass spectrometer is a device which would be able to calculate the masses and compute the relative absorptions of molecules and atoms. It is used in the magnetic force on a shifting charged particle. In, mass spectrometer, a selector of velocity is used by mass spectrometers to choose only charged particles by an exact velocity analysis. It is used for geometry where opposite, equivalent magnetic and electric forces are measured for speed of a specific particle. If a charge shifts into a magnetic field with direction at a 90 degree angle to the field, it will go in a circular path. The magnetic force, at a 90 degree angle to the velocity, supplies the centripetal force.

\[ F = qvB \]
\[ r = \frac{(mv)^2}{qB} = \frac{mv}{qB} \]
\[ \frac{1}{2}mv^2 = qv; \quad v = \sqrt{2mv/m} \]
\[ r = \frac{1}{B} \sqrt{2mv/q} \]

"Mass spectrometers are sensitive detectors of isotopes based on their masses. They are used in carbon dating and other radioactive dating processes" (Nave, 2001). The grouping of a mass spectrometer and a gas chromatograph creates a great instrument for the detection contaminants or toxins of measured trace. Mass spectrometers are included in some satellites and spacecraft for the classification of the few amounts of particles which are intercepted in the space. For instance, a mass spectrometer is used by the SOHO satellite for analyzing the solar storm. Mass spectrometers are applicable for the analysis of remaining gases in high vacuum structure (Nave, 2001).

A firm called Smart Holograms found in Cambridge, England, has started a technique to store two holograms together in a single portion of photosensitive material. The material is a kind of extremely absorbent synthetic polymer, known as a hydrogel that includes silver halide grains of the type used in some photographic procedures. The hydrogel itself extends and contracts, depending on the contained water in it. In its extended state, it creates an image, and in its contracted state, it creates the second (More to it than meets the eye, 2008)

A spectroscopic's basic principles are: if something is shifting it to a one side force, instead of shifting in a straight row, it will shift in a curve. For example, you have a cannonball shifting past you and you wanted to repel it instead of going through you, you could get a water jet from a hose-pipe that you could squeeze at it. Honestly, it is not going to create much difference because the cannonball is so weighty, and it will not easily be repelled at all from its original course. Atoms are deflected through magnetic fields, supplying an atom that is initially turned into the ion. Although electrically neutral ones aren't influenced through a magnetic field, electrically charged particles are. The sequence is in different stages: first ionization, second acceleration, third deflection, and fourth detection. In stage one; the atom is ionized by reducing one or other electrons to provide a positive ion. This is still true for things from which negative ions are normally expected to form, such as chlorine, or it would not form ions at all, such as
argon. All the time, mass spectrometers work with positive ions. In stage two, the ions are accelerated; therefore, everyone has equal kinetic energy. In the third stage, a magnetic field deflects the ions according to their masses. They are more deflected as they are lighter. The total deflection depends on the amount of positive charges on the ion as well. The more the ion is charged, the more it gets deflected. In stage four, the beam of ions traveling is electrically detected by the machine (Clark, 2000).

Holography is a technique of duplicating a three-dimensional picture of an object by means of light wave patterns created on a photographic film or plate. It is also occasionally called "lens less photography" because there is no use of lenses to create the image. The plate or film with the recorded patterns of waves is called a hologram. The term has been taken from Greek words "holos" (whole) and "gramma" (message). Most people will imagine the three-dimensional image seen on credit cards and banknotes as soon as referring to the word "hologram," but now holography has uses in some new fields. A hologram is a particular interference pattern produced in a photosensitive medium. The pattern has frequently been produced by a quick trick using lasers. "This involved combining two beams, one of which has been bounced off the object to be holographic. The combined beam then strikes the photosensitive medium and the result is the interference pattern that generates the 3-D picture" (Biedermann, 2005).

The system enlightens the object and an amplifier in the center from the mirror and the lens at the higher left. The light of the amplifier is enlarged towards the photographic plate facing. As the lens is not meant to develop an image, the incident flux of radiant energy per unit area from the loudspeaker to the plate is fairly uniform. Nevertheless, a part of the laser beam has been separated as a reference field on the partly see-through mirror. After almost equal travel time, the laser beam has now met the object field on the photographic plate. Then, the two fields get in the way and expose simultaneously the wave pattern in the composition. The reference field only stands out on the plate and, turn in modulate the structure once it is developed, which is the hologram. The light is spread into some diffracted fields; from these fields, one is identified as the reconstructed field that spreads from the plate as a duplicate copy of the object field which hit the plate before. Thus, the hologram acts as a window with a memory (Biedermann, 2005). Birefringence of material and large molecules can be visualized from the capture of a single hologram beams. This invaluable property of holography makes possible the detailed study of stresses and strains inside dielectric materials (Springer, 2006).

To observe light in diffraction and interference, spectroscopy is useful tool for that. To build a spectroscope, I used diffraction grating 2 cm square slit, paper tube (I used tube from toilet paper), poster board square (little bigger size than the tube surface), masking tape, scissors, razor blade knife, spectrum tubes and power supply (fluorescence bulb), laser and pencil (these all is per one spectroscope). First, from pencil we draw round about size of tube surface, and then from scissor, I cut this out in circle. The circle should be little larger than the tube surface. I already had about 15 diffraction grating slits. I did not have to cut it about 2 cm. Then, I tape the diffraction grating slit with tube, and tape the circle other side of the tube. While holding it in place, view a light like a fluorescent tube. The spectroscope is complete now.

However, I have some difficulty with finding a fluorescent bulb, I do not understand how I am going to place bulb in spectroscope. Also, I was wondering about the lighting because even though my house light was on, I could see the rainbow by the spectroscope what I have made. The other question how the florescent bulb is helpful for spectroscope even though I could see the rainbow. In beginning, I could not see the rainbow because I was looking at laser. Then, I
found out that I should not have looked at the light. I am also planning to give spectroscope to all students in my class on presentation day.

**Conclusion.**

The creator of the monograph was Joseph Fraunhofer, who is normally recognized as an inventor of diffraction grating. Fraunhofer mentioned the difficulties in actually inventing the diffraction grating. Reflection is an alteration in the direction of waves when they jump off an obstacle; where refraction of waves is an alternation in the direction of waves as they go from one medium to another, *diffraction* is a change in direction of waves as they go by an opening or pass a barrier in their pathway.
A light wave is known to vibrate in a multitude of directions ...

... In general, a light wave can be thought of as vibrating in a vertical and in a horizontal plane.

Wave Interference

Constructive Interference

Polarization of light waves (glenbrook)

Destructive Interference (Glenbrook)

Single Slit Diffraction

Double Slit Diffraction

hyperphysics

Photoelectric Effect

Davison-Germer Experiment

Wave-Particle Duality (hyperphysics)
Wave Interference

After ionization, acceleration, and selection of single velocity particles, the ions move into a mass spectrometer region where the radius of the path and thus the position on the detector is a function of the mass.

If the velocity $v$ is produced by an accelerating voltage $V$:

$$\frac{1}{2}mv^2 = qV$$

Substitution gives:

$$f = \frac{1}{B} \sqrt{\frac{2meV}{q}}$$

Diffraction Grating in Spectroscopy

Polariscope (adbn.)

Spectrum

Color
Diffraction of light


Obesity in America

Prepared for
Dr. Hank Mancini
CHM236
Khushboo Dave
April 18, 2008
Abstract

The word *obesity* refers to the overall body weight of a person and also tells us about the overweight. Excess bodyweight comes from muscle, bone, heavy fat, and/or water. Obesity contains a great amount of excess fat of the body. BMI is the most important tool for the obese people to measure their weight level.¹ The obesity is risky for some heart diseases and kidney disease and also creates some other problems and diseases as well. The obese people often have Cohen syndrome.

Introduction

The word “obesity” refers to the overall body weight of a person and also tells us about the overweight. Excess bodyweight comes from muscle, bone, heavy fat, and/or water. Obesity contains a great amount of excess fat of the body. The body mass index (BMI) is a very helpful tool to measure the body whether overweight or obesity. BMI depends on how much height and weight is, and it is useful for adults, children, and adolescents. Obesity is the most common problem for most Americans; however, there are many problems and risks for some diseases caused by obesity. The more extra body fat that you have, the more you are overweight, and the more likely you to have heart disease, high heart blood pressure, diabetes, gallstones, breathing problems, and some types of cancers.¹ “Studies in over 5000 identical twins demonstrated that childhood obesity has a strong (77%) inherited component.”² There were 41 percent BMI in 342 males, and 40 % BMI in 356 females. Obesity is a major health problem in America. U.S. Government found out that 5% of health care costs are responsible for obesity related diseases; such as diabetes, cardiovascular disease, gall-bladder disease, hypertension, and cancer. Large number of adults have problem of excess body weight, and so “the interest for the genetics of human obesities has increased considerably during the last decade partly because of the realization that some forms of obesity were associated with high risks for various morbid conditions and mortality rate.”³

Symptoms/diagnosis

There are some symptoms that people can observe to determine the obesity. Most of the time people can tell by knowing their weight if they are obese, but sometimes it is kind of hard to tell. If you are obese, you should measure the scale and see if you have gained your weight. If you are tall, and if you have gained some weight, you should not be worried about this too much. Also, you can tell if you have too much fat around your waist that you are obese. If your weight is more than the normal body mass index and circumference of weight, you can also tell if you are obese. Here is the body mass index for adults, and you can estimate from this how much you are overweight and how much your weight should be according to your age.¹

<table>
<thead>
<tr>
<th>Body Mass Index (BMI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
</tr>
<tr>
<td>4'10&quot;</td>
</tr>
<tr>
<td>5'0&quot;</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>5'1&quot;</td>
</tr>
<tr>
<td>5'3&quot;</td>
</tr>
<tr>
<td>5'5&quot;</td>
</tr>
<tr>
<td>5'7&quot;</td>
</tr>
<tr>
<td>5'9&quot;</td>
</tr>
<tr>
<td>6'0&quot;</td>
</tr>
<tr>
<td>6'1&quot;</td>
</tr>
<tr>
<td>6'3&quot;</td>
</tr>
</tbody>
</table>

### Stature-for-age and Weight-for-age percentiles

2 to 20 years: Boys

<table>
<thead>
<tr>
<th>NAME</th>
<th>RECORD #</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Mother's Stature</th>
<th>Father's Stature</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Age</th>
<th>Weight</th>
<th>Stature</th>
<th>BAP</th>
</tr>
</thead>
</table>

### To Calculate BMI:

- Weight (kg) = Stature (cm) * Stature (cm) / 10,000
- Weight (lb) = Stature (in) * Stature (in) / 703

**GROWTH CHART**

Published May 22, 2000 (revised 1/31/02).

**SOURCE:** Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2002).

https://www.cdc.gov/growthcharts

(picture is taken from chartgraphdiagrams.com)
To measure children’s weight, doctors also use the “Growth Chart”, which is also a very important tool to check the obesity level if your children have it. This chart has height and weight, and it compared to children who are the same age, to observe children’s body changes more time. “The number plotted on a growth chart - greater than the 95 percentile is considered overweight or obese. A child who falls between the 85 percentile and 95 percentile is considered at risk for becoming overweight.”

The BMI’s result is reliable, but there are some limits also for body mass index: sometimes, it calculate more body fat for athletes and some other people who are well built, and it also sometimes calculates less body fat for old people and some others who are missing some muscle mass. If your BMI (units of Kg/m^2 where Kg is the person’s weight, and m in the person’s height in meters.) calculation is between 25.0 to 29.9, then you are overweight. If your BMI calculation is 30.0 or above, then you know that you are obese.

In adolescents, the obese or overweight is observed by different symptoms, such as skin of well face often seeming abnormal; white and purple marks being easy to see on skin; external genitals appearing very small in males. One can see adiposity (fat cells) in areas of the breast in boys. There will be more fat cells in upper arms and thighs, which looks uneven. Some obese adolescents experience social pressure and stress. Usually, they look mentally disturbed.

Causes

In Western society in the latter part of the 20th century, most researchers have found that people with inactive lifestyles and people who intake too much nutrients, are more susceptible to becoming obese. Obesity includes an inactive life style, such as lack of sleep, “endocrine disruptors” - lipid metabolism is interfered by food material, decreased changeability in room temperature, trying to stop smoking, which causes low appetite, more use of medication that increases the weight, becoming a pregnant at a later age, and selecting healthy nutrients with overweight, assortative pairing (overweight people trying to make relationships with the same type of people).

(Pictures are taken from Wikipedia.org)

With several medical situations, the high calories do not balance, which in obesity is most likely the result of a composition of genetic and environmental factors. In some genes, Polymorphisms prevent to let appetite, metabolism, and adipokine go affect to obesity; however, the situation needs enough calories, and probably some other factors, to expand. “Various genetic conditions that feature obesity have been identified (such as Prader-Willi syndrome, Bardet-Biedl syndrome, MOMO syndrome, leptin receptor mutations and melanocortin receptor mutations), but known single-locus mutations have been found in only about 5% of obese individuals”. It thinks that still, the causative genes’ huge proportion is recognized.

(Structure of the coenzyme adenosine triphosphate, a central intermediate in energy metabolism) On a population stage, the “thrifty gene hypothesis” hypothesizes that some specific ethnic people are probably more likely to be obese than others. People, who have high adipose saved, were more possible to remain famished.

In most population, not having balanced energy could be the one cause for high weight and obesity. When you have less energy in and more energy out, then you lose weight; when you have more energy in and less energy out, then you gain weight; and, when you have the same
amount of energy in and out, then your weight stays same. When you use fewer calories and take more calories, then obesity takes place. The other causes are not being physically active, environment (easy schedule, more restaurants in neighborhood, lack of healthy food, and food advertising), and genes and family history. Obesity belongs with parents and families. If your parents or one of your parents is obese, then your possibility of being obese is much greater. Genes also have an effect where the amount of fat is stored in a body and where the extra fat is holed. The reason of inheritance is because you have the same habits as your families, and they have the same amount of physical activity and food shared. If parents eat high caloric food, then children are going to eat the same type of food. Finally, the result becomes over weight, which is unlikely with healthy food and physically active parents. If parents take healthy food and are more physically active, then the possibility for being obesity is low. Taking medicine would become the cause for the obesity; medicines such as:

**Prednisone**

![](image1.png)

**Amitriptyline**

![](image2.png)

**Gabapentin**

![](image3.png)

<table>
<thead>
<tr>
<th>Chemical structure of synthetic corticosteroid drug, 17-hydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-7,8,9,10,12,13,14,15,16,17-decachydro-6H-cyclopenta[a]phenanthrene-3,11-dione, C_{22}H_{26}O_{5} (358.428 g/mol)</th>
<th>Chemical structure of Amitriptyline (or Amitypyline) hydrochloride is a tricyclic antidepressant drug. 3-(10,11-dihydro-5H-dibenzo[a,d]cycloheptene-5-ylidene)-N,N-dimethyl-1-propanamine, C_{20}H_{25}N (277.403 g/mol)</th>
<th>Chemical structure of Neurontin (medication treatment for epilepsy), 2-[1-(aminomethyl)cyclohexyl]acetic acid C_{8}H_{17}NO_{2}, 171.237 g/mol</th>
</tr>
</thead>
</table>

All these medicines let your body burn slowly, and causes greater appetite, which makes you become obese.¹

By genetics, “Studies have shown that a predisposition toward obesity can be inherited. One study reported in 2004 found that 48 percent of children with overweight parents became overweight. Where a person carries weight - the hips or around the middle - is also strongly influenced by heredity.”⁶ Hormonal factors and metabolic factors are different for each one; however, all factors cooperate to find out gained weight. Appetite regulator known as a
peptide hormone, and other peptides in the stomach, cooperate to produce appetite and make a feeling that you are full. The weight of the body is the effect of genes, metabolism, activities, atmosphere, culture, and socioeconomic status. Behavior and atmosphere is related to people causing the obesity.

Cohen syndrome

One can get this syndrome from parents; it is a genetic disorder, which creates problems in many parts of your body. This is the most common syndrome along with the people in America. For Cohen syndrome, the symptom is white blood cells which are also known by neutropenia. This kind of people has a small amount of white blood cells. People with obesity in childhood and adolescence also have the same problem about white blood cell. When people have obesity, it usually expands white blood cell around the chest and legs and arms remains thin/slender. Victims of Cohen syndrome also have slender hands, feet, and fingers. The cause of Cohen syndrome is VPS13B gene, which is usually called the COH1gene. The other names of Cohen syndrome are hypotonia, obesity, Norio syndrome, obesity-hypotonia syndrome, and prominent incisors-obesity-hypotonia syndrome.

Treatment / Prevention

Obesity also could be treated by some changing a life style, a low calorie diet (1,000 to 1,200 for women and 1,200 to 1,600 for men), planning healthy food, limiting in food, engaging in physical activity, changing behavior, taking some medicines for losing weight, and having surgery to lose weight. Adults with obesity should lose 5-10% of current weight in about six months. Children with obesity should be active physically and also refer to doctor for pediatric obesity treatment center. Physical activity benefits in some ways, such as preventing the risk of any heart disease causing by obesity, making lungs stronger, and getting more energy.

Also, some types of surgery can be helpful to lose weight. For people who have severe obesity (40 or greater BMI) and another treatment would not work, then surgery is the last option that doctor would prefer. It also works for the people who have 35 or greater BMI and are having problems with sleeping disorder, obesity related heart muscle diseases, or extreme type 2 diabetes. There are two types of surgery for obese people: Banded gastroplasty and roux-en- Y gastric bypass. In Banded gastroplasty surgery (weight lose surgery), a stapler device creates a small pouch in the top of the stomach. This surgery helps because your stomach can hold a limited amount of liquids and food. There are some long term side effects from this surgery, such as food intake is severely limited and effects on your health and body. On other hand, for roux-en-Y gastric bypass, a bypass in the region of the small intestine (calorie absorbs over). Food intake and less absorbed calorie from body can be limited by this surgery. Both these surgeries are helpful to reduce weight and improve health. However, there are more side effects than banded gastroplasty.
also by this surgery, such as swelling stomach, diarrhea, nausea, and faintness.4

Some approved medicines by FDA (Food Drug Association) are also helped for the obese and overweight people. People who have 30 or greater BMI, may use the weight loss medicines. It is also beneficial for 27 or greater BMI and heart risks. Some medicines are used for weight prevention, such as: sibutramine, and orlistat. These medicines are helpful for losing up to 22 pounds and sometimes, even more. Sibutramine (Meridia®) helps to command your brain to control your appetite. This medicine makes your blood pressure and pulse heavy, so high blood pressure patients should not take this medicine.

