18th Annual Science Symposium

May 10th, 2012
Volume I
Foreword

The 18th Annual Science Symposium was held on May 10, 2012. Students enrolled in my Organic Chemistry classes and Dr. Casey Durandet's Physics classes from Paradise Valley Community College (PVCC) participated in the event. Each contributor was responsible for selecting and researching their topic and preparing a paper. A few orally presented their project to their peers. This booklet contains each of those papers.

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

Since I am retiring in June, this will be my last Science Symposium. I want to thank all who have contributed and assisted with these Symposia. The Science symposium show cases the great students that we have at PVCC. Dr Casey Durandet and Professor Jenny Weitz have agreed to continue the Science Symposium in the future. I want to thank both of them for continuing this legacy.

William L. “Hank” Mancini, PhD
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Nuclear Medicine:

How Radioactive Tracers Can Effectively Locate and Treat Thyroid Imbalance

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General Physics II – Physics 112

17 April 2012
ABSTRACT

The thyroid gland is an essential component of the endocrine system. The hormone it secretes regulates and controls many physiological processes of the body. Abnormalities of the thyroid gland can cause a plethora of homeostatic imbalances. The use of radiation can be used to detect such abnormalities. Radioactive iodine tracers are commonly used concurrently with other testing methods to determine thyroid function and performance.

THYROID GLAND

Of the eleven organ systems within the body, the nervous system is deemed the greatest control structure. Working alongside this distinguished system is the endocrine system which controls the body’s metabolic activity. While the nervous system uses neurons as a primary means of control, the endocrine system uses hormones to regulate several physiological processes. “The nervous system sends electrical messages to control and coordinate the body. The endocrine system has a similar job, but uses chemicals to ‘communicate’. These chemicals are known as hormones” (Carter 1996). The production of hormones targets several organ systems. As a result, the endocrine system has diverse and extensive effects on almost all cells within the body.

Located on the trachea of the anterior neck, the thyroid gland is an integral component of the body. This two-lobed gland is shaped like a butterfly and is considered the largest gland of the endocrine system. The thyroid gland secretes a chemical known as thyroid hormone. Thyroid hormone is comprised of two iodine-containing hormones referred to as thyroxine and triiodothyronine or T₄ and T₃, respectively. The nomenclature of their names implicates the amount of iodine atoms bounded to the amino acid, tyrosine – T₄ has four bounded iodine atoms, whereas T₃ has only three iodine atoms.

The production of thyroid hormone is a multistep process. The hypothalamus first releases a chemical called thyrotropin-releasing hormone or TRH. The release of TRH stimulates the anterior pituitary gland to excrete thyrotropin-stimulating hormone or TSH. Once TSH has been released, it stimulates the thyroid gland to produce thyroid hormone or T₃ and T₄. Like many systems within the body, the thyroid is regulated by a negative feedback system. T₃ and T₄ levels in the blood determine the regulation of thyroid hormone. “Circulating serum T₃ and T₄ levels exert a feedback effect on both TRH and TSH secretion. When serum T₃ and T₄ levels increase, TRH and TSH secretion decrease. When thyroid hormone levels decrease, TRH and TSH secretion increase” (McAuley 1993). This negative feedback system ceases only when proper levels of thyroid hormone within the blood are reached. Precision Nutrition (2010) exemplifies this process in the figure above.
On a microscopic scale, the synthesis of thyroid hormone within the thyroid gland is a complex process. Thyroid tissue is composed of follicle cells which synthesize a glycoprotein called thyroglobulin. Two essential parts of thyroglobulin are tyrosine amino acids and iodine atoms. These molecules form the substance found in the follicle's lumen called colloid. Hochn and Marieb (2010, p. 609-610) provide a detailed diagram and seven essential steps that occur during the synthesis of thyroid hormone on a microscopic level:

1. The thyroglobulin is synthesized and discharged into the follicle lumen,
2. Iodide is trapped in the follicle cell and discharged into the lumen,
3. Iodide is oxidized to iodine by the removal of electrons,
4. Iodine is attached to tyrosine amino acids that form part of the thyroglobulin colloid,
5. Iodinated tyrosines are linked together to form T3 and T4,
6. Thyroglobulin is endocytosed, and
7. T3 and T4 hormones diffuse into the bloodstream.

This process continues until the proper amounts of thyroid hormone are reached in the blood. TSH production then ceases, and the feedback system is turned off.