![Chemical structure of Sibutramine](structures from Wikipedia.org)

The medicine, Orlistat (Xenical®), does not let the body absorbs as many fats, calories, vitamins A, D, E, and K. This drug has minor side effects like diarrhea. The structure of this drug is above. There is also a program for losing weight, which is Alli. FDA found out that people can lose weight up to 10 pounds in about six months. Alli also works the same as orlistat like losing fat and calories.4

**Mechanism/Reaction for Sibutramine (Meridia®)**

Grignard Reagent attacks the + charge carbon of the cyano group.
In childhood, obesity or overweight is prevented by asking the doctor or a nutritionist for “24-hour food recall”. This is a tool that doctors or a nutritionist give you all information about food intake, mean types, use of sugar-beverages, and breakfast routine. Physical activity is the most helpful for the obese or overweight children.² They should do exercise every morning at least for an hour; this is helpful to make your child to be active. We can make our children eat healthy food and intake fewer calories by changing the food habits in families.⁴

Risks

There are a huge number of people in America who qualify as obese. The risk of death is increased as obesity increases. If your BMI is over 32, then it is the most danger for death. Diseases are related with the either dependent or independent divided of adipose tissue. There are so many diseases which are caused by obesity, such as diabetes mellitus type 2, heavy blood pressure, and heavy blood cholesterol. Obesity is also associated with some different types of diseases. If you are obese, you are at a greater risk for developing one of these diseases: heart failure, infertility, fatty live disease, Hernia, colorectal cancer, breast cancer (female), hypogonadism (male), back pain, stretch marks, disorder in sleep apnea, depression, low self-esteem, and body dysmorphic disorder.² To be obese is not only a cosmetic problem, but it is so risky to have some disease for adults in future. Heart disease takes a place in your body when there are some fatty foods on the inner wall of coronary arteries (blood and oxygen supplier in body). These fatty materials narrow the blood and oxygen supplier, and that causes to not blood flow to your heart. When the blood force is more than enough to push next to the wall of the arteries, then high blood pressure occurs in your body. Fatty materials build up in your arteries, which create a blood clot, when you are obese or overweight. If this clot is next to your brain, it will not allow the blood and oxygen to flow in your brain, and it causes a Brain hemorrhage. This happens because of increased BMI. When the level of blood sugar (glucose) is extremely high, then type 2 diabetes occurs. The cells do not react sufficient to the insulin that the body makes. Diabetes is the top cause of early death, diseases of heart and kidney, stroke, and blindness. “More than 80 percent of people with type 2 diabetes are overweight.”¹ You have more possibility of not having normal stages for blood fats if you are obese, which have bigger number of triglycerides and low-density lipoprotein (LDL) cholesterol, and low high-density lipoprotein (HDL) cholesterol. Not having normal blood fats levels becomes a risk for heart disease. Risk for colon, breast, endometrial, and gallbladder cancers are somehow causing from the obesity. There are also some other diseases like osteoarthritis, reproductive problems, and gallstones.¹

Genetics

“The interest for genetics of human obesities has increased considerably during the last decade partly because of the realization that the some forms of obesity were associated with high risks for various morbid conditions and morality rate.”¹³ We do not see obesity anymore in
homogeneous phenotype. Phenotype of the obesity does not exist yet. We have recognized that there are four different types of obesity in the human body, which is described the following. From the table above, we know that there are four types of obesity. Type one obesity is associated with excess body mass or percent fat; type 2 obesity is associated with excess subcutaneous truncalabdominal fat (android); type 3 obesity is associated with excess abdominal visceral fat; and type 4 obesity is associated with excess gluteo-femoral fat (genoid). One character of type 1 obesity is poor absorption body fat in a particular part in the body. They are on the anatomical classification of overweight of the body, in the additional group that has to do with extremely overweight bodies. Type 2 is described by overweight in the trunk, mainly which pertaining to the abdomen area, and similar to the suspected android or male type deposited of fat. The characteristic of type 3 is by an extreme overweight in the abdominal area where pertaining to a viscus area, and can be called by abdominal visceral obesity.

For 27 men of 28 to 30, the average BMI percent body fat is 28; however, the range was from 15 to 41 percent. Women have been observed the same as men. In adult males, there was heterogeneity of body fat content for a given BMI class.

<table>
<thead>
<tr>
<th>BMI</th>
<th>N</th>
<th>Mean</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-22</td>
<td>27</td>
<td>17</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>23-25</td>
<td>76</td>
<td>22</td>
<td>11</td>
<td>35</td>
</tr>
<tr>
<td>26-27</td>
<td>46</td>
<td>26</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>28-30</td>
<td>27</td>
<td>28</td>
<td>15</td>
<td>41</td>
</tr>
</tbody>
</table>

UCSF children’s hospital made an assumption if one parent has obesity; there is 50% possibility for his or her child to have obesity. When both parents have obesity, their children have 80% possibility to have obesity.

**Conclusion**

In 2003-2004, the National Health and Nutrition Examination Survey (NHANES) found that the population of overweight people was about 33.33% (one-third) in adults in America, and the population of obese people was slightly more than 33.33%. The population of the obese non-Hispanic Black Women was about 82%, Mexican American Women about 75%, and non-Hispanic White Women about 58%. The obesity or overweight children’s population is about 19% of school-ages and 17% of teens in America. These are not a normal statistic; it is
dangerous for the next generation if the rate of the obesity will stay the same. So the only way we can prevent obesity, as it is said in “prevention/treatment” like is to take in fewer calories, and start taking the medicine which helps one to lose weight. Obesity should be prevented in some decades otherwise it will cause extreme problem for our next generation.
Works Cited

Vytorin: A Look at the Drug and the Study that says it may not work

Sarah Fields

April 18, 2008
Abstract

Vytorin is a cholesterol-lowering medication that was approved by the Food and Drug Administration (FDA) in 2004. It is a combination of two cholesterol-lowering medications, simvastatin (Brand name: Zocor) and ezetimibe (Brand name: Zetia). Recently in a study conducted by the makers of this drug, Merck and Schering-Plough, it has been concluded that Vytorin is no more effective at lowering cholesterol in patients than if patients were to take simvastatin or another statin alone.

Cholesterol is maintained by mostly two organs in the body, the liver and the small intestine (Earl & Kirkpatrick, 2003). The liver gets cholesterol from mainly three sources (“Facts & Comparisons,” 2008). It either synthesizes cholesterol, takes up cholesterol that is absorbed by the small intestine or takes up cholesterol from lipoproteins that are circulating in the blood (“Facts,” 2008). Cholesterol in the small intestine is mainly derived from cholesterol that is secreted in bile and also from cholesterol that is in food (“Facts,” 2008). There is total cholesterol, low-density lipoproteins (LDL-C), high-density lipoproteins (HDL-C), triglycerides and apolipoprotein B (apo B), a major protein constituent of LDL (“Facts,” 2008). Elevated levels of total cholesterol, LDL-C and apo B, contribute to atherosclerosis or the hardening of arteries due to plaque (Earl & Kirkpatrick, 2003). Low levels of HDL-C can also contribute to the development of atherosclerosis (Earl & Kirkpatrick, 2003). For people with diabetes, kidney disease, cardiovascular disease or have had a coronary artery procedure, the current recommended LDL level is 100 mg/dL or less (Anonymous, 2005). If a person has one of those mentioned before and also additional risk factors like smoking or high blood pressure, then the recommended level is 70 mg/dL or less (see table 1 for list of recommended levels for each risk category and when a person should exercise or go on medication) (Anonymous, 2005). People can try and lower their cholesterol naturally by changing their diet, like eating less saturated and trans fats and also cut back on the amount of actual cholesterol that they eat (Anonymous, 2005). Exercise is also a good option, but this is better at raising HDL more than lowering LDL (Anonymous, 2005). For some people though, like the people who have these high-risk factors, natural ways of lowering their cholesterol is not enough, so they must add prescription drugs in order to reach their goals (Anonymous, 2005).

Table 1:

<table>
<thead>
<tr>
<th>RISK CATEGORY</th>
<th>LDL GOAL (mg/dL)</th>
<th>WHEN TO START EXERCISE/DIET</th>
<th>WHEN TO CONSIDER DRUGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>&lt;100 or &lt;70*</td>
<td>&gt;140</td>
<td>&gt;140</td>
</tr>
<tr>
<td>Moderately high risk</td>
<td>&lt;130</td>
<td>&gt;130</td>
<td>&gt;130</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>&lt;130</td>
<td>&gt;130</td>
<td>&gt;160</td>
</tr>
<tr>
<td>Low risk</td>
<td>&gt;160</td>
<td>&gt;160</td>
<td>&gt;160</td>
</tr>
</tbody>
</table>

*Lower goal is optional.

There are quite a few prescription drugs on the market today to lower cholesterol. There are fibrate drugs like gemfibrozil and niacin (Anonymous, 2005). There is also a large class of drugs called statins, which include drugs like atorvastatin (Lipitor) and simvastatin (Zocor), and this is the class that physicians usually prescribe first (Anonymous, 2005). When a person is put on one of these drugs, they are usually started on a strength between 10 and 40 mg, however, if this strength is not working, doctors will increase the dose to a more aggressive 80 mg strength (Anonymous, 2005). Of course, all drugs have side effects and the higher doses of these statins can put people at a greater risk for the side effects that can occur while taking a statin (Anonymous, 2005). These side effects are muscle weakness and stiffness and more seriously is rhabdomyolysis, which is the breakdown of muscle tissue (anonymous, 2005). Since there is a higher risk of these side effects, physicians began to give combinations of lower strength statin drugs with another cholesterol-lowering medication like gemfibrozil or niacin (Anonymous, 2005). The fibrate-statin combo did not work because this seemed to increase the risk of the muscle-related side effects and the niacin combo did not work because a high dose of niacin is needed, and high levels of this can often cause flushing (Anonymous, 2005). Since these combos did not work, researchers created a new combination, which is Vytokin (Anonymous, 2005).

Vytokin was approved by the FDA in July of 2004 (“Facts,” 2008). Vytokin is a combination of simvastatin and ezetimibe (Zetia). It comes in four strengths, 10 mg ezetimibe/10 mg simvastatin, 10/20, 10/40 and 10/80. Vytokin is effective in both men and women (“Facts,” 2008). It has also been through many trials to test its safety and seems to be well tolerated with mostly everyone who takes Vytokin (“Facts,” 2008). It is supposed to reduce total cholesterol, “bad” cholesterol or LDL, apoB, triglycerides, and non-high-density lipoproteins (non-HDL-C) (“Facts,” 2008). It can also increase “good” cholesterol or HDL (“Facts,” 2008). These responses can be seen within two weeks of starting the mediation and of course can be maintained with continued therapy (“Facts,” 2008). Since the drug is a combination, both drugs will be discussed below.

The first drug in Vytokin is ezetimibe. Ezetimibe is now only available as the brand name of Zetia, separately. It was approved by the FDA in 2002 and comes in one strength; 10 mg (“Facts,” 2008). Ezetimibe is a drug that, for now, is in a class of its own (Perl & Kirkpatrick, 2003). It is a selective cholesterol absorption inhibitor which means it inhibits the absorption of biliary and dietary cholesterol in the small intestine but it does not affect the absorption of fat-soluble vitamins or bile acids (Davis & Veltre, 2007). In a study conducted with mice, it is assumed that ezetimibe inhibits the absorption of cholesterol by binding to the Niemann-Pick C1-like 1 gene (NPC1L1), which is a putative intestinal sterol transporter, and by binding to this, it keeps the cholesterol in the intestinal lumen for excretion (Kosoglou et al., 2005; Davis & Veltre, 2006; Field, Watt & Mathur, 2005). Ezetimibe stays along the brush border of the small intestine, which therefore decreases the delivery of this intestinal cholesterol to the liver (“Vytokin,” 2008). In turn, the amount of cholesterol stored in the liver is decreased
and there is also an increase in the clearance of cholesterol from the blood ("Vytorin," 2008). This mechanism is complementary to the mode of action of simvastatin ("Facts," 2008). Ezetimibe is metabolized primarily in the small intestine and the liver via glucuronide conjugation ("Facts," 2008). When the drug is in the body, it is quickly metabolized to ezetimibe-glucuronide, which is pharmacologically active, which means it has a higher affinity to bind to NPC1L1, and this accounts for 80-90% of the total drug in the plasma (see Fig 1) (Kosoglou et al., 2005; "Facts," 2008; Davis & Veltri, 2006). It is then slowly eliminated from the plasma with a half-life of about 22 hours ("Facts," 2008).

![Molecular structures of ezetimibe and ezetimibe-glucuronide](image)

Fig 1: Molecular structures of ezetimibe and ezetimibe-glucuronide. Source: Kosoglou et al.

The second drug in Vytorin is simvastatin (see Fig 2), which is available as this generic name, separately. It was approved by the FDA in 1991 and comes in five strengths; 5, 10, 20, 40 and 80 mg ("Facts," 2008). Simvastatin is part of a large class of drugs called statins. Statins have been around for over a decade and have been shown, through many clinical trials, to prevent episodes like heart attacks, strokes and cardiovascular deaths (Nissen, 2004). Simvastatin has been proven to be highly effective at reducing total cholesterol and LDL-C in heterozygous familial and non-familial forms of high cholesterol ("Facts," 2008). It also has been proven to decrease triglycerides and also increase HDL-C ("Facts," 2008). When administered, a marked response is seen in two weeks and the maximum therapeutic response is seen within four to six weeks, which can be maintained with continued therapy ("Facts," 2008).
Simvastatin is an inactive lactone that is hydrolyzed to the β-hydroxyacid form, which is an inhibitor of HMG-CoA reductase (“Facts,” 2008; Diwan, 2008). Hydroxymethylglutaryl-coenzyme A (HMG-CoA) is the starting point in the making of cholesterol (Diwan, 2008). HMG-CoA is formed by the condensation of acetyl-CoA and acetacetyl-CoA, which is catalyzed by HMG-CoA synthase (Diwan, 2008). After this step, the HMG-CoA is catalyzed by HMG-CoA reductase which forms mevalonate (Diwan, 2008). After many steps and reactions, mevalonate is synthesized into different molecules and eventually cholesterol is formed (Diwan, 2008). Since HMG-CoA reductase is inhibited, mevalonate is never able to be formed and therefore, cholesterol is not formed.

There are quite a few drug interactions that can occur when a patient is taking Vytorin. Most of them seem to affect the simvastatin levels in the patient. The first is between Vytorin and amiodarone, which may increase the risk of myopathy (a neuromuscular disease which causes muscle weakness) and rhabdomyolysis (“Facts,” 2008). If a patient is taking both drugs, the Vytorin dosage should not exceed 10/20 mg (“Facts,” 2008). Another is the interaction between aluminum- and magnesium-containing antacids, which can decrease the maximum
concentration of ezetimibe by 30% in the body but did not decrease the overall amount of the drug in the body ("Facts," 2008). There can also be an interaction when taking carbamazepine. This could lower the plasma concentration of simvastatin, which in turn decreases the therapeutic effect ("Facts," 2008). Another is between Vytorin and cholestyramine. Cholestyramine can decrease the mean value amount of total ezetimibe in the body by 55% and ezetimibe by 80% ("Facts," 2008). Simvastatin can bind to cholestyramine, which reduces the gastrointestinal absorption ("Facts," 2008). It can also cause a reduction in the lowering of LDL-C, so it is recommended that Vytorin be taking two hours before or four or more hours after taking cholestyramine ("Facts," 2008). There is also an interaction between CYP3A4 inhibitors (i.e., clarithromycin, itraconazole, ketoconazole), which can raise the levels of simvastatin in the body and therefore increase the risk of myopathy ("Facts," 2008). It is recommended that a patient should avoid taking these drugs together but if absolutely necessary, the patient should stop taking Vytorin until the antibiotic or antifungal regimen is completed ("Facts," 2008). Danazol is another drug that can have an interaction ("Facts," 2008). It can increase the risk of myopathy/rhabdomyolysis, especially with high dosages of Vytorin so the Vytorin dose should not go above 10/10 mg ("Facts," 2008). Delavirdine is another interaction that can occur ("Facts," 2008). This can increase simvastatin levels to where severe myopathy can occur ("Facts," 2008). Diltiazem can also increase the levels of simvastatin in the body, so again the risk of myopathy is increased ("Facts," 2008). Efavirenz can actually reduce the levels of simvastatin because it induces CYP3A4 metabolism ("Facts," 2008). Fibric acid derivatives (i.e. fenofibrate or gemfibrozil) can increase the total ezetimibe concentration and also significantly increase simvastatin acid and plasma concentration ("Facts," 2008). Even though it is not recommended to take both this and Vytorin together, if they are, the dose of Vytorin should not exceed 10/10 mg per day ("Facts," 2008). Nisocin can also cause an interaction by increasing the risk of severe myopathy ("Facts," 2008). Propranolol with Vytorin saw a significant decrease in the maximum concentration of simvastatin but no change in the overall amount in the body, the clinical relevance of this combination is unclear ("Facts," 2008). Rifampin can reduce the levels of simvastatin and therefore decrease its pharmacological effects ("Facts," 2008). St. John's Wort also has an interaction by decreasing simvastatin levels and therefore could decrease the effectiveness of simvastatin in the body ("Facts," 2008). Verapamil can increase the risk of myopathy, so the dose of simvastatin should not exceed 10/20 mg per day ("Facts," 2008). Adding a Vytorin regimen can also affect other drug regimens that a person may be on from working properly. These drugs are Bosantan, Cisapride, Cyclosporine, Digoxin and Warfarin ("Facts," 2008).

There are also some interactions between Vytorin and some foods. The maximum concentration of ezetimibe was increased by 38% when a person consumed a high-fat meal ("Facts," 2008). A person should not consume large quantities of grapefruit juice (at least a quart daily) because this can increase the plasma levels of simvastatin and therefore increase the risk of myopathy ("Facts," 2008). There is also an interaction between oat bran and pectin ("Facts," 2008). These can cause a decrease in the pharmacological effects of simvastatin.
because it decreases the absorption of simvastatin in the gastrointestinal tract ("Facts," 2008). Peppermint oil should be used with caution because this can increase simvastatin levels and also increase pharmacologic and adverse reactions ("Facts," 2008).

Some adverse reactions with can also be seen with Vytorin. The adverse reactions of ezetimibe can include gastrointestinal issues like diarrhea or abdominal pain ("Facts," 2008). People can also experience issues like back pain, fatigue, sore throat, sinusitis, coughing and fatigue ("Facts," 2008). Some adverse reactions that can occur with simvastatin is eczema, abdominal pain, cataracts and itching ("Facts," 2008).

A study that was released on January 14 of this year has found that there is no significant advantage to taking Vytorin, when it comes to lowering the development of atherosclerosis, than by taking simvastatin alone (Mitka, 2008). The study, which was conducted by Merck and Schering-Plough (the makers of the drug), was a multinational double-blind study conducted with 720 participants (Greenland & Lloyd-Jones, 2008). It used a surrogate endpoint of using a vascular ultrasound to see results rather than a clinical endpoint of heart attack or stroke (Greenland & Lloyd-Jones, 2008). The study was called ENHANCE, Effect of Ezetimibe plus Simvastatin versus Simvastatin alone on Atherosclerosis in the Carotid Artery (Greenland & Lloyd-Jones, 2008). ENHANCE was a two year study that took participants with heterozygous familial hypercholesterolemia and some patients were given Vytorin and others only simvastatin (Greenland & Lloyd-Jones, 2008). The researchers conducting the study looked at both the right and left carotid arteries of these participants with an ultrasound in three sites (the common carotid, the internal carotid and the carotid bulb) and studied the change in intimal-medial thickness in these areas (Greenland & Lloyd-Jones, 2008). After two years, researchers again looked at the carotid arteries of these participants to see if there were any changes in the intimal-medial thickness (Greenland & Lloyd-Jones, 2008). By looking at this primary end point, which is a surrogate marker for atherosclerosis, the study concluded that there was no significant decrease of thickness in the carotid artery (Mitka, 2008). However, the study also looked at the decrease of LDL cholesterol, the secondary end point, and found that Vytorin did decrease this more significantly than plain simvastatin (Mitka, 2008). There was a 54% decrease in LDL-C in patients using Vytorin versus a 41% decrease in patients taking simvastatin alone (Greenland & Lloyd-Jones, 2008).

These study results have received a lot of controversy in the last couple of months throughout the medical community (Mitka, 2008). The one problem is that this study was completed in April 2006, yet the results were not released until January 2008, almost two years (Mitka, 2008). Now that the results have been released, some physicians question if Vytorin should still be in use, while others say that these results should be taken with a grain of salt because larger trials are still in the works for answering questions about the efficacy and safety of Vytorin (Mitka, 2008). There has also been questions surrounding Merck and Schering-Plough and if either of the companies manipulated the results prior to the public release of the results (Mitka, 2008). The companies do admit that there was a recommendation to change the
study end points but that it was done through the request of an unnamed advisory panel (Mitka, 2008). The companies also failed to register the study with the National Institutes of Health only after the study had been completed and not before they began to register patients for the study (Mitka, 2008). Both companies dismiss these concerns and say that the delay in the release of the results was from the unexpected time it took to interpret all of the results, about 40,000 ultrasound images (Mitka, 2008). Though the companies tried to explain these questions, there are still some skeptics (Mitka, 2008).

The big question that remains on the minds of people with high cholesterol is if they are on Vytorin, should they continue to take it? The American Heart Association and the American College of Cardiology recommend that patients and physicians do not need to switch from Vytorin to another cholesterol-lowering medication based on this trial’s results (Mitka, 2008). They say that since the trial focused only on the surrogate end points of LDL-C levels and intimal-medial thickness, and not on clinical outcomes, such as heart attack or stroke, the results are not a sure answer that Vytorin does not work (Mitka, 2008). The current guidelines for cholesterol-lowering medications is to target elevated LDL-C levels, which Vytorin does, and therefore the risk of cardiovascular disease is reduced (Mitka, 2008).

Conclusion: As for where my drug is going in the future, I cannot really give a definitive answer. Since ezetimibe and Vytorin are both new drugs to the market, there still is a lot of research and studies that are being conducted on whether these drugs are effective or not. I think the research will find that the drug does work well but maybe only for certain people. There have been no studies concluding that Vytorin is unsafe in any way, so unless a patient is directed by their physician to switch medications, I think a patient should stay on Vytorin, if they are already taking it, they can afford it and it is working for them.
Bibliography


GARDASIL: Could you be one Less Person to Deal with Cervical Cancer?

Prepared for
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Organic Chemistry 236
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Prepared by
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April 19, 2008
Abstract

Human Papillomavirus (HPV) is the most common sexually transmitted disease. HPV causes cervical cancer in most women and they don’t even know they have it. In 2006 the FDA approved GARDASIL which is a new vaccine intended to prevent against cervical cancer. This paper will discuss what HPV is, how it becomes cervical cancer, what the treatments are, and how GARDASIL could make you one less person to deal with cervical cancer.

Human Papillomavirus (HPV) and Cervical Cancer

Cervical cancer is cancer of the cervix (9). It is caused by certain types of Human Papillomaviruses (HPV). Papillomaviruses are a diverse group of DNA-based viruses that infect the skin and mucous membranes of humans and a variety of animals (9). There have been 130 human papillomavirus (HPV) types that have been identified; however, there are still several that haven’t been identified. Some types may cause warts while others may cause an infection resulting in precancerous lesions. All HPV types are transmitted by skin-to-skin contact and/or by fomites. High risks of HPV can lead to precancerous cells later turning into invasive cancer (9).

HPV virions infect epithelial tissues through micro-abrasions, whereby, the virion associates with putative receptors such as alpha integrins and laminins, leading to entry of the virions into basal epithelial cells through endocytosis (8). At this point, the viral genome is transported to the nucleus by unknown mechanisms and replicates itself to about 10-200 viral genomes per cell. Then the host keratinocyte begins to divide and become differentiated in the upper layers of the epithelium. The viral oncogenes, E6 and E7, are thought to modify the cell cycle to retain keratinocyte in a state that allows genome replication (8). Once cells are invaded by HPV, a latency (quiet) period of months to years may occur. The latency period means the HPV virus is in an incubation period. Having sex with a partner whose HPV infection is in the incubation period still leaves people to get infected. HPV virus can last from 3 months to 2 years without visible changes, making it difficult for an infectee to establish the source of infection (8).

For most women who become infected with HPV, their bodies own immune system can fight it off. However, if the virus persists abnormal cells can develop in the lining of the cervix and if not treated early can become precancerous and eventually cancerous cells (9). HPV that is precancerous is like a silent killer if it’s not caught at an early stage. Most people who become infected with HPV don’t even know they have it. In 2005, the Centers for Disease Control and Prevention (CDC) estimated that 20 million people in the U.S. had this virus (6). At least 50% of sexually active people will get HPV at one point in their lives and won’t even know it because their body fought it off.
How HPV turns into Cancer:

![Diagram of HPV process](image)

(2)

Types of HPV

Over 100 different HPV types have been identified and are referred to by number.

- Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 are "high-risk" sexually transmitted HPVs and may lead to the development of cervical intraepithelial neoplasia (CIN), vulvar intraepithelial neoplasia (VIN), penile intraepithelial neoplasia (PIN), and/or anal intraepithelial neoplasia (AIN).
- HPV Types 16 an 18 cause 70% of cervical cancers, and HPV types 6 and 11 cause 90% of genital warts (s).
<table>
<thead>
<tr>
<th>Disease</th>
<th>HPV type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common warts</td>
<td>2, 7</td>
</tr>
<tr>
<td>Plantar warts</td>
<td>1, 2, 4</td>
</tr>
<tr>
<td>Flat cutaneous warts</td>
<td>3, 10</td>
</tr>
<tr>
<td>Anogenital warts</td>
<td>6, 11, 42, 43, 44, 55 and others</td>
</tr>
<tr>
<td>Genital cancers</td>
<td>16, 18, 31, 33, 35, 39, 45, 51</td>
</tr>
<tr>
<td>Epidermodysplasia verruciformis</td>
<td>more than 15 types</td>
</tr>
<tr>
<td>Focal epithelial hyperplasia (oral)</td>
<td>13, 32</td>
</tr>
<tr>
<td>Oral papillomas</td>
<td>6, 7, 11, 16, 32</td>
</tr>
</tbody>
</table>

(s)

How to Detect HPV

There are various tests that can be done to detect if you have HPV. The first and very effective way is to get an annual Pap Test. The Pap test is a procedure used to collect cells from the cervix for cervical cytology (the study of the structure and function of cells) testing (i). The Pap test is done by a doctor by first placing a speculum inside the vagina. The speculum is a metal or plastic instrument that keeps the vagina open so that the cervix can be seen clearly. Next, using a small spatula, a sample of cells and mucus is lightly scraped from the exocervix (the surface of the cervix that is closest to the vagina). A small brush or a cotton-tipped swab is then used to take a sample from the endocervix (the inside part of the cervix that is closest to the body of the uterus) (i). Then the cells will be examined under a microscope in the laboratory. The next step is to see what your results are.

Doctors use The Bethesda System (TBS) test to determine your results. The general categories are:
- negative for intraepithelial lesion or malignancy,
- epithelial cell abnormalities, and
- other malignant neoplasms (1).

**Negative for intraepithelial lesion or malignancy:** This first category means that no signs of cancer, pre-cancerous changes, or other significant abnormalities were found. Some specimens in this category appear entirely normal. Others may have findings that are unrelated to cervical cancer, such as signs of infections (with yeast, herpes, or Trichomonas, for example). Some cases may also show "reactive cellular changes", which is the way cervical cells respond to infection or other irritation (1).

**Epithelial cell abnormalities:** The second category, epithelial cell abnormalities, means that the cells of the lining layer of the cervix show changes that might be cancer or a pre-cancerous condition. This category is divided into several groups for squamous cells and glandular cells (1).

**Atypical squamous cells:** This category includes atypical squamous cells of uncertain significance (ASC-US). This term is used when there are cells that look abnormal, but it is not possible to tell (by looking at the cells under a microscope) whether the cause is infection, irritation, or precancer. Sometimes a colposcopy is recommended to get further information (1).

**Squamous intraepithelial lesions (SILs):** These abnormalities are divided into low-grade SIL and high-grade SIL. High-grade SILs are less likely than low-grade SILs to go away without treatment. High-grade SILs are also more likely to eventually develop into cancer if they are not treated. Treatment can cure all SILs and prevent true cancer from developing. A Pap test cannot tell for certain whether a woman has a high- or low-grade SIL. A colposcopy is needed (1).

**Squamous cell carcinoma:** This result means that the woman is likely to have an invasive squamous cell cancer. Further testing will be done to be sure of the diagnosis before treatment can be planned (1).

This following picture shows what a normal cell looks like and how it turns into cancer:
How to Treat HPV

Currently there is no cure for cervical cancer; however, the abnormal cells can try to be removed. The options for treating each patient with cervical cancer depend on the stage of disease, its size, depth of invasion, and how far it has spread (1). The three main methods of cancer treatment are surgery, radiation therapy, and chemotherapy. Sometimes it's best to use two or more of these methods for better results. Although there is not a cure for HPV there is a new vaccine that was approved by the FDA in 2006. The Vaccine is called GARDASIL. This vaccine is not meant to cure HPV but it is meant to prevent it (1).

GARDASIL

GARDASIL is manufactured by MERCK & CO., INC., and got approved by the Food and Drug Administration (FDA) on June 8, 2006. GARDASIL is a non-infectious recombinant, quadrivalent vaccine prepared from the highly purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, and 18. The L1 proteins are produced by separate fermentations in recombinant Saccharomyces cerevisiae and self-assembled into VLPs (5). The quadrivalent HPV VLP vaccine is a sterile liquid suspension that is prepared by combining the adsorbed VLPs of each HPV type and additional amounts of the aluminum containing adjuvant and the final purification buffer (5).

GARDASIL is a sterile preparation for intramuscular administration. Each 0.5-mL dose contains approximately 20 mcg of HPV 6 L1 protein, 40 mcg of HPV 11 L1 protein, 40 mcg of HPV 16 L1 protein, and 20 mcg of HPV 18 L1 protein (5). Each 0.5-mL dose of the vaccine contains approximately 225 mcg of aluminum (as amorphous aluminum hydroxyphosphate sulfate adjuvant), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, and water for injection. The product does not contain a preservative or antibiotics (5).

INDICATIONS AND USAGE

GARDASIL is a vaccine indicated in girls and women 9-26 years of age for the prevention of the following diseases caused by Human Papillomavirus (HPV) types 6, 11, 16, and 18:

• Cervical cancer
• Genital warts (condyloma acuminata) and the following precancerous or dysplastic lesions
• Cervical adenocarcinoma in situ (AIS)
• Cervical intraepithelial neoplasia (CIN) grade 2 and grade 3
• Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3
• Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3
• Cervical intraepithelial neoplasia (CIN) grade 1 (5).
GARDASIL should be administered intramuscularly as 3 separate 0.5-mL doses according to the following schedule:

First dose: at elected date  
Second dose: 2 months after the first dose  
Third dose: 6 months after the first dose

GARDASIL should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh. Do not inject intravascularly. Subcutaneous and intradermal administrations have not been studied, and are not recommended (5).

Drug Interactions

Before receiving the HPV vaccine, tell your doctor about all other vaccines you have recently received. Also tell your doctor if you have recently received drugs or treatments that can weaken the immune system, including: an oral, nasal, inhaled, or injectable steroid medicine; medications to treat psoriasis, rheumatoid arthritis, or other autoimmune disorders, such as azathioprine (Imuran), efalizumab (Raptiva), etanercept (Enbrel), leflunomide (Arava); medicines to treat or prevent organ transplant rejection, such as basiliximab (Simulect), cyclosporine (Sandimmune, Neoral, Gengraf), muromonab-CD3 (Orthoclone), mycophenolate mofetil (CellCept), sirolimus (Rapamune), or tacrolimus (Prograf) (5). These drugs can weaken the immune system; therefore, decreasing the vaccines efficiency.

Precautions

Vaccination with GARDASIL may not protect everyone who takes it. This vaccine is not intended to be used for treatment of genital warts or cervical cancer. This vaccine will not protect against diseases that are not caused by HPV (5). GARDASIL has not been shown to protect against diseases due to non-vaccine HPV types. Appropriate medical treatment should always be available in case of rare anaphylactic reactions. Syncope (fainting) may follow any vaccination, especially in adolescents and young adults (5). Individuals with impaired immune response may have reduced antibody response to active immunization. GARDASIL should not be given to individuals with bleeding disorders such as hemophilia or thrombocytopenia. GARDASIL is not recommended for use in pregnant women (5).

Adverse Reactions:

In 5 clinical trials (4 placebo-controlled), subjects were administered GARDASIL or placebo on the day of enrollment, and approximately 2 and 6 months thereafter. Few subjects (0.1%) discontinued due to adverse experiences. In all except 1 of the clinical trials, safety was evaluated using vaccination report card (VRC)-aided surveillance for 14 days after each injection of GARDASIL or placebo (5). The subjects who were monitored using VRC-aided surveillance included 5088 girls and women 9 through 26 years of age
at enrollment who received GARDASIL and 3790 girls and women who received placebo. Table 7 shows the most common side effects these girls and women noticed (5).

<table>
<thead>
<tr>
<th>Adverse Experience</th>
<th>GARDASIL (N = 5088)</th>
<th>Placebo (N = 3790)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia</td>
<td>13.0</td>
<td>11.2</td>
</tr>
<tr>
<td>Nausea</td>
<td>6.7</td>
<td>6.0</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6.4</td>
<td>6.4</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4.0</td>
<td>3.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Cough</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Toothache</td>
<td>1.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Malaise</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>1.1</td>
<td>0.9</td>
</tr>
</tbody>
</table>

(5)

**CLINICAL STUDIES**

There was a phase II, randomized, double-blind, placebo-controlled study that evaluated the efficacy of GARDASIL in preventing infection from the types of HPV responsible for 70 percent of all cases of cervical cancer and 90 percent of all cases of genital warts (4). In the study, 552 women in the United States, Europe and Brazil between the ages of 16 and 23 were randomized to receive vaccine or placebo at Day 1, Month 2, and Month 6. The primary endpoint of the study was to assess the efficacy of the investigational vaccine in reducing the combined incidence of persistent HPV 6, 11, 16, and 18 infections and related diseases, including cervical pre-cancers (cervical intraepithelial neoplasia, or CIN), cervical cancer, and/or external genital lesions (genital warts) (4). Over the two and a half years of follow-up after vaccination, GARDASIL reduced the combined incidence of persistent infection from HPV 6, 11, 16, or 18 and related genital disease including new cervical pre-cancers and genital warts by 90 percent compared with placebo among women who were naive to the relevant HPV types (4). Thirty-six cases of disease, persistent infection, or detection of HPV on the last visit on record were seen in the placebo group compared to four in the group who received GARDASIL. Of the four cases seen in the group who received GARDASIL, one was confirmed as persistent infection; in the other three cases HPV was detected on the last study visit but was not later confirmed as a persistent infection (4).

There are currently studies being done on the longevity of this vaccine (3). There haven’t been any studies on it thus far. It has been working for 5 years without a difference in impact, further studies are being done. Studies are also being done for a vaccine for boys and men. GARDASIL only protects against cervical cancer for girls and women.
Future of Cervical cancer and GARDASIL

GARDASIL has only been around for a couple of years. Further studies should be done before making children take the vaccine in schools. The longevity of the vaccine hasn’t been identified and no clinical studies have been done. Unfortunately, cervical cancer has been one of the most common deaths in the world. This vaccine has a way to prevent it. Studies show that most women who have gotten the vaccine are 95% protected against cervical cancer and some types of herpes. The more studies that are done, the more effective this vaccine will be. There are some side affects that go with the vaccine; however, they can be tolerated. GARDASIL will be around for many years and hopefully cause the rates of cervical cancer to decrease.

Conclusion

I believe that there should have been more studies done on the effectiveness and longevity of GARDASIL. The reason why no one has been able to find a vaccine for cervical cancer is because it mutates numerous and there are over 100 different strands of it. That is way too many to keep track of. I don’t think children should be given this vaccine in school. I wouldn’t say GARDASIL is for me. I just don’t believe it. It’s like the flu, we get it every year and yet we have to find a new vaccine for it every year. This might happen with GARDASIL. Overall I think that there should be more studies done on it and see how long it lasts before we test it out on ourselves.
Bibliography


Why Airplanes Fly

Karli Henry

PHY 111 SEC 2542

Dr. Casey Durandet

November 26, 2007
In this report I will explore the development of the airplane and the fundamentals that keep them in flight. I will demonstrate the process man has gone through and discovered to make this dream a reality. Flight is not made possible by merely the machinery, and the sheer science of it all, but the people, and brains working behind them, to understand this physics and make it work for us.

The idea of flight has been around since 1000 BCE inspiring us, even as we struggled to make sense of our natural world and the other people in it. The Chinese experimented with kites, using them both as measuring instruments, and weapons of war. The Greeks tell us of Daedalus and Icarus, who escaped on man-made wings. And of course even Leonardo da Vinci’s infamous drawings of the possibility of flight, continue to be awe inspiring and subject to study today. With how far we have advanced, we have to look back to a time when man flying was just a thought, a dream, a scientific vision.

The modern aircraft, as we know it today, is attributed to Sir George Cayley who created the first design of an airplane and established the basic principles of flight. As a young man he engraved the principles of weight, thrust, lift, and drag onto a silver disc, the size of an American quarter and proceeded to experiment with wing air foil shapes, to determine the most efficient design for flight. He created a hand-launched model glider in 1804—the first of which to fly with the basic design still used today. In 1849 Sir Cayley began experimenting with full-scale aircraft with a tri-plane glider, and in 1853 he created a monoplane that successfully went into free flight (Kinney 3-5).

What makes him important is his emphases on the principles of thrust, drag, lift, and weight. These four principles are essential to flight—even after one hundred years they have not changed. Thrust is a force that is exerted by the engine and its propeller(s) which push the air backward and, as a result, move the aircraft in a forward direction. Thrust can be explained as the force that makes the airplane move through a linear plane, or linear momentum, it only pertains to the forward motion, so even when an aircraft is on the ground it has thrust. Linear momentum is how a mass moves along a straight path (P=mass * velocity).

Drag is the resistance of the airplane to advancing motion, or the opposing force to thrust; which is a reiteration from Newton’s Third Law (1687)—for every force, there must be an equal and opposite force. Drag is not created, but can be utilized to decrease the thrust. Which can also be described in everyday physics—when you lean against a wall, the wall is pushing against your weight to keep you upright. Drag can be increased and decreased by the flaps on the wings of the aircraft, which slow it down, as well as by the simple action of flying against the wind instead of with it. As drag increases the velocity—or speed—decreases along with the thrust. Drag, or wind resistance is considered a frictional forces—which is a force that oppose the acceleration of an object (F=μg * normal and F=μk * normal).

A Swiss physicist, John Bernoulli’s experiments with water proved that as air pressure decreased the velocity of the fluid flow increased, which later provided the basis for understanding the creation of lift. Bernoulli’s equations explained that pressure is inversely proportional to the velocity (p + ¼ ρV² + ρgh = constant, where p is pressure, ρ is the density of the fluid, V is the velocity, h is the elevation, and g is the gravitational acceleration) (Bernoulli’s Equation); therefore the faster the liquid or air is moving, the less pressure there is. Sir Cayley used Bernoulli’s discovery towards his four principles of flight. Lift is the upward force created by the wings moving through the air. An airplane wing is designed to be rounded at the front and curved on the top while the bottom portion is a straight line. If one takes into account the
chemistry of air, it is important to emphasize that each particle of air needs to maintain its positioning. Therefore, if an object were to "cut" the air, when the object is no longer present, the particles must remain in the same order they were before they were disrupted. Because of these known facts, the shape of the wing would cause the air speed above the wing to be faster than the air speed below the wing. According to Bernoulli’s principal, these facts would cause the pressure below the wing to be greater than the pressure above the wing, which would result in the force of lift. To oppose the weight of the craft and maintain its levity, the force of lift is required to be equal to or greater than the aircraft’s weight, or gravity (U.S. Centennial... n.d.); Sir Cayley used his skills as an inventor to test the most efficient way to increase lift (Kinney 3).

Weight is described as the force of gravity working to pull the aircraft back towards the ground. The weight is actually an acceleration, and is the product of the mass of the object multiplied by the constant acceleration of gravity (-9.8 m/s^2). The lift is required to be a greater number than the weight for any object to remain in flight. The weight, just as the drag, is an opposing force to the flight of the aircraft. If these two factors were not discovered or taken into consideration, flight would still elude man today.

The only thing that Cayley seemed unable to create was power for his flight. With the technology that was around it was impossible for his invention to successfully stay in flight, but the basic founding principles of fully directional powered flight were there. Many others followed Cayley’s example. John Smeaton observed the workings of a windmill and noted the advantages of having a curved, or cambered, surfaces over straight ones. He created a new tool, which spun objects around an arm to test the surfaces. He is most well known for discovering the density of air from his tests in 1759 (Kinney 3).

The following years the source of the power grew to steam power. In the 1840s, William Henson patented his “Aerial Steam Carriage.” In France, Felix du Temple de la Croix constructed a hot-air or “steam-powered monoplane” which briefly flew in 1874. Clement Ader built a steam-powered aircraft which took off and flew for 54 yards, though not much resulted from his success (Buckley 26).

Hiram Maxim built a steam-powered device which would lift straight off the ground in 1894, but due to some design flaws, the machine would not lift off the ground any higher than two feet (though it did fly within the barrier for 40 feet). It was Otto Lilienthal in Germany who fostered the development of fixed-wing powered flight with his creation of a series of over two thousand glider flights. Lilienthal believed that the key to power flight was an ornithopter (a device that replicates a bird’s movement by flapping mechanical arms). He wanted to first learn to fly before adding power; he was unable to do so, however, because of his tragic death in the crash of one of his gliders in 1896. As a result from Lilienthal’s successful glider flights, Percy Pilcher patented a design which was based off of Lilienthal’s gliders, but powered by a petrol engine. Pilcher did beat the Wright brothers to creating controlled powered flight, but he was killed in a glider crash in 1899 (Buckley 26).

Any object that is moving is experiencing a type of energy called kinetic energy, which is the energy of motion (KE=1/2 * mass * volume^2). Centripetal forces cause an object to change direction, but not its speed—causing it to move in a circular pattern (F_c=m * v^2/r). Inertia is defined as the property of an object which opposes change in velocity—described by Newton’s first law.

It took several years for these innovative minds to apprehend everything involved in flight and utilize those concepts to their fullest. We are still learning about different applications,
but for the most part things haven’t changed much at all. Designs have been modified for the different purposes of flight, yet all the same parts remain.

Now that one has become familiarized with some of the basic physics of an aircraft, one must look at the different parts of an aircraft that makes it work. Of course each type of airplane will have some parts unique to that specific design; however, all airplanes have the same basics. In the beginning all that made the aircraft move was the propeller which is a set of rotating wings, which can also be called blades; and a simple internal engine, much like those found in the cars of the time. A jet engine was later created to increase the speeds. The gas turbine works by taking in air, compressing it, mixed it with fuel in a gaseous state, and would burn to create thrust. The actual structure of the aircraft is called an airframe and is characteristic for its light weight and strength. The fuselage is present in both jet, as well as strut type aircraft. It is the center body of the vehicle and is used to house the passengers, luggage, fuel, landing gear, and the cockpit, which is where the pilot directs his flight of the plane. The wing and tail can sometimes contain an engine, but their importance is mainly on creating lift. On the outer edge of the wing there is what is called an aileron. The aileron makes it possible to turn in flight.

Besides the fact that an airplane is heavier than air, there are several other reasons why the vehicle shouldn’t work in migrating from one location to the next through the air. To explain some of the hindrances, there are a few more definitions that still need to be explained. Firstly, the angle of attack—or the “angle between chord line [within the airfoil wing] and the relative wind,” which can also be described by stating that the angle of attack is the angle between where the wing is pointing and the direction of where the airplane is going. Now if the angle of attack is too extreme, the air is no longer able to stream-line against the wing a “bubble effect” is the result. The air that flows across the top of the wing will begin to circulate and cause the aircraft to stall (Flight Instructor 87). If ice has accumulated on the wings it can reduce the lift as well as increase drag due to the abnormal and textured surface (Flight Instructor 123).

Air density is also a major factor in flight. Higher up in the atmosphere air density decreases—that is, there is less air particles for an equal amount of space closer to the surface of the earth. With less particles, there is less oxygen for the engines to pull in and burn, decreasing the thrust as well as lift. Flying at certain heights can be extremely dangerous (Williams NP).

The FAA regulates the air space and “divides” the heights of flight like layers of a cake. Only authorized aircraft are allowed to fly near airports or other specified zones as well as each type of aircraft and pilot is restricted to a specific height. This is to minimize air collisions as well as controlling the planes so that they can fly at the best height for that aircraft.

Aircraft and flight are common in today’s world, whether it’s a daily commute to a job, or a way to save oneself a family drive across the desert, or a way to cross the ocean for that vacation in Paris. There is no child who has not wondered, at some point, how something so large stays up in the sky. Throughout the years, man’s perception of flight has changed with the introduction of technology and the imaginative spark of the media.

To test out a prototype of a new airplane, what’s known as a flight simulator these virtual environments use the controls that are in the aircraft and a pilot “flies” the object in the realistic
settings. Digital technologies were created and advanced with the main concern to research goals and technical problems; the concept of using such devices for entertainment was not a concern for the developers at the time. With the advancements of graphics as well as reaction speeds the simulator was developed and utilized (Darley 12). The reactions of the pilots when handling the plane and the simulations help the designers fix any major flaws and potentially save lives (Shiphandling Simulation).

The Federal Aviation Administration (FAA) has also designed realistic simulators to represent air traffic patterns that occur at airports to train incoming air traffic controllers who work under extreme pressure and have to be alert to the hundreds of planes that come and leave not only the airports but also while flying to their destinations—it's decisions that their trained to make and practice in their simulated environment that can prevent catastrophic disasters (Michael 85).

So many things go into the assembling and testing of planes, and yet one of the most important factors still remains. The pilot. The pilot needs to understand all of these concepts as well as utilize them in case of a mechanical failure. Who are these men and women who control these beasts of the air?

It takes a surprisingly short amount of time to become a pilot, relative to the several years in college a doctor or nurse must weather. Most pilots learn the concepts of flight through self-study. While some do attend classes, these classes are usually provided for other specific areas of interest during flying—such as air-traffic control. Rick Koril, one of the pilots I interviewed, informed me that all a person must do to become a private pilot is pass a written test as well as log at least fifty-eight hours with an instructor, while the FAA only requires forty hours of flight time. Very basic physics (examples of which were discussed in this paper) and a knowledge of aerodynamics are needed to be known to fly.

What appears to be very little academics required is compensated with the practical skill of actual flight. Lou Ferzacco, a licensed flight instructor as well as an airline transport pilot, told several different stories about his experiences with flying. Lou Ferzacco began flying in 1985 and has been so since, whether for his career (as an instructor as well as a pilot for major airlines like America West, now US Airways, or as his hobby while he works in an office. He has flown a wide variety of planes, including the Citation X, which is the fastest civilian aircraft flown, as well as officer training by the Air Force, and has had the privilege of flying famous athletes, singers, and actors; such as Bill Joy, Lance Bass, Arnold Schwarzenegger, and Tiger Woods around. He stated that a pilot must always be aware of what is going in, with, and around the plane. While flying a Jetstream 32 at a height of 17,000 feet he experienced a total hydraulic failure. The failure caused all of his controls to no longer respond to his commands. Brakeless and without flaps he and his copilot had to land the plane while the passengers were experiencing a lack of cabin pressure. Lou explained that his copilot was required to manually lower the landing gear—by pumping the control that resembled a butter churner almost two hundred times. A hydraulic failure is rare because there are fail safes within the containment to prevent leaks (ball bearings). The hose has only one weak point, and that was where it had ruptured; the hydraulic fluid flooded the baggage compartment, and the nitrogen ate through all of the luggage that was on board. There were still able to land safely, thanks to his quick thinking and the assistance of his copilot. It's just as he said, "Flying is extremely safe, [but there's] not a lot of space for stupidity," there really isn't a better way to put it. Mr. Ferzacco laughed as he joked, yet still with a serious tone, that the thing he fears most about flying is driving on the freeway to the airport.
Mr. Ferzacca has flown many different types of planes for different situations. There are several different types of airplanes, and each has its own purpose, from the smallest twin engine to the largest wide body.

Twin engines are usually small and are used for hobby or day-trip flights. Rick Koril owns his own airplane and chooses to fly it for a few different reasons. When he lived in Chicago he used his aircraft for business and also became a member of the FBO (fixed-base operation) with people who recently received their instrument rating. When he moved to Arizona it wasn’t as practical to use his plane for business and the weather conditions were nowhere near necessary to fly in bad conditions for his instrument rating (though he still does the minimum hours to maintain it), and so he began volunteering with United Blood Services and uses his aircraft to transfer blood from Flagstaff down into Phoenix before the blood is no longer usable. He also is a member of the Flying Samaritans—a group of private pilots, doctors, nurses, and medics who travel down into Mexico and give much needed medical attention.

The next type of flight would be for military purposes. Flight was extremely important during World War II, effectively ending it after the bombing of Nagasaki and Hiroshima, but flying and training is just as important today. The Air Force has developed and now uses an unmanned plane to scout out possible danger areas.

Another type of aircraft is used to transport people in commercial flight. They can be as small as a City Jet that holds no more than fifty passengers to as large as a Boeing 747 which holds over eight hundred people. These wide variety of planes perform an aerial ballet depending on where you are traveling to you can be stuffed like sardines in a can or spread out in the luxury of first class with your own personal television. They are intended to make their passengers as comfortable as possible for the smallest amount—which includes offering standbys as well as sometimes overselling a flight. Many people use commercial flights for their own personal needs, whether it be business or vacation.

The knowledge of flight has been harnessed by man in the past, perfected for flights now, and even performed by unmanned air vehicles. The questions still remain—where’s the limit? Is there a limit? Is flight in shuttles even possible? When will discover the next big accomplishment? With all that has been known only more questions can be asked and wait for the answers to return in time.


Sildenafil (Viagra), Tadalafil (Cialis), and Vardenafil (Levitra): The New Sexual Revolution

By: Ricardo Hernandez  
April 18, 2008  
Organic Chemistry  
Dr. Hank Mancini
Abstract

To provide a description of what the drugs Sildenafil, Vardenafil, and Tadalafil do. I will include the usage the Structure and how have these drugs have changed the revolution of sex for people that suffer Erectile Dysfunction. Also what is the outlook for a drug that will work in similar ways for women.

Background

In order to understand how drugs like sildenafil, vardenafil, and tadalafil work and what the effect of these drugs have been we have to know the disease first. This disease that I will explain is Erectile Dysfunction. According to an article on the National Kidney and Urologist information center “Erectile Dysfunction, sometimes called “impotence”, is the repeated inability to get or keep an erection firm enough for sexual intercourse.” (National Institute) According to Bernie Zilbergeld, a sex expert, “Most of the penis is filled with two large cylinders of spongy tissue surrounded by a tough fibrous covering. In a healthy male, the spongy tissues become engorged with blood during sexual excitement, causing the penis to expand. As the spongy tissue fill with blood they push out to make the penis hard.” (Zilbergeld 58) More specifically the chambers on the penis are called the corpora cavernosa. A membrane called the tunica albuginea surrounds these chambers. The whole process begins with either or both sensory and mental stimulation in the brain that sends signals to the corpora cavernosa to relax letting an inflow of blood to go into the spaces. There are many factors that contribute to erectile dysfunction. An erection requires a specific sequence of events so when any of the process are involved it can have a great effect on it. Damage to the nerves around the penis due to surgery or trauma can cause it. Diseases like chronic diabetes, alcoholism, vascular disease, neurological disease, and multiple sclerosis can lead to ED. Lifestyle choices like being overweight, avoiding exercise and psychological factors like stress, depression, and anxiety are causes. Even worse, some of the medicines that you take to help with the diseases have ED as a side effect.

In order to diagnose ED doctors go through a series of tests that help determine the leading cause of this disease. These include looking at family history, and physical and psychological examination. “Monitoring erections during sleep can help rule out certain psychological causes.” (National Institute) This is due because healthy men have
erectations when we are at our REM cycle of sleep. If a man doesn’t have them, it is deduced that it is a physical cause rather than a psychological one.

History

We can say that the era of sexual revolution started well before the discovery of Viagra. This happened at a 1983 American Urology Association meeting that took place in Las Vegas. Giles Brindley, who was a fifty seven year old British Physician, left people speechless.

Brindley stepped from behind the lectern at a Las Vegas medical conference, dropped his pants, and showed his erect penis to hundreds of colleagues. Brindley had just presented work on injectable drugs to treat impotence and was displaying an erection he had induced by injecting his own penis. The results were quite good. (Loe 36)

This was important because before that people saw this problem as something to do with the mind. Men that had this problem didn’t go to urologists to seek treatment. Men suffering from Erectile Dysfunction went to psychologists. Men were ashamed to admit to this problem. They were labeled as impotent. But even before this, blame had been passed back and forth between men and women. Before the 1940’s the blame was put on women. It was said that the women were at fault because they weren’t sensual enough to cause an erection. They were labeled as rigid and if a man didn’t get a full erection it was due to the woman inability to arouse the man. With the help of feminists’ movements it was then shifted to men as the sole person to blame for their impotence. And so forth men blamed this on a psychological problem and the way society viewed the male species, they felt that they weren’t man because they could not sexually satisfy women.

The date that turned the tables on this belief of impotence having to do with the mind was really 1983. After this the focus was completely shifted to a medically solution to the problem of impotence. The actual term “impotence began to loose its value and was replaced by the more widely accepted term Erectile Dysfunction. It was better accepted by men everywhere because it did not have the connotation that you were less of a man which the term impotent had, but instead it was seen as a disease where there was hope for men that had it.

The year was 1998. What do you remember the most about that certain year? During that year there were two big stories that grab everybody’s attention. One was the White House scandal known as MonicaGate involving then President Bill Clinton and the
other was the drug Sildenafil more widely known as Viagra. The following paragraph from 2001 presidential candidate Sandra Leiblum.

Who knows this date? March 29, 1998. What Happened on that day? That was when we all celebrated and benefited from the first FDA recognition of an oral therapy for male sexual dysfunction... Now we are in a decade of the Medicalization of sex, with many different approaches. (Loe 132)

Sildenafil was the first drug that was approved by the FDA in 1998. But since then there have been two other that have been approved. Pfizer was the one that open up the gates for other companies like Bayer and Eli Lilly and Company to create their own ED drugs.

Sildenafil was first synthesized and studied for the use in hypertension and angina pectoris, which is a symptom of ischemic cardiovascular disease. In an article in Medline plus it said “Sildenafil (Revatio) is used to improve the ability to exercise in people with pulmonary arterial hypertension (PAH; high blood pressure in the vessel carrying blood to the lungs, causing shortness of breath, dizziness, and tiredness”. (Medline Plus 2007) Revatio and Viagra are the same drugs; the distinction made by Pfizer is to differentiate in that one treats ED while the other treats PAH. Sildenafil was synthesized by a group of pharmacists working at Pfizer’s research facility in England. Now it is mostly advertised as an ED treatment all over the world. According to the family doctor website one tablet is taken 30 minute to 1 hour before planning to have sex and the tablets come in 25, 50, and 100 mg doses. (06/2006)
The FDA first approved Tadalafil also known by the trade name Cialis in December of 2003. It was synthesized, advertised, and sold by the Eli Lilly and Company. “Tadalafil is in the class of medications called phosphodiesterase (PDE) inhibitors and it works by increasing blood to the penis. (Medline Plus 12/2007) It has the chemical formula C$_{22}$H$_{19}$N$_{5}$O$_{4}$ and its mass is 389.404g/mol. This is the most different on structure of the three. It contains less mass and it does not contain the sulfur group.

Another phenomenon that has started due to use of these drugs is women wanting something similar. Now that men have found a cure for their problem they want the same thing. According to a study conducted, 564 percent of women suffer from a sexual problem compared to only 343 of men. I don’t think that it will ever be possible to create a pill similar to Viagra for women. Even though their sexual organs follow a similar path.

The final drug on the list is the drug vardenafil, which is made by the Bayer Company. According to Medline.org it should be taken 60 minutes before sexual activity. (Medline 12/2007) It had has the chemical formula C$_{23}$H$_{32}$N$_{6}$O$_{4}$S and its mass is 488.604g/mol. It is heavier than Viagra due to its extra Carbon and extra couple of hydrogens.
Which is best for you?

Viagra, Levitra and Cialis each have a slightly different chemical make up. These minor differences affect the way they work, such as how quickly they take effect and wear off; how they interact with other medications; and side effects. Your doctor will consider these factors when deciding if one of these medications is a good choice for you. Your doctor will also consider any other health problems you have and whether any of your current medications could cause problems when taken with Viagra, Levitra or Cialis.

Chart and Caption from MayoClinic.com (4/2008)

Mechanism

The mechanism for all three drugs is the same. To create an erection the nervous system causes nitric oxide to be release into the corpus cavernosum of the penis. Nitric acid binds to the enzyme guanylate cyclase and this causes an increase amount of cyclic guanosine monophosphate (cGMP). This cause the smooth muscle that leads to the penis to relax letting an inflow of blood causing the penis to go erect. All three drugs are potent inhibitors of phosphodiesterase type 5 (PDE5). PDE5 is responsible for the degrading of cGMP’s. These drugs are similar in structure to cGMPs and act as competitive binding agents in the corpus cavernosa creating a better erection.

<table>
<thead>
<tr>
<th></th>
<th>Viagra (sildenafil)</th>
<th>Levitra (vardenafil)</th>
<th>Cialis (tadalafil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How to take</td>
<td>Without food, no more than once a day</td>
<td>Without food, no more than once a day</td>
<td>With or without food, no more than once a day</td>
</tr>
<tr>
<td>When to take</td>
<td>30 to 60 minutes before sex</td>
<td>30 to 60 minutes before sex</td>
<td>30 minutes before sex</td>
</tr>
<tr>
<td>Time an erection is possible</td>
<td>Up to four hours</td>
<td>Up to four hours</td>
<td>Up to 36 hours</td>
</tr>
</tbody>
</table>
The impotence drug Viagra blocks the enzyme, specific phosphodiesterase (PDE5), which is responsible for degradation of cGMP. The molecular structure of Viagra is similar to that of cGMP and thus it acts as a competitive inhibitor of PDE5. It blocks the degradation of cGMP, prolonging the NO signal.

Risks

It is better to consult your doctor before taking any of the drugs to determine which one is for you. It is very dangerous if you are taking other drugs that contain nitrates for other problems to take them with these drugs. The combined effects can lead to low blood pressure and the loss of consciousness. Other common side effects are headache, indigestion, diarrhea, muscle aches and temporary vision changes. If the erection lasts more than 4 hours you should consult a physician as fast as possible because it can cause permanent damage.

Many things have been said about making a similar drug that would work on women. Pharmaceutical companies spend millions of dollars trying to come up with a pill that will have the same effect on a woman in the sexual context. Women themselves are pushing for something like it to be created because they see how it has affected men in a positive way. But I honestly think that it will never be possible. A woman’s sexual process is so much different than a man’s that it is impossible to try to find a common point where it would be best controlled. The three drugs that I talked about above I think will continue to have great success. It will get to a point in the near future that
everybody, even the ones without ED will use it as a recreational drug to enhance their sex lives. The only thing that is holding it back is the fear of possible side effects and the price. Both of these things will have a solution and the drug will take off even further than they are now.


The History, Uses, and chemistry of Ibuprofen

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Abstract

Ibuprofen is one of the best selling drugs on the world market today, primarily due to its success as an anti-inflammatory, fever-reducing pain reliever. It has become the most popular drug in the NSAID (Nonsteroidal Anti-Inflammatory Drug) market. Throughout this paper we will discuss what makes this drug such a modern wonder. The drug was presented to the market in the 1960's and its use quickly became widespread. Through hours of laboratory testing, scientists now know exactly how it works. This group of drugs (NSAID's) work by interaction with cyclooxygenase (COX) enzymes that through a series of interactions with prostaglandins in the body serve to inhibit inflammation and block pain signals. Also, the stereochemistry, chemical composition, Infra Red Spectroscopy and the reactions by which ibuprofen is synthesized in a lab will be discussed throughout this paper.

The drug ibuprofen is a very important and well known drug that is used every day in the homes of millions of Americans. Ibuprofen is a medication (commercially known as Advil) that acts to do an array of interesting and amazing things in the human body. This medication is primarily used for mild to moderate pain relief, inflammation of tissues, and fever reduction. Ailments that it is used to combat are rheumatoid arthritis, osteoarthritis, dysmenorrhea, ankyllosing spondylitis (degenerative arthritis of the spine), gout, and psoriatic arthritis. Ibuprofen can be bought over the counter and is also available as a prescription drug in a higher dosage.

The history of ibuprofen is extensive; this drug has many origins but only a few successful creators. It has been proven an effective and safe medicine for nearly anyone. The drug was first synthesized in the early 1960's by a medication manufacturing company located in Britain. The company was known as the Boots Company and is now a very prominent drug store chain all across the United Kingdom. (5) The chemists of Boots were able to take aspirin, which was readily available, and identify the portion of the drug that was causing the anti-inflammatory properties seen in the aspirin of the day. The scientists found that the inflammation fighting component was primarily due to the carboxylic acid. Below is the structural component of a carboxylic acid and shown on the right is the structure of ibuprofen with the carboxylic acid highlighted.

The scientists then looked at a wide array of chemicals with carboxylic acids in their structure and tested 600 different ones. They came to the conclusion that ibuprofen – the direct derivative of aspirin - was the most effective. (5) In 1964 the drug was released as a prescription drug throughout the United Kingdom called Brufen.

Due to the extreme popularity of the drug in the UK, it began expanding into other areas of the world. In 1974 ibuprofen emerged in American pharmacies
when a non-exclusive license was given to the America-based Upjohn Company. Upjohn would later market the drug as an arthritis pain reliever called Motrin. The drug was soon given approval by the Food and Drug administration to be sold as an over-the-counter drug in a lesser dosage than the prescription counterpart. The drug was only to be manufactured by those given direct rights by the Boots Corporation. By 1986 though, the worldwide patent was lifted and the drug was free to be made by anyone. At this point there was an array of companies ready to try to take a piece of the exciting new market. (5)

Ibuprofen appears to be a relatively straightforward drug, which it arguably is, to some degree. As you delve into the how and why it works, however, it becomes complex and interesting. Ibuprofen is classified as a Non-steroidal anti-inflammatory drug (NSAID) of the propionic acid chemical class. (4) This means that the drug is not a steroid in the way it functions as an anti-inflammatory agent, though its effects can be very similar to those of a steroid hormone. Ibuprofen in its marketed form is a racemic mixture containing both the (R) and (S)-isomers of the drug. Clinical experiments have shown that only the (S)-form of the medication is very useful in the human body. The (R)-form of ibuprofen does, however, help in pain relief and inflammation because once in your body it is incompletely turned into the (S)-form. In children this may be used as a “reservoir” for the active drug in the body. (4) NSAID’s are very effective drugs but also do pose serious risks.

The Food and Drug Administration has an online guide that informs readers about NSAID’s and the dangers they pose. The following warnings are included.

“NSAID medicines may increase the chance of a heart attack or stroke that can lead to death.” (9) “NSAID medicines can cause ulcers and bleeding in the stomach and intestines at any time during treatment [with ibuprofen]...” (9)

The FDA has also posted an extensive list of serious side effects that can be caused by prolonged use of ibuprofen. The list includes kidney failure, anemia, heart attack, life-threatening skin reactions, liver failure, and asthma attacks. These are all only possible side effects. Though this is a disconcerting list, the FDA has tested the OTC form of the drug and found that the risk of cardiovascular events in the study did not increase with the use of ibuprofen. No warning label, therefore, is needed on the medication packaging. (9)

The mechanism of action that ibuprofen takes as an anti-inflammatory pain reliever and fever reducer also has an effect on blood platelets and the renal system. The primary effect of ibuprofen occurs due to the collective inhibition of cyclooxygenase (COX) enzymes. (4) These enzymes are responsible for the production of certain prostanoids such as prostaglandins. These prostaglandins are created by cells and are used to carry messages to areas directly around the cell until they are broken down or dissipated. The enzyme acts by instigating cells around it to also become inflamed which causes pain to the individual. The prostaglandins control numerous processes, such as: accumulation of platelets during clotting, strengthening and delivery of pain signals, and introduction of inflammation. The way in which ibuprofen disrupts this is, as stated above, by inhibition of the cyclooxygenase enzyme. More specifically, the ibuprofen is able to bind to the cell in which the COX enzymes have their effect—arachidonic acid. If uninhibited, this acid will initiate the production of prostaglandins from a single common fatty acid. The
COX enzyme adds two oxygen molecules to and therefore oxidizes arachidonic acid (an unsaturated fatty acid) to turn it into the beginning molecule of a prostaglandin. Ibuprofen will attack this arachidonic acid and bind to it, which means that it will no longer be able to bind to its neighboring cells and act on them to induce pain. The addition of O₂ is shown in the image below, next to the three dimensional and linear structures of arachidonic acid.

![Addition of 2 O molecules to arachidonic acid. (Source: 3)](image)

When analyzing the anti-inflammatory feature of ibuprofen, the two different types of COX enzymes must be explained - COX-1 and COX-2. COX-1 is used for the “general housekeeping” of the body which involves signaling for the increase of gastric mucosa and also some properties involved in kidney function. The COX-2 enzyme is only in the specific cells of the body and is used to signal pain and inflammation. This is the enzyme that, once inhibited, is very effective at reducing pain and swelling. Ibuprofen unfortunately inhibits both enzymes. Scientists have not yet been able to selectively inhibit only COX-2, leaving us with the less pleasant effects of COX-1 inhibition, as well. This is the culprit for most of the side effects cited earlier.

When it comes to the aspect of pain relief, Ibuprofen functions just as it does as an anti-inflammatory. Much of the pain a person feels is due to swelling or inflammation of cells in the body which causes the hyper-sensitivity of pain receptors. As shown above, COX inhibition prevents prostaglandins involved with inflammation from being produced, which reduces inflammation and, therefore, does not allow pain.

Ibuprofen also works as a fever reducer by suppressing a different prostaglandin - PGE₂. The PGE₂ prostaglandin is a very important one in retention of heat within the body. PGE2 causes vasoconstriction of the capillaries in skin and muscle which reduces heat escape through skin, leaving a person with increased internal temperature, otherwise known as a fever. This vasoconstriction is caused by a change in the hypothalamus’ standard resting temperature set point. When body temperature goes up, it is due to a signaling cascade set off by the binding of PGE₂ to the PGE₂ receptor in the brain. Ibuprofen is able to block the production of the PGE₂ prostaglandin, therefore reducing the effect of the fever or even masking it all together.
Ibuprofen affects other parts of the body, as well, including the blood and kidneys. The kidneys serve to filter and remove unwanted materials from blood such as urea and other by-products of bodily processes. Prostaglandins which are produced by the COX-1 and COX-2 enzymes play a role in the re-absorption of water and sodium in the kidneys. Some of these prostaglandins can affect the rennin-angiotensin system which is responsible for blood pressure and blood flow into the kidneys. In certain cases, ibuprofen can lead to a decrease in blood flow to the kidneys leading to acute renal failure. (4)

Platelet (clotting cell) aggregation can also be affected by ibuprofen. The COX enzyme is responsible for the production of thromboxane which facilitates the clotting of platelets. The lack of thromboxane means that a wound will bleed longer due to the decreased action of the platelets in the clotting of the wound. One interesting fact is that ibuprofen binds to the COX enzyme reversibly so the affects of the drug will wear off after 24 hours, as opposed to the well-known drug, aspirin. Aspirin irreversibly binds to these COX enzymes making them useless for the life of the cell, which is the primary reason why aspirin is so effective as a blood thinner. (4)

A great deal of information about the structure of ibuprofen was learned from Infrared Spectroscopy. In this process a machine is able to pass a beam of concentrated infrared light through the sample. A detector then reads how much energy was absorbed at each wavelength and plots it on a graph. This works because of the fact that all functional groups have very specific frequencies where they will easily vibrate. The IR Spectra for ibuprofen is as follows, with the higher wavelengths to the left and lower ones to the right.

The two separate spectra above show different regions of absorption and are from the same IR spectra originally. If we break these spectra down, we can determine the functional groups of ibuprofen. On the IR to the right, the thinner line corresponds to ibuprofen. There is a very sharp and strong peak at 1700cm^-1. This reveals that there is a carbonyl (C=O) group, which can be seen as a carboxylic acid on Carbon number 1 on the structure of ibuprofen on the first page. Another very distinct peak is seen at 3400cm^-1 on the left IR (dotted line). This is a very strong and broad peak and encompasses the hydroxyl group (OH) on carbon 1. It is also
apparent on the left IR that there is a sharp peak at roughly 3000 cm\(^{-1}\). This reveals that there is either an aromatic group (benzene) or an alkene. It can be observed that at 600-800 cm\(^{-1}\) (which is not visible on this IR) there is another peak. With the peak at 3000 cm\(^{-1}\), along with the peak at 600-800 cm\(^{-1}\), an aromatic ring is identifiable. The aromatic ring is also apparent in the structure. From this simple process we are able to determine that there is an aromatic benzene ring, a hydroxyl group, and a Carbonyl group. This includes all of the functional groups in ibuprofen.

The images above show the structure of ibuprofen as it is known today. The IUPAC name is 2-[4-(2-methylpropyl)phenyl]propanoic acid. It is labeled as an acid because of the carboxylic acid group. Ibuprofen is a fairly simple molecule composed of only 13 carbons, 2 oxygens, and 18 hydrogens. It also has the relatively small molecular mass of 206.13 g/mol. In addition, as can be seen from the 3D model, it contains a chiral carbon in the alpha position of the carboxylic acid making this molecule a stereoisomer - having more than one three-dimensional arrangement. The medication contains a para-substituted aromatic (benzene) ring with the carboxylic acid on the right side, named more specifically as p-n-propionic acid. On the left side of the ring there is an isobutyl group. Due to the chiral center we find in the molecule, there are actually two different arrangements or enantiomers, \(R\) and \(S\). The two different arrangements are pertaining to the difference in location in space of the methyl and \(H\) on the number 2 carbon. The following illustration shows the different enantiomers and the way in which the structures are different.

Though the change between the two enantiomers seems very small, it plays a huge role in how the human body uses it. As discussed earlier, the \((S)\)-form of ibuprofen is the only useful one—the \((R)\)-form does nothing unless it is converted into the \((S)\)-form. The drug is currently sold as a racemic mixture containing equal amounts of both of the forms for the following two reasons:
1. It was found that the isomerase 2-arylpropionyl-CoA epimerase is able to slowly convert the (R)-form to the (S)-form in the body. (4)
2. It is very costly to remove the R-Enantiomer from the racemic mixture and would not make sense economically. (4)

The creation of ibuprofen in a laboratory is not merely a one-step process. A total of three steps are needed in today’s quickest process and a total of seven outside chemicals to make the drug.

The entire process is shown in an illustration to the right taken from the Wisconsin Center for Education Research. There are many different routes to creating ibuprofen but this one is the most popular and is used most often today. It is the process that was first patented by the Boots Company in Great Britain. The starting material for the medication is isobutyl benzene (C₁₀H₁₄). The isobutyl benzene is added to propionyl chloride through a Friedel-Crafts acylation as shown in detail in figure 1 to the right. In this reaction, the starting materials are brought together and through a reaction with the catalyst aluminum chloride (AlCl₃) and a solvent (CH₂Cl₂ – which is not involved in the reaction) the para-substituted benzene is made. The first step is to prepare an electrophile from the propionyl chloride and AlCl₃. This yields AlCl₄⁻ and the electrophile which is now the acyli group with a net + charge. This acyl group then acts as an electrophile and attacks the electron-rich benzene ring at the para position due to the ortho-para activating group (isobutyl) on the opposite side of the ring. This in turn frees a proton that binds to one chlorine atom from the aluminum tetrachloride (AlCl₄⁻) to restore the catalyst (AlCl₃) unaltered. (10)

Through this reaction, the product of the first step is formed: 1-(4-isobutyl-phenyl)propan-1-one (Figure 1). From this product, the second reaction of the process is run. The new reactant is reacted with iodine and trimethyl orthoformate (HC(OH)C₃H₃) turning it into methyl ibuprofen. In the last step of the synthesis methyl ibuprofen is caused to react with potassium hydroxide (KOH) and water, producing the final product in its enantiomeric R and S form. (10) This final product is then be added to a whole list of inactive ingredients, such as carnauba wax, colloidal silicon dioxide, corn starch, hylpromellose, iron oxide, magnesium stearate, polydextrose,
polyethylene glycol and many more before it is sold in stores across the world. (10) There are other processes used to make the drug, though the principles are each the same and, in most cases, only different catalysts and solvents are involved.

Ibuprofen is an effective drug that has improved the world. Time, money and effort were needed, though, to unravel how exactly this medication works and how to make it in an economical and safe manner. Ibuprofen was discovered in the 1960’s but at the time was synthesized in a much more laborious manner that it is today. As modern technology and knowledge have progressed, the process of making ibuprofen has grown shorter and less wasteful. Ibuprofen is a simple, fairly non-complex drug that has significant effects in the realms of pain, fever, and inflammation. The development of ibuprofen has increased the body of information about the enzymes and receptors involved in pain reception. An example of this is how ibuprofen led to the understanding that COX enzymes and arachidonic acid are both precursors of prostaglandins, and that with the right chemicals such as ibuprofen, containing the right molecular weight and functional groups, can bind to and disrupt the actions of those molecules. As science and medicine advance we will see more revolutionary breakthroughs in the drug industry and will see lives changed and diseases cured. Ibuprofen is just one simple example of how the world was changed forever by a single small medication. There is still a lot to learn about how the body works but we are slowly chasing down and uncovering its wonderful complexities. This knowledge allows the synthesis of medications that can target very specific components of the body and be one hundred percent effective. Although we are not there yet, no doubt we will be someday.
Bibliography


Zoloft

Daniel Isaac

April 18, 2008
Abstract – Zoloft is an antidepressant that many people in America are prescribed. It has been on the market for over twenty years and millions presently are taking it. In this paper, the history of this medication will be discussed, how it was derived, how it works on the brain chemistry, and what the possible side effects could be. Side effects vary from binine to very serious, such as suicidal thoughts. Brain chemistry is very sensitive, so this medication should not be taken lightly, a qualified physician should be notified if any severe side effects occur. This drug has helped many people deal with the symptoms of depression, by allowing nerve cells in the brain to communicate properly. Zoloft regulates serotonin reuptake, which allows for more serotonin to arrive at the desired location.

"In 2007 it was the most prescribed antidepressant on the U.S. retail market with 29,652,000 prescription.”(2) The Antidepressant that holds that title is Zoloft. With so many Americans on this medication, it is important to know exactly what this medication is and what it does that has made it so popular. Many different antidepressants have come onto the market, with their promises of a better, happier life, and many have failed to live up to their billing. Zoloft makes a similar claims, but does it live up to its billing? Perhaps this medication is overly prescribed, and the millions that take it are looking for happiness in a bottle of pills? On the other hand, maybe the new and different stresses and problems that come along with our ever changing world has created a necessity for chemical assistance for a more peaceful existence.

Zoloft, which is also known as sertraline, was developed in the 1970 by biochemist Kenneth Koe and chemist Willard Welch. These men worked for Pfizer, and were looking to generate a new antidepressant, by taking up the work of their predecessor Reinhard Sarges. Sarges synthesized a norepinephrine reuptake inhibitor, it was called tametaline. Sarges administered tests on animals with the tametaline, and he did not get the desired effect.

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Tametaline, the compound that was first developed by Reinhard Sarge, and then used to derive sertraline by Kenneth Koe and Willard Welch.
Years later at Pfizer, biochemist Kenneth Koe and chemist Willard Welch took the development of this drug further. Koe and Welch generated derivatives of tametraline, then Welch prepared stereoisomers of the most promising candidate, which were then tested on animals. The most active cis-isomer was taken into development and then it was named sertraline. Sertraline was approved by the Food and Drug Administration in 1991.

![Chemical Structure of Sertraline](image)

Sertraline Hydrochloride, (Zoloft Lustral)

(1S)-cis-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine

Chemical Formula – C\textsubscript{17}H\textsubscript{17}Cl\textsubscript{2}N  

Molar Mass – 306.229 g/mol

Zoloft is an anti-depressant medication known as SSRIs, selective serotonin reuptake inhibitors. Like other medications in this class, such as Prozac and Paxil, Zoloft claims to relieve symptoms of depression without the side effects that many people experience with the older tricyclic antidepressants and MAO inhibitors.

Zoloft is used to treat symptoms of major depressive illness, including bipolar disorder and manic depression. Depression can be a serious medical illness causing mood and physical changes that could seriously alter a person's daily functioning. A sad mood accompanies changes in appetite, sleep, and activity level. One may lose interest in activities he or she normally enjoy, decrease their sexual desire, find difficulty concentrating and remembering. Thinking, movement and general motor skills may slow down as well, and one may experience feelings of hopelessness, worthlessness and guilt for no rational reason. In extreme cases there could be suicidal thoughts.

In order to be diagnosed with depression several of these symptoms must be present for an extended period of time. Zoloft has also been shown to work in relieving
anxiety, insomnia, and psychomotor agitation that sometimes come along with depression. Recently, tests have shown that Zoloft was effective in treating Obsessive-compulsive disorder in both children and adults. This success was not across the board however; in the cases that the Zoloft was effective it outshined the standard for Obsessive-compulsive treatment, clomipramine. However, with patients that did not receive the benefits of Zoloft for whatever reason, they still did not receive any help for their condition when the dosage was increased.

Depressive symptoms are the result of a biochemical imbalance in the brain, a disturbance in the brain's chemical messengers called neurotransmitters. Zoloft deals with the neurotransmitter serotonin, allowing electrical messages to be processed more efficiently. This helps relieve symptoms of depression, because the messages that are being sent are being received. Zoloft is a selective serotonin reuptake inhibitor, which means it helps correct the chemical imbalance of serotonin in the brain. Serotonin is a naturally occurring chemical in the brain that is involved in the transmission of messages between nerve cells.

Zoloft is slowly absorbed from the gastrointestinal tract, and then is travels through the liver. Zoloft is then metabolized in the liver to N-desmethylsertraline, which is ten times less active as an inhibitor of serotonin reuptake. Reuptake is when the nerve ending that is releasing the neurotransmitter, serotonin in this case, receives the message that it sent out, not allowing the message to be sent to the corresponding nerve ending.

"Sertraline specifically inhibits central nervous system neuronal re-uptake of serotonin, thus increasing the concentration of the serotonin at the synapse and enhancing of serotonergic neuronal transmission. The increased availability of serotonin is thought to be linked with the improvement in depression accounted for by sertraline treatment. Sertraline has no direct effect on the re-uptake of noradrenaline, dopamine or GABA. Unlike most tricyclic antidepressants, it has no significant affinity for alpha_1-adrenergic, H_1-histamine, and muscarinic receptors. Furthermore, sertraline does not show significant affinity for D_1 and D_2 dopaminergic, alpha_2 and e adrenergic, benzodiazepine and opioid receptors. The selectivity of sertraline may account for the lower incidence of some adverse effects such as sedation, orthostatic hypotension and anticholinergic effects. Like tricyclic antidepressants, MAOIs, and other SSRIs, sertraline significantly reduces REM (rapid eye movement) sleep density, REM time and the REM percentage of total sleep time in patients with major depression.” (3)

Zoloft deals with the serotonin levels that are administered in one's brain. "In the central nervous system serotonin is believed to play an important role as a neurotransmitter, and helps regulate anger, aggression, body temperature, mood, sleep, sexuality and appetite as well as stimulating vomiting”(1) Having so much responsibility in the human body, one can see why being deprived of this essential chemical can lead to depression and other problems.

People that have normal brain chemistry do experience neurotransmitter reuptake, but reuptake only occurs with a small percentage of the serotonin sent. In the diagram,
the serotonin is being released by nerve A and traveling to nerve B. In a person with normal brain chemistry, the majority of the serotonin is able to reach its destination on nerve B. The blue arrows represent the serotonin that successfully travel to nerve B, the red arrows represent the serotonin that was released from nerve A and experienced reuptake and returned to the nerve that sent it out, nerve A.

People that are suffering from depression, or another condition caused by a chemical imbalance in the brain experience serotonin reuptake far more often. In result of this, the nerve cells cannot communicate properly. In the diagram below, one can see that virtually all of the serotonin that has been sent out by nerve A are not making it to nerve B. Reuptake by nerve A has not allowed for the majority of serotonin to make it to its destination and to deliver its message. Again the blue arrows represent the serotonin being released from nerve A and the red arrows represent the serotonin experiencing reuptake.
Zoloft blocks the serotonin from returning back to the nerve cell that it was released from, allowing the message to arrive at its proper destination. When reuptake is blocked the serotonin has no option but to travel to the corresponding nerve cell, the gates of communication are open and one’s body and brain can function as normally. The blue arrows represent the serotonin leaving nerve cell A and the red arrows represent the serotonin trying to return to the nerve cell of its origin, but the sertraline is blocking it from returning. Since the serotonin can not return, it has no other option but to go to nerve B.
Like other medications, Zoloft relieves depressive symptoms, but it produces fewer side effects than other classes of antidepressant medication. The side effects that are experienced are mild and easily managed in most cases. However, people are all different, and some people that take it may find that the other antidepressants work better for them. The chemistry of the human brain is not a fully understood yet, so it is not surprising that one medication will not help everyone. Zoloft has slightly different side effects than other drugs that deal with the same problem, so it is up to the patient to determine which is right for them.

There is no way of knowing in advance which medication will work the best for a given person. Unfortunately, because the chemistry of the brain is not an exact science, a certain amount of trial and error is involved in finding the right medication and the right dose. People that are taking this medication should discuss symptoms and side effects with their doctor, to make sure that he or she is receiving the right medication and the right dosage. A standard dose of Zoloft is 50 to 200 mg per day. It is taken once a day, either in the morning or evening. People taking Zoloft, should probably continue to take the medication six months to a year after the depression has ended to insure that the communication between the nerve cells remains free flowing.
Zoloft is no a magic pill, it will not start working immediately after the first time that one takes it. Any positive effects directly after taking it would probably be attributed to the placebo effect. Zoloft is a medication that takes time to build up in your system. Even though some symptoms may get better within a couple of days, it is important to allow four to six weeks for the medication to be fully effective. If a person does feel any different after the four to six weeks that person may want to look into another medication.

The most common side effects of Zoloft include nausea, diarrhea, loose stools, tremor, insomnia, drowsiness, dry mouth, increased sweating and sexual problems. Although other antidepressants often cause weight gain, Zoloft on the other hand has been shown to make patients lose a couple pounds. Other antidepressants have a history of causing dizziness or light headedness, but no such side effects have been attributed to Zoloft. Also, other antidepressants in the past have been known to cause heart problems, but Zoloft does not seem to have this effect.

Zoloft is not for everyone, there are medical conditions that may eliminate someone from taking this drug. This drug should rarely be used by children for depression, however those diagnosed with Obsessive compulsive disorder can benefit. Patients with epilepsy, liver, and kidney dysfunction should not use Zoloft. Women should stop using or use with caution in most cases if they become pregnant, intend to become pregnant, or are breastfeeding an infant, because Zoloft maybe harmful to an infant and a mother could be retaining some harmful chemical for the baby in her breast milk. “If you are taking sertraline during the third trimester until the time of delivery, your baby may experience some complications for the first few days of life, requiring extra care. Symptoms of withdrawal such as problems breathing, jitteriness, increased muscle tone, irritability, altered sleep pattern, tremors and difficulty eating may occur.”(8)

One should reduce or eliminate consumption of alcohol, caffeine, and tobacco while taking any psychiatric medication. These substances may interfere with the way the medication is metabolized in the body and may make a higher dose necessary. Body chemistry is very sensitive, so nearly every other medication should be checked by one’s doctor if Zoloft is being taken as well. There are medications that should never be taken with Zoloft.

One type of drug that should never be taken with Zoloft are antidepressants that are MAOIs, monoamine oxidase inhibitors. “It is very important that Zoloft not be taken in combination with MAOIs, such as Nardil, Parnute, or Marplan. These combinations have caused extreme reactions that could be lethal.”(4) Therefore, when one is switching from an MAOI to Zoloft, or from Zoloft to an MAOI, they should wait for two weeks between stopping one and starting the other.

Zoloft has been used with children and adolescence that have shown signs of OCD, and has been shown to treat childhood depression in some cases. On the other hand, some parents of children that have committed suicide while on this medication would differ with that opinion. “Tom and Kathy Woodward, the parents of Julie, blame
SSRIs for the death of their 17-year-old daughter. She committed suicide seven days after she began taking Zoloft."(5) There is no way of knowing for certain in a case like this if Zoloft was the factor responsible for the young girl's suicide, but it does raise a question about Zoloft's effect on children.

Zoloft is a drug that has helped many people to find a way to manage their feelings of depression. The communication of nerve cells in the brain is vital to a healthy and happy life, and without this free flowing communication between nerve cells life can become intolerable. Zoloft is another example of man, through the advancements of modern science, overcoming a problem that would have been a life long affliction in the past. I believe that Zoloft is a good drug for the treatment of depression and other ailments associated with an imbalance of chemicals in the brain. Although there are negative accounts of Zoloft's effectiveness, the good seems to outweigh the bad. Millions of people are prescribed Zoloft, and a majority find it to be helpful in the alleviation of depression symptoms.

Photograph of Sertraline under the microscope. (9)
Bibliography

Leukemia

Prepared for
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April 18, 2008
Abstract

The word leukemia refers to cancers of body’s blood-forming tissues, including the bone marrow and lymphatic system. Leukemia typically originates when bone marrow produces a very large number of abnormal white blood cells.11 These abnormal white cells then build up both in the blood and throughout other organs of the body. These abnormal white blood cells are not capable of carrying out their normal functions. Leukemia is used as a general term to describe four different types of this disease that are classified by their speed of progression (acute or chronic) and by the type of white blood cells affected (lymphocytes or myeloid cells).11 Today the researchers have not found a single definite cause for this disease. However they have considered some possible causes.

Introduction

Leukemia typically originates when bone marrow, that produces three major types of blood cells, starts to produce a very large number of abnormal white blood cells (leukemia cells) that do not mature correctly but continue to reproduce themselves.11,12,15 White blood cells are part of the immune system that help the body fight different types of infections. These dysfunctional cells grow faster than normal cells and tend to collect in certain parts of the body causing pain, swelling, and other problems. After some time, the abnormal white blood cells outnumber the normal blood cells and at that time a person starts to experience symptoms of leukemia, such as anemia, different types of infections, and excessive bleeding.1 Identifying the type of leukemia is very important because that determines what type of treatment a patient will be given. There are four major types of leukemia: Acute Lymphocytic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Acute Myelogenous Leukemia (AML), and Chronic Myelogenous Leukemia (CML). There is also a very rare type of leukemia called Hairy Cell Leukemia (HCL). According to the Leukemia and Lymphoma Society website, the estimated number of new cases for 2007 was 44,240.13 There was 7 percent more cases of chronic leukemia than acute leukemia.13 For 2008 an estimated number of new cases for AML is 13,410, for CLL is 15,340, CML is 4,570 and for ALL is 5,200.13 The definite cause for leukemia is still unknown, but many studies have shown that people who were exposed to certain risk factors are at higher risk for developing this disease. Some of the risk factors include high levels of radiation, being exposed to certain chemicals (such as benzene), and certain genetic diseases.12

![Normal White Blood Cells](http://science.tsu.edu/ledocs/whitebloodcells.html)

![Abnormal Leukemia Cells](http://www.dailyfacts.org/leukemia-or-blood-cancer-facts/)
Four major types of Leukemia and Hairy Cell Leukemia

Leukemia has four major types that are classified by the speed of progression and by the type of white blood cells it affects. There is acute and chronic leukemia that further divides into myelogenous and lymphocytic leukemia. The four major types are: Acute Lymphocytic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Acute Myelogenous Leukemia (AML) and Chronic Myelogenous Leukemia (CML). In Acute Myelogenous Leukemia abnormal cells develop inside the bone marrow and they quickly replicate and start to replace the healthy blood cells. Eventually abnormal cells overcrowd the normal cells and bone marrow stops working correctly.\(^5\) This type of leukemia is most common among adults.\(^1\) Acute Lymphocytic Leukemia is also a fast growing cancer where body produces extremely large number of abnormal immature white blood cells (leukemia cells) that cause damage to the bone marrow and eventually bone marrow failure.\(^1,\,12\) Because of such a fast progression of disease, it could be very fatal if left untreated. This type of leukemia is commonly seen in young children and elderly.\(^1\) Chronic Lymphocytic Leukemia is caused by DNA mutation of B cells (type of white blood cells) in the bone marrow that later replicate themselves, infect normal blood cells and continue to spread through the bone marrow, affecting the lymph nodes and some other organs. Chronic Lymphocytic Leukemia usually affects adults and almost never affects children. Chronic Myelogenous Leukemia is caused when too many immature cells develop abnormal white blood cells that build up in the bone marrow and in the blood, over crowding the normal blood cells. People that have this type of leukemia, often have a chromosome abnormality called Philadelphia chromosome. Philadelphia chromosome develops when chromosome 22 breaks off and attaches to chromosome 9. “The break on chromosome 9 involves a gene called ABL, “and the break on chromosome 22 involves a gene called BCR.”\(^5\) The attachment of these two pieces of chromosomes make BCR-ABL cancer gene.\(^5\) This new cancer gene initiates the cell to make the protein that will later lead to Chronic Myelogenous Leukemia. This type of leukemia mainly occurs in adults and only affects a very small number of children. The fifth type of leukemia is called hairy cell leukemia. It is a very rare type of chronic lymphocytic leukemia.

It is caused by an abnormal change in a B cell within the bone marrow. The name Hairy Cell leukemia comes from the way these abnormal cells look like under the microscope.\(^5\) They have short, fine projections that look like hairs coming from their surface. This type of leukemia usually affects adult men and it is incurable. The patient with Hairy Cell Leukemia has a very low count of white blood cells.\(^1\)

Symptoms

Depending on how many abnormal white blood cells the bone marrow produces and where these blood cells collect throughout the body, each person might have a number of different symptoms. The first indications of leukemia are usually nonspecific and indistinguishable: unexplained fevers, frequent infections, night sweats, fatigue, easy bleeding
and bruising, weight loss, bone and joint pain. In acute leukemia’s symptoms usually develop very quickly and abnormal cells tend to collect in the brain and spinal cord causing headaches, vomiting and difficulty seeing. Chronic leukemia often goes undetected for many years and symptoms develop gradually and are not as severe as in acute leukemia. Since their antibody making cells do not function properly, people that have chronic leukemia tend to be more susceptible to different types of infections such as pneumonia, colds and cold sores. In some cases of chronic leukemia, a patient will develop autoimmunity which means their immune system will start producing defected anti body cells that attack normal blood cells. Autoimmunity can lead to hemolytic anemia where the defected anti bodies attack healthy red blood cells, thrombocytopenia or attack of cells that make platelets, and leucopenia or attack of white blood cells. The symptoms in leukemia are caused by a lack of normal blood cells or collections of abnormal cells in different organs and tissues. When the abnormal cells collect in tissues and organs they often cause the following symptoms: pale skin, shortness of breath, tiredness, enlarged spleen and liver, swollen lymph nodes in the neck and poor appetite.

**Diagnosis**

To diagnose leukemia, a medical provider will perform one or more of the following tests: a complete blood count, physical exam, cytogenetic analysis and bone marrow sample. Acute leukemia is usually diagnosed after a person visits a medical provider after becoming ill. Chronic leukemia is detected after performing a routine blood test but a lot of times a person does not have symptoms at the time their disease is diagnosed. The complete blood count will determine if there is an abnormal level of white blood cells, platelets or hemoglobin that is found inside red blood cells. These counts are very important because white blood cells help body fight infections, therefore abnormal levels cause these cells to not function properly and the body is not capable to fight different infections and sometimes start to attack other cells in the body.

Red blood cells carry oxygen to different tissues in the body and platelets help form blood clots that control bleeding. In acute leukemia red blood cells and platelets levels are usually very low, and cause the person to bruise easily, bleed excessively and become anemic. With blood work a medical provider is able to determine if abnormal cells are affecting other organs, such as liver, spleen and kidneys. Physical exam consists of a check up for swelling of the lymph nodes that store white blood cells, spleen that filters the blood, stores blood cells, and destroys old blood, and liver that cleanses the blood. In many cases to diagnose leukemia, a doctor might want to take a sample of bone marrow just to make sure that this is what he/she is suspecting. When a sample is taken, a doctor will look under the microscope for abnormal cells. Depending on the extent of leukemia in your body sometimes a doctor is able to classify the disease into stages that indicate the severity of the disease. Cytogenetic analysis is the analysis of blood or bone marrow cells that focuses on chromosomal rearrangement. The doctor looks under the microscope and tries to detect any changes in chromosomes, such as presence of Philadelphia chromosome that gives rise to certain types of leukemia. This test is essential to the diagnosis and treatment of different forms of cancer, such as leukemia. Sometimes one test is enough to diagnose leukemia, especially if patient has very severe symptoms, but in many cases a doctor will order multiple tests just to make sure the diagnosis is correct.
Causes

The researches and doctors have not found one definite cause for leukemia, but they are suspecting that leukemia develops from a combination of both genetic and environmental risk factors. Some of the risk factors that tend to increase the chance of developing leukemia are previous radiation, chemotherapy, exposure to certain kinds of chemicals (benzene and formaldehyde), and genetic diseases that are caused by abnormal chromosomes such as Down’s Syndrome.11 The researchers have found that people who were exposed to these risk factors are more likely to develop leukemia then those who were not exposed. However, in many cases people who developed leukemia were not exposed to any of the risk factors, and those who were exposed to these risk factors never developed leukemia. Acute leukemia develops when an original abnormal cell starts to produce more and more copies of itself. In acute leukemia cells never mature, they are very abnormal and they do not function like normal cells, but they still have the ability to multiply in very large numbers.4 Since these cells do not mature and they do not die like normal cells do, they build up in the body and start to interfere with functions of vital organs. In chronic leukemia abnormal mature blood cells replicate and replace normal blood cells within the bone marrow, which then start to build up in the body at a very slow pace. After a while the body does not have enough of healthy blood cells that can fight the infections, which causes a person’s immune system to work inadequately and puts them at higher risk for contracting different types of infections.5 One of the very important discoveries that help us understand the possible cause of leukemia was the certain changes in DNA that cause the bone marrow to produce abnormal white blood cells (leukemia cells). Some of our DNA cells contain instructions for the control of the cell growth and division. The genes that promote cell division are called oncogenes and genes that slow down cell growth and cause them to die at the suitable times are called tumor suppressor genes.11 DNA mutation causes oncogenes to turn on, or tumor suppressor genes to turn off, which leads to cancers or leukemia. A translocation of DNA is another chromosomal abnormality that leads to leukemia. It happens when one of the chromosomes breaks off and attaches its DNA to a different chromosome. A translocation is similar to mutation, which means it can cause oncogenes to turn on or tumor suppressor to turn off. This type of chromosomal abnormality is often seen in chronic leukemia’s.

Treatment

The main goal of treatment for leukemia is to destroy abnormal blood cells and allow the normal blood cells to grow in the bone marrow. Leukemia treatment is often complex and it depends on patients overall health, age, the type and stage of leukemia they have and if it has spread to the other organs of their body. Patients diagnosed with leukemia are usually in shock, stressed and unprepared for this. Often the doctors recommend medical clinics that have a specialized and experienced team in treating leukemia. They are able to help the patient understand the treatment path as well as expected results and possible risks and side effects. Depending on what type of leukemia patient has, the few possible treatment choices are: chemotherapy, radiation therapy, biological therapy, use of different combination of medications and bone marrow transplantation.16

Chemotherapy

Chemotherapy is one of the most common treatments used to treat leukemia. This treatment uses chemical drugs/agents to kill the abnormal blood cells in the bone marrow and in
the blood. Sometimes a patient can receive a single drug, but in other cases there can be a combination of one or more drugs given to the patient. The medications can be given to the patient in several different ways, such as by mouth in a pill form, directly injected into a vein, through a catheter placed in a large vein or by an injection directly into the cerebrospinal fluid. Chemotherapy is sometimes received for a long periods of time and is given in cycles. It usually lasts until the bone marrow and blood cell counts are back to a normal level, which sometimes does not happen during the first course of chemotherapy. During chemotherapy treatments some of the healthy blood cells are harmed which causes some of the side effects such as: temporary hair loss, mouth sores, nausea, vomiting and dizziness.

**Biological Therapy**

Biological therapies are treatments that stimulate and restore the ability of immune system to fight the infections and diseases. Patients are sometimes treated with monoclonal antibodies which are special proteins made in laboratories. Monoclonal antibodies job is to attack and kill abnormal blood cells in the blood and bone marrow. Interferon is a natural substance produced by the white blood cells that is used in biological therapy. Interferon slows down the growth of abnormal cells and often helps strengthen the immune system.

**Radiation Therapy**

Radiation Therapy uses high energy rays that destroy abnormal blood cells that cause leukemia and other cancers. The energy rays are usually placed on the target areas (tissues that have extremely large number of abnormal leukemia cells) or towards the whole body, and they work by destroying abnormal cells genetic material and making it harder for them to reproduce and replicate. This type of therapy usually destroys both healthy and abnormal cells, but healthy cells often recover from radiation and continue their normal functions. Radiation therapy can be used alone or in combination with chemotherapy.

**Drug therapy**

Today there are few drugs that are used in treating different types of leukemia and their symptoms. One of them is Gleevec (Imatinib Mesylate), which is a kinase inhibitor (enzyme inhibitor) that works by turning off an enzyme that causes normal blood cells to become abnormal and dysfunctional. Imatinib is a 2-phenylaminopyrimidine derivative that functions as a specific inhibitor of a number of tyrosine kinase enzymes. Gleevec is the only drug that works by directly turning off the signal of a protein that is known to cause cancer.
Gleevec has shown to work better than any other drug used for treatment of Chronic Myelogenous Leukemia and sometimes it is used for the patients with Acute Lymphocytic Leukemia. Sprycel (Dasatinib) and Tasigna (Nilotinib) are another two kinase inhibitors that are used in patients that were not successful with Gleevec in treating leukemia and its symptoms. Both of these drugs work by blocking the growth of abnormal cells and reduce the number of dysfunctional cells found in the blood and bone marrow. Some of the drugs are used in combination with chemotherapy, which gives the patient a better chance of treating leukemia and its symptoms. Some of the drugs are vincristine (Oncovin), corticosteroids (such as prednisone), idarubicin (Zavedos), cyclophosphamide (Cytoxan), hydroxyurea (Hydrea), and many more. Furthermore, there are a lot more possible drug treatments out there. However, some of them still require further research and clinical trials before their benefit can be determined. In addition to the cancer drugs, often there are other supportive medications given to the patient during his/her cancer treatment. They often include antibiotics and immunoglobulin that help in prevention of infections since the patient does not have enough white blood cells to fight the infections.

"Transfusion of red blood cells and platelets," epoetin, and hematopoietic stimulants help the patient’s body in producing new healthy cells. Along the treatment path, patients are expected to take care of themselves the best way they can. Good nutrition, maintaining a healthy diet, family support, and a follow up with their doctor on a regular basis are the main components to the success of their treatment.

**Bone Marrow Transplantation**

This type of treatment is used when chemotherapy and radiation therapy have destroyed bone marrow and healthy blood cells within the bone marrow, and the only way for the patient to survive is to receive a bone marrow transplant. Bone marrow transplant is used to replace dysfunctional bone marrow with a large source of healthy blood cells. There are three different types of bone marrow transplant: autologous, allogeneic and syngeneic. Autologous bone marrow transplant involves collecting and freezing patients’ own bone marrow and the blood cells. After an intensive treatment of chemotherapy and radiation therapy, the bone marrow and the blood cells are defrosted and put back into the patient. This treatment destroyed the abnormal blood cells and gives stem cells a chance to develop into normal blood cells. Allogeneic bone marrow transplant is a very complicated treatment and it involves using someone else’s bone marrow that closely matches another patient’s bone marrow. First, drugs are given to the patient to suppress the body’s immunity and to allow the body to accept the donor’s bone marrow or stem cells. The marrow is collected from the donor and later the patient receives marrow by a drip (similar to blood transfusion). After the patient receives the transplant, the bone marrow cells are able to find their way to the bone marrow where they start to grow. Sometimes a patient receives additional drugs that help the body accept the transplant and stops the cells from rejecting it. Syngeneic is a very rare type of bone marrow transplant because it uses the bone marrow of identical twin as a transplant. After transplantation, the patient is at high risk for developing infections and rejecting the new bone marrow. Different combination of drugs are given to the patient to prevent this from happening. Bone marrow transplant is intensive and does not succeed all the time.

**Side Effects of the Leukemia Treatments**

Medications used during the leukemia treatments can cause certain side effects. Most of the treatments work in a way that they kill both abnormal blood cells and normal, healthy blood
cells. Side effects depend on the type of the treatment patient is receiving, as well as the extent of the treatment. Each person reacts differently to the medications given and the side effects change from treatment to treatment. In chemotherapy side effects depend on the drug and dosage given. Usually during the chemotherapy the patient faces temporarily hair loss. The hair grows back later, but it will have a different color and texture than before. Furthermore, nausea, vomiting, and mouth sores are possible side effects. All these side effects can be treated with medications, but in many cases these medications cause the patient to feel weak and tired. During biological therapy, the patient often experiences a rash or swelling at the injection site and sometimes patient is susceptible to vein inflammation. For the patients that use interferon in biological therapies, they often experience flu-like symptoms such as: chills, fever, body aches, and fatigue. The same symptoms show up in radiation therapies, but the only difference is that the radiated areas become red, tender and dry. If radiation therapy is combined with chemotherapy these side effects become worse. During bone marrow transplantation patient faces a higher risk of infections, bleeding and sometimes rejection of the transplant. Some patients need to receive red blood transfusions during their treatments, which gives them more energy and strength to pull through the therapy. A very small number of people obtain an allergic reaction when given certain drugs, but some of them can be fatal.

Conclusion

Today’s science and technology have allowed researchers to take a step forward in finding more successful methods of treatments as well as anticancer drugs. The researchers are on the right path of discovering and developing more drugs such as Gleevec and Sprycel, which attack only specific parts of cancer cells that cause leukemia. These drugs would cause fewer side effects to the patient, and they would not affect normal blood cells. The studies are being done to see if these drugs can be combined with chemotherapy and other treatments, in hope for a better outcome. Also there are big studies done on medications used in other types of cancers, which seem to be working on the patient with certain types of leukemia. With today’s technology, those drugs could be altered into new drugs that would work better and give hope to leukemia patients. There are many people who are willing to join clinical trials and help the researchers find a cure for this disease. One of the promising approaches to help fight leukemia is stem cells from the umbilical cord. Umbilicus contains a very large number of stem cells that are designed to become blood cells. With a couple of successful cases of using stem cells from the umbilical cord to treat patients with leukemia, this could be a new step in the finding the cure for leukemia patients.
References


15. "Radiation Therapy for Cancer: Questions and Answers." National Cancer Institute. 25

    Retrieved 1 Apr. 2008
Ritalin

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April 18, 2008
Abstract

Ritalin (methylphenidate) marketed by Ciba Geigy Pharmaceutical Company and Novartis, is an amphetamine-like central nervous system stimulant, that affects chemicals in the brain and nerves that contribute to hyperactivity and impulse control (1). Methylphenidate was approved by the Food Drug Association (FDA) in 1955 for the treatment of attention deficit hyperactivity disorder (ADHD), attention deficit disorder (ADD), and narcolepsy. Methylphenidate, like many other schedule II controlled substance (C-II) drugs can be administered orally, via a patch, liquid form, and chewable tablet, but Ritalin can only be administered orally. This paper will discuss the history of methylphenidates, the mechanism of the action, possible side effects and the future of Ritalin.

Brief History of Ritalin (Methylphenidate)

Ritalin was first synthesized in 1944; at that time commonly known as Methylphenidate (MPH) then improved by 1950, and by 1954 it was being tested on humans. In 1957, Ciba Pharmaceutical Company began marketing MPH as Ritalin to treat chronic fatigue, depression, psychosis associated with depression, narcolepsy, and to offset the sedating effects of other medications. For a short time MPH was sold in combination with other products, particularly a tonic of MPH, hormones and vitamins, marketed as Ritoric in 1960, intended to improve mood and maintain vitality (2). Production and prescription of methylphenidate rose significantly in the 1990s, especially in the United States, as the ADHD diagnosis came to be better understood and more generally accepted within the medical and mental health communities. After making Ritalin, the Novartis Pharmaceuticals manufactured Ritalin SR, which is the extended release version of Ritalin (methylphenidate).

Description

Ritalin is available in a variety of short, intermediate, and long acting forms. The regular Ritalin is the short acting, lasting from anywhere between three to five hours. Then there is Ritalin SR which is the intermediate form of Ritalin, and those tablets last anywhere between three to eight hours. Furthermore, Ritalin LA is the long acting form, lasting anywhere between eight to twelve hours long. Ritalin in the SR tablets is more slowly but as extensively absorbed as in the regular tablets. Relative bioavailability of the SR tablet compared to the Ritalin tablet, measured by the urinary excretion of Ritalin major metabolite (a-phenyl-2-piperidine acetic acid) was 105% (49%-168%) in children and 101% (85%-152%) in adults. The time to peak rate in children was 4.7 hours (1.3-8.2 hours) for the SR tablets and 1.9 hours (0.3-4.4 hours) for the tablets. An average of 67% of SR tablet dose was excreted in children as compared to 86% in adults (3).

The following table shows the difference between the various dosage of Ritalin.

- **Ritalin 5 mg - round, yellow tablets**
- **Ritalin 10 mg - round, pale-green, scored tablets**
- **Ritalin 20 mg - round, pale-yellow, scored tablets**
- **Ritalin SR 20 mg - round, white, coated tablets**
- **Ritalin LA 20 mg - white capsules** (4)
- Ritalin LA 30 mg - yellow capsules
- Ritalin LA 40 mg - light brown capsules

**Chemical Formula/Ingredients**

Methylphenidate hydrochloride is methyl α-phenyl-2-piperidineacetate hydrochloride chemical formula is C14H19NO2HCl. The molecular weight of methylphenidate is 269.77 grams and it is covalently bonded to all of the atoms. In addition, there are four double bonds in the compound methylphenidate, and three of the double bonds are between the carbons and one is between one carbon and one oxygen.

The inactive ingredients in Ritalin tablets is lactose, magnesium stearate polyethylene glycol, starch, sucrose, talc, and tragacanth.

![Chemical structure of methylphenidate hydrochloride](image)

C14H19NO2

**Mechanism of Action:**

Like other stimulants, such as cocaine and amphetamine, Ritalin increases the activity of dopamine, a neurotransmitter associated with pleasure and important for reinforcement of behavior. While amphetamines stimulate the release of dopamine, cocaine and Ritalin block the transporters that reuptake dopamine into the neuron that released it. One of the theories as to why Ritalin helps people with ADHD is that they may have more dopamine transporters than others. The excess of transporters removes dopamine from the synapse before it can reach a dopamine reward receptor in the receiving neuron, so the attention circuitry in the ADHD brain is under stimulated. By blocking transporters, Ritalin allows more dopamine to reach receptors, thus increasing attention signaling, which helps people with ADHD to focus. Ritalin, when taken orally, slowly raises dopamine levels over the course of an hour or so. By contrast, when inhaled or injected, cocaine reaches the brain in seconds, producing a high.

**Dosage and Indications:**

Ritalin (Methylphenidate) is a central nervous system stimulant that is chemically similar to amphetamines, but the difference between the two is, methylphenidates' peripheral pharmacologic actions are milder than those of the amphetamines; it has more noticeable effects
on mental function than on motor activities. Also, Ritalin is clinically used for the treatment of attention deficit hyperactivity disorder (ADHD) in children and for narcolepsy in adults; epically the cancer suffering patients. ADHD is one of the most common mental disorders that develop in children. Children with ADHD have impaired functioning in multiple settings, including home, school, and in relationships with peers. If untreated, the disorder can have long-term adverse effects into adolescence and adulthood. Furthermore, narcolepsy is a chronic neurological disorder caused by the brain's inability to regulate sleep-wake cycles normally. At various times throughout the day, people with narcolepsy experience fleeting urges to sleep.

Methylphenidate dosage should be individualized according to the needs and responses of a patient. For children ages six years old and over, Ritalin tablets should be initiated in small doses such as 5 to 10 mg three times daily before breakfast, lunch and dinner with weekly increments of 5 to 10 mg in the daily dosage. Dosage should be individualized on the basis of factors such as age, body weight and individual response. Timing of drug administration should be (4). Furthermore, daily dosage of 60 mg of Ritalin is not recommended and if the improvement is not observed after appropriate dosage adjustment over a period of one month, then the drug should be discontinued and something else should be replaced instead of it. In addition to Ritalin tablets, there is also Ritalin SR tablets, which have a duration of action of approximately 8 hours. Therefore, Ritalin-SR tablets may be used in place of Ritalin tablets when the 8-hour dosage of Ritalin-SR corresponds to the titrated 8-hour dosage of Ritalin. Ritalin-SR tablets must be swallowed whole and never crushed or chewed. Ritalin SR, is to be taken once daily approximately 45 minutes before breakfast. The dosage of methylphenidate varies slightly in adults then that of children. Adult dosage is usually 20 to 30 mg daily and is divided two or three times daily, usually 30 to 45 minutes before meals. Some adult patients may even require 40 to 60 mg daily. Furthermore, in order to avoid sleeplessness patients should not take this medication late in the day and the last dose should be before six in the evening.
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<td>Adderall IR</td>
<td>15, 20 mg tablets</td>
</tr>
<tr>
<td>Focalin</td>
<td>2, 4, 6 mg tablets</td>
</tr>
<tr>
<td>Focalin XR</td>
<td>5, 10, 15, 20 mg capsules</td>
</tr>
<tr>
<td>Daytrana</td>
<td>10, 15, 25, 30 mg patches</td>
</tr>
</tbody>
</table>

*Note: All dosages are for children aged 6 years and older. The above information is a summary and should be used as a guide. For detailed information, please refer to the package insert.*
Pharmacokinetics

Methylphenidate drugs are quickly and extensively absorbed from the tablets following oral administration; however, because of the extensive first-pass metabolism, bioavailability is low, usually approximately 30%. Furthermore, methylphenidate is eliminated from the plasma with a mean half-life of 2.4 hours in children and 2.1 hours in adults. The apparent mean systemic clearance is 10.2 and 10.5 L/h/kg in children and adults, respectively for a 0.3 mg/kg dose. These numbers indicate that the pharmacokinetic behavior of methylphenidate in hyperactive children is similar to that in normal adults. The apparent distribution volume of methylphenidate in children was approximately 20 L/kg, with substantial variability (11 to 33 L/kg). When Ritalin is administered orally 78% to 97% of the dose is excreted in the urine and 1% to 3% in the feces in the form of metabolites within 48 to 96 hours. In addition, once methylphenidates and its metabolites reach the blood, they are distributed between the plasma (57%) and erythrocytes(43%). Methylphenidates, also show a low plasma protein bonding of approximately 15%.

Methylphenidate in the extended release tablets, such as Ritalin SR, are more slowly but as extensively absorbed as the regular strength Ritalin. The relative bioavailability of the Ritalin SR tablet, compared to the Ritalin tablet, measured by the urinary excretion of the methylphenidate major metabolite (PPAA), was 105% (49 to 168%) in children and 101% (85% to 152%) in adults. The time to peak rate in children was 4.7 hours (1.3 to 8.2 hours) for the extended-release tablets and 1.9 hours (0.3 to 4.4 hours) for the regular tablets. The elimination half-life and the cumulative urinary excretion of PPAA are not significantly different between the two dosage forms. An average of 67% of the extended-release tablet dose was excreted in children as compared to 86% in adults.

Drug Interactions

There are some rare, but severe drug interactions that’s can occur while taking Ritalin or any methylphenidate drug. Serious adverse events have been reported with the use of
methylphenidates and clonidine at the same time; and the safety of using methylphenidates in combination with clonidine or other centrally alpha-2-agonists has not been systematically evaluated. Also, methylphenidate is not recommended for use with lithium, be the effects of either agent in treating mood disorders may be altered. Ritalin should not be used in patients who are being treated with Monoamine Oxidase Inhibitors (MAO Inhibitors). Furthermore, because of the possible effects on blood pressure, patients taking Ritalin should use it cautiously with pressor agents. Also, methylphenidates may have a slight effectiveness on drugs that treat hypertension. Studies have shown that racemic methylphenidates may inhibit the metabolism of coumarone anticoagulants, anticonvulsants and tricyclic drugs.

That is why a downward dose adjustments of these drugs may be required when given concomitantly with methylphenidate. It may also be necessary to adjust the dosage and monitor the plasma drug concentration when initiating or discontinuing methylphenidates (3).

Methylphenidate is classified as FDA pregnancy risk category C, meaning the safety of this drugs for pregnant women has not yet been established. Therefore, women who are pregnant should avoid taking this drug during pregnancy and if breast feeding.

**Side Effects and Warnings:**

The most common adverse side effects reported while taking Ritalin and other methylphenidates are nervousness and insomnia, but those are usually controlled by reducing the dose and omitting the drug in the afternoon or evening. Other side effects include hypersensitivity, including skin rash, fever, exfoliative dermatitis and urticaria. Furthermore, children and adolescents taking prescription drug Ritalin have been noted to have nausea, dizziness, and at times even anorexia. Also, more so in children than in adults, abdominal pain, loss of appetite, weight loss, tachycardia, and insomnia may occur more frequently (2).

Sufficient data on the safety and efficacy of long-term use of Ritalin in children are not yet available. A causal relationship has not been established, but suppression of growth such as weight gain or height has been reported with long-term use of stimulants in children. Thus, careful monitoring of those requiring long-term therapy is recommended. Ritalin should not be used in children under six years of age, as there is no substantial data for the safety and efficacy in this age group. As well, Ritalin should not be used for severe depression of either exogenous or endogenous origin. Clinical information suggests administration of Ritalin to psychotic children may exacerbate symptoms of behavior disturbance and thought disorder (2).

**Clinical Studies**

Two well-controlled experiments performed by the National Institute of Mental Health, demonstrated that roughly 70-80% of children treated with stimulants had improvements at the end of the treatment phase; to a point that the child was no longer meeting the criteria for the diagnosis of ADHD. “Methylphenidate has been shown to have a strong effect on measures of attention, distractibility, and impulsivity (effect sizes: .75-.84; and mean .78) and social and classroom behavior (effect sizes: .63-.86; mean .81)” (3). Furthermore, children with ADHD taking Ritalin have been reported to have major improvement in academic achievement.

Yet, in another carcinogenicity study carried out in B6C3F1 mice, methylphenidate
caused an increase in heptocellular adenomas and, in males only, an increase in heptoblastomas, at daily dose of approximately 60mg/kg/day. This dose is approximately 30 times and 4 times the maximum recommended human dose on a mg/kg basis. Even though, there was an adverse side effect with mice; when methylphenidate was administered to F344 rats, there was no increase in tumors in them. The highest dose used on rats was approximately 45mg/kg/day, which is approximately 2 times and 5 times the maximum recommended human dose on a mg/kg basis (3).

**Future of Ritalin(Methylphenidate)**

Methylphenidates have been around for a few decades now. Obviously, as with most drugs there has been some adverse side effects in adults and children who were on Ritalin, but those side effects do not compare to the actual number of patients that have had drastic improvements in their social and academic life. Furthermore, because Ritalin has a generic the costs are quite reasonable and affordable and most insurance companies, including the government paid insurances are adding Ritalin to their approved drug list; thus making it more affordable for ADHD suffering patients.

**Conclusion**

Ritalin (methylphenidate) marketed by Ciba Geigy Pharmaceutical Company and Novartis, is an amphetamine-like central nervous system stimulant, that affects chemicals in the brain and nerves that contribute to hyperactivity and impulse control. Ritalin is prescribed to patients who have Attention Deficit Hyperactivity Disorder(ADHD) and narcolepsy. Like many ADHD drugs, Ritalin is a schedule C-II controlled substance and can only be administered orally. In addition, there are some other drugs in the group of methylphenidates that can be administered orally, in chewable tablets, in liquid form, or via a patch. Therefore, I believe that Ritalin will be on the market for years to come because despite of some adverse side effects; overall this drug is a savior for ADHD suffering patients.
Works Cited


The Effect of pH on Algal Metabolism and Community Composition

Jamshid Kiumarsi
Dr. Mancini
CHM 236 Project Paper
April 18, 2008
Abstract

This experiment explores the effects of pH on activities of Cyanobacteria, Green Algae and community composition. The main hypothesis is that pH does not have any effect on respiration and community composition. The Experiment took between 6 to 8 weeks. In the experiment, two separate flasks were given different values of pH (one with 5.5 and the other one with 8.5). Cyanobacteria and Green Algae was added and allowed to grow. The flasks were placed near the window and after 6 weeks, the changes in the amount of Oxygen were measured to determine the amount of photosynthesis and respiration. Later, the abundance of species was measured and the T test was performed, which disproved the hypothesis that pH has no effect on photosynthesis and abundance. Therefore, according to this experiment, pH does have an effect on photosynthesis, respiration and community composition.

Introduction

Photosynthesis is defined as the changing the energy of light to the form of chemical energy. The needed materials for photosynthesis are carbon dioxide($\text{CO}_2$) and water($\text{H}_2\text{O}$); the source of energy for this action will be the sunlight. The leftovers from photosynthesis are oxygen and carbohydrates. Photosynthesis is a group of many things which are connected with each other in a complicated way that happen in higher plants, phytoplankton, algae, as well as bacteria such as cyanobacteria. A simple equation for photosynthesis can be written as:

$$6 \text{CO}_2 \text{(gas)} + 12 \text{H}_2\text{O} \text{(liquid)} + \text{photons} \rightarrow \text{C}_6\text{H}_{12}\text{O}_6 \text{(aqueous)} + 6 \text{O}_2 \text{(gas)} + 6 \text{H}_2\text{O} \text{(liquid)}$$

Carbon dioxide + water + light energy → glucose + oxygen + water

Green algae and cyanobacteria are very small and can be found in all aquatic environments. In addition, they make their own food; they are unicellular but can be observed during growth as they grow in colonies. They are the most valuable members of the food chain, which are the run of nutrients among the organisms. Phytoplankton has a main role in carbon addiction and global warming. Organic molecules in the ocean are produced by phytoplankton because they fix carbons. Carbon passes through organisms by getting CO$_2$ from the air and resulting in sedimentary rocks or petroleum (Freeman, 2005). By this important role which phytoplanktons have in our life, there are biological and environmental factors that affect their life. For example, photosynthesis and respiration rate and their profusion will be important. In this experiment, the effect of pH on phytoplankton's photosynthesis, respiration and community composition was studied for examining the validity of the suggested hypothesis, which was pH, has no effect on photosynthesis, respiration and community composition of phytoplankton (Middelboe & Hansen, 2007).
Relationship between pH and net photosynthesis of *E. nuttallii* measured in unbuffered media. Individual points were plotted as O2 evolution vs. pH, and the curve was fit by eye (15_C, DIC 2.4 mM, O2 281 mM, PAR 290 nmol m⁻² s⁻¹).

In another experiment, we saw that the growth of *C. marina* remain unchanged in the normal range of pH, when pH is between 7.5 to 8.5, but if the pH increases beyond 9, we see the significant reduction in growth of *C. marina* (Liu, W.T. Au, Anderson, Lam, S.S, 2007). In terms of effects of pH on respiration of cyanobacteria: the effect of changing environmental variables in the surrounding water on the physiology of *Elodea Nuttallii*, which is a cyanobacterium, indicates that low pH response has a very specific effect. (Colman, Nalcwajko & Olaveson, 1997)

Effect of pH in the incubation medium on the net O2 evolution in the light and uptake in the dark of *E. nuttallii* (S.E. n = 4). (15_C, DIC 2.4 mM, O2 281 mM, PAR 290 nmol m⁻² s⁻¹).

When a comparison is made between the results it appears that there is little difference in the response to the environmental variables tested. When growing together, there is little difference in their response to pH, except below pH 6 (Iwan, J. et al., 2000) we see that significant penetration starts only at pH 8 and increases with evolution of the pH (Abeliovich, A. Azov,
The direct effect of pH on species composition in marine macroalgal habitats has been unnoticed due to assumption of the relatively constant pH of water with an average of 8.2. However, high pH is important in distribution and production of marine macroalgal communities because species with a low maximum pH limit would not be able to survive in high levels of pH (Middleboe and Hansen, 2007).

Respiration is one of the processes used during the experiment. It is a process where energy is released from food while carbon dioxide and water are also produced (Kohler & Kuhl, 2000). According to an experiment to search the effect of pH on taxonomic composition of 17 genera of algal species, it has been found that the more acidic the water was, the fewer algal taxa were present, but there was no difference in the total number of algal genera (Horne and Dunson, 1995). All of this research about the effect of pH on phytoplankton is background information. This experiment was performed to understand the effect of pH on phytoplankton’s photosynthesis, respiration and also to look at the validity of the suggested hypotheses which were pH does not have any effect on photosynthesis, respiration and community composition of phytoplankton.

What are green algae and cyanobacteria?

The term 'algae' is used for some lower plants and many, often unrelated groups of microorganisms that are able to perform photosynthesis. Photosynthesis (converting light energy into chemical energy) is performed in parts of the cell called chloroplasts. They can be found in different shapes and colors and in many different organisms. Not all these organisms are green. Diatoms, Chrysophytes and dinoflagellates have yellow to brown chloroplasts. There are brown algae (Phaeophyta), red algae (Rhodophyta) and many other groups of unicellular algae in many shades of green. The blue green Cyanobacteria also photosynthesize.

Very diverse groups of freshwater algae are the Chlorophytes or Green algae. Based on the compounds of the photosynthetic pigments and several other characteristics, they seem closest related to plants.

The "green algae" is the most diverse group of algae, with more than 7000 species growing in a variety of habitats. The "green algae" is a paraphyletic group since it excludes the Plantae. Exactly like the plants, the green algae have two forms of chlorophyll, which they are usefull to
capture light energy to fuel the manufacture of sugars, but unlike plants they are primarily aquatic. Because they are aquatic and manufacture their own food, these organisms are called "algae," along with certain members of the Chromista, the Rhodophyta, and photosynthetic bacteria, even though they do not share a close relationship with any of these groups.

Cyanobacteria are aquatic and photosynthetic—that is, they live in the water, and can manufacture their own food. Because they are bacteria, they are quite small and usually unicellular, though they often grow in colonies large enough to see. They have the distinction of being the oldest known fossils, more than 3.5 billion years old, in fact! It may surprise you then to know that the cyanobacteria are still around; they are one of the largest and most important groups of bacteria on earth.

Many Proterozoic oil deposits are attributed to the activity of cyanobacteria. They are also important providers of nitrogen fertilizer in the cultivation of rice and beans. The cyanobacteria have also been tremendously important in shaping the course of evolution and ecological change throughout earth's history. The oxygen atmosphere that we depend on was generated by numerous cyanobacteria during the Archaean and Proterozoic Eras. Before that time, the atmosphere had a very different chemistry, unsuitable for life as we know it today. The other great contribution of the cyanobacteria is the origin of plants. The chloroplast with which plants make food for themselves is actually a cyanobacterium living within the plant's cells. Sometime in the late Proterozoic, or in the early Cambrian, cyanobacteria began to take up residence within certain eukaryote cells, making food for the eukaryote host in return for a home. This event is known as endosymbiosis, and is also the origin of the eukaryotic mitochondrion. Because they are photosynthetic and aquatic, cyanobacteria are often called "blue-green algae". This name is convenient for talking about organisms in the water that make their own food, but does not reflect any relationship between the cyanobacteria and other organisms called algae. Cyanobacteria are relatives of the bacteria, not eukaryotes, and it is only the chloroplast in eukaryotic algae to which the cyanobacteria are related.

Algae are single celled organisms and they can photosynthesize. Photosynthesis, the process of producing glucose from air and water, is an enzyme controlled process. Enzymes are biological catalysts. (Catalyst is a chemical that can speed up the rate of a reaction but cannot initiate
They are sensitive to pH and usually work in small range of a pH scale. Optimum pH is the pH at which a particular enzyme works best. Since algae produce enzymes, they are indirectly affected by pH.

Materials and Methods

First year science students of Ryerson University did this experiment in September 2007 to November 2007. The experiment contained 250 mL of sterile growth medium buffered at pH of 5.5 and 8.5. There were 8 different species: Cyanobacteria (Microcystis, Anabaena), Green Algae (Pseudokirschenriella, Chlorella, Spirogyra) and Diatoms (Aulacoseira, Navicula). The Experiment took about 6 to 8 weeks. Two different flasks were given different values of PH (one with 5.5 and the other one with 8.5)

Method of measurement for O2 production or consumption

Photosynthesis was calculated by change in the amount of dissolved oxygen through respiration in the dark or photosynthesis under 100 W lights. The calculation for photosynthesis was done with the Winkler Titration method (Grasshoff, 1983). Four BOD bottles were filled with algae and another bottle to do the calculation for initial dissolved oxygen concentration and the other three bottles were kept one in the dark, the other one in a low light of 200 W and the last one under high light of 100 W to calculate the oxygen concentration after one hour. Adding 0.5 ml started the use of oxygen MnSO4 and 0.5 ml alkaline iodide azide reagent to the BOD bottles was containing algae. The bottle was upturned the flock settle and then inversed again for many times. At the third time the flock was settled, 0.5 ml of H2SO4 was transferred with a transfer pipette below the surface and inversed until the floc got disappeared, the content of BOD was moved to a 250 ml flask and titrated with 0.0125 N standardized sodium thiosulfate. Two drops of starch indicators was then added to get a blue color and this would show the endpoint. Then the volume of titrant was used to calculate the oxygen concentration by this formula.

Method of estimating the species abundance

Microscope slides from samples of each culture prepared and examined under microscope for approximation of the relative abundance of species after 8 weeks.

Results

After performing the experiment, the result came up to a conclusion that average of net respiration of 30 replications for pH 5.5 and pH 8.5 are 1.35 and 1.78 and these would result in variance of 0.57 and 0.23 respectively. The standard error was 0.16. Thus, the t test would give a value of 2.58.
The mean values for respiration at pH 5.5 and pH 8.5 are 0.66 and 0.84 respectively their variance are 0.10 and a 0.22. Then based on what we got as result our standard error would be 0.10 and the t would be calculated as 1.68.
The averages for % cyanobacteria at pH 5.5 and pH 8.5 are 75.0 and 42.0 respectively and have variance of 50.00 and 237.24. The calculated standard error is 3.10. Thus, based on all these the achieved value for t test is 10.66.
The average for % green algae in pH 5.5 and 8.5 are 20.0 and 53.00 and their variance values are 50.00 and 237.24. Standard error was calculated and it got to be 3.10. So, the obtained value for t is 10.66.
By according to the result, the null hypothesis would be rejecting. The calculations below show us that how we can reject the null hypothesis.

% Cyanobacteria:

<table>
<thead>
<tr>
<th>pH 5.5</th>
<th>pH 8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average=75</td>
<td>Average=42</td>
</tr>
<tr>
<td>Variance=50</td>
<td>Variance=237.2</td>
</tr>
</tbody>
</table>

Standard error=3.09
T=10.67
Probability is p<0.01. Therefore reject the null hypothesis.

% Green Algae:

<table>
<thead>
<tr>
<th>pH5.5</th>
<th>pH8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average=20</td>
<td>Average=53</td>
</tr>
<tr>
<td>Variance=50</td>
<td>Variance=235.3</td>
</tr>
</tbody>
</table>

Standard error=3.08
T=10.7
The probability is p<0.001. Therefore reject null hypothesis

% Respiration:

<table>
<thead>
<tr>
<th>pH5.5</th>
<th>pH8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average=0.6633</td>
<td>Average=0.84</td>
</tr>
<tr>
<td>Variance=0.104</td>
<td>Variance=0.225</td>
</tr>
</tbody>
</table>

Standard error=0.105
T=1.7
Since the p value is greater than 0.05, therefore accept the null hypothesis.
Net Respiration:

<table>
<thead>
<tr>
<th>pH 5.5</th>
<th>pH 8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average=1.35</td>
<td>Average=1.776</td>
</tr>
<tr>
<td>Variance=0.57</td>
<td>Variance=0.245</td>
</tr>
</tbody>
</table>

Standard error=0.165
T=2.6
Reject the null hypothesis.

Discussion

By explanation the result of the T test which is probability that the null hypothesis would be false. At the end of this experiment the photosynthesis and respiration are important because they showed how phytoplankton was being affected by different pH. So pH does have effect on Photosynthesis and activities of green algae and cyanobacteria but not on respiration. The resultant probability for the t value of net photosynthesis (0.02) which was less than 0.05, therefore pH affected on phytoplankton’s photosynthesis. The probability of null hypothesis for respiration was 0.1, which was bigger than 0.05, so pH had no effects on respiration of phytoplankton. At the end the probability value for % cyanobacteria and % green algae was the same for both which was 0.0001 and would be concluded that pH affects community composition. Also the rate of photosynthesis can be affected by sunlight, temperature, CO₂ and O₂. Algae produces oxygen as a by-product of photosynthesis and Temperature also influences the amount of oxygen dissolved in water and the rate of photosynthesis by Algae (which can be one of the factors that may cause some Errors in our measuring and calculation of photosynthesis). PH can greatly affect the respiration of algae. In some cases a higher pH can increase respiration, and in others it decreases it. It mostly depends on the type of algae, its location, and other biotic factors (what other organisms are present) and other biotic factors (what nutrients are present, such as nitrogen, carbon, phosphorous, potassium, etc.). So when algae photosynthesize they consume CO₂ from the liquid and CO₂ is supplied to liquid from Respiration of the Algae and Bacteria in the liquid. Therefore if PH effects on photosynthesis then for sure Respiration part does not continue regularly because if the consumption rate of CO₂ by the algae exceeds the supply rate of CO₂ to the liquid then the CO₂ concentration in the liquid will go down and the pH will go up. Every other hypotheseses of photosynthesis was in agreement with the studies done before about on phytoplankton’s photosynthesis, respiration and community composition on (Macroalgal and Chattonella Marina) and on cyanobacteria such as (Elodea Nuttalli). The difference between some of the theoretical results and the obtained results from the experiment might be caused by several factors such as different light which were provided for different cultures which were 20 W and 100 W, which is different from natural light. Another reason would be the different waters because distilled water is different from lake waters.
References

Abeliovich, A., Avoz, Y. (1976); Toxicity of Ammonia to algae in Sewage Oxidation Ponds, Applied and Environmental Microbiology, 31:801-806


J. Iwan Jones; John W. Eaton.; Keith Hardwick; (2000); The effect of changing environmental variables in the surrounding water on the physiology of Elodea nuttallii, Aquatic Bonaty 66:115-129