Thyroid hormone is essential in controlling the body's metabolic activity. As a result, thyroid hormone affects nearly all systems of the body. Tulane University (2012) firmly states: "Almost all body functions carried out in nearly every tissue rely on thyroid hormones. Their actions and influence are so wide-ranging that vertebrates cannot live without them."

Furthermore, Dr. Richard Bowen of Colorado State University (2010) argues that "It is likely that all cells in the body are targets for thyroid hormones." He continues by stating that "Thyroid hormones have profound effects on many 'big time' physiologic processes...and deficiency in thyroid hormones is not compatible with normal health." The largest gland in the endocrine system ultimately carries a large responsibility in the regulation of the body's health. Thyroid hormone promotes normal regulation of the body's basal metabolic rate and metabolism. Furthermore, it promotes normal development in the nervous, cardiovascular, muscular, skeletal, gastrointestinal, reproductive, and integumentary systems. Without the thyroid and ultimately thyroid hormone, the body would exhibit several homeostatic imbalances.
THYROID ABNORMALITIES

Abnormal functioning of the thyroid gland can be an occurring problem. “Both overactivity and underactivity of the thyroid gland can cause severe metabolic disturbances” (Hochn and Marieb 2010, p. 611). An overactive thyroid gland is referred to as hyperthyroidism, while an underactive thyroid gland is hypothyroidism. As can be expected, hypothyroidism occurs when the thyroid gland does not produce enough thyroid hormone. Myxedema is the most severe disease due to an underactive thyroid gland. This can result from a variety of factors. The problem could have nothing to do with thyroid hormone itself but rather an insufficiency in either thyrotropin-releasing hormone or thyrotropin-stimulating hormone. If either TRH or TSH is unable to secrete, thyroid hormone will not be stimulated and will not release. This occurrence ultimately results in a decrease of T3 and T4 throughout the body. Hypothyroidism could also result from a deficiency in iodine. Since thyroid hormone relies on the binding of iodine atoms to tyrosine amino acids, a lack of iodine could decrease the levels of thyroid hormone within the body. An autoimmune disease called Hashimoto’s Thyroiditis is yet another result of an underactive thyroid. This occurs when the body’s own immune system attacks its thyroid gland and ultimately reduces the amount of thyroid hormone produced. Other causes of hypothyroidism include physical defects and surgical removal of the thyroid gland.

Hyperthyroidism or an overactive thyroid occurs when there is an excess or increase of thyroid hormone. When the thyroid gland produces too much thyroid hormone, the thyroid is considered to be overactive. The leading cause of hyperthyroidism is an autoimmune disease called Graves’ disease. “Graves disease is the most common cause of hyperthyroidism. It is caused by an abnormal immune system response that causes the thyroid gland to produce too much thyroid hormones” (Medline Plus 2010). Like most autoimmune diseases, Graves’ disease occurs when the body produces an antibody called thyrotropin receptor antibody. This antibody has the ability to excessively promote thyrotropin-stimulating hormone which ultimately leads to an overproduction of thyroid hormone.

One very common symptom that arises from either hyperthyroidism or hypothyroidism is goiter. Goiter is referred to as an enlarged or swollen thyroid gland. It can occur from either an overactive or underactive thyroid. The three common causes of goiter are Graves’ disease, Hashimoto’s Thyroiditis, and iodine deficiency. When the thyroid is overactive it produces a plethora of thyroid hormone. According to the Mayo Clinic (2011), “In Graves’ disease, antibodies produced by your immune system mistakenly attack your thyroid gland, causing it to produce excess thyroxine. This overstimulation causes the thyroid to swell.” Goiter also can be caused by an exact opposite process in Hashimoto’s Thyroiditis. In this disease, the autoimmune system attacks the thyroid gland. This self-attack process ultimately decreases thyroid hormone levels. “Sensing a low hormone level, [the] pituitary gland produces more TSH to stimulate thy lobby, which then causes the gland to enlarge” (Mayo 2011). Goiter can also occur when the body is deficient of iodine. This deficiency causes the thyroid to work overtime in an effort to produce normal levels of iodine. This causes the thyroid to swell.

Goiter is not the only symptom caused by a homeostatic imbalance of the thyroid gland. Abnormalities in body temperature, appetite, weight, metabolism, brain development, heart rate, blood pressure, skeletal growth, GI motility, ovarian function, and integumentary components can also occur from thyroid imbalances. Other symptoms include edema, depression, memory impairment, irritability, insomnia, sluggishness, muscle cramping and weakness, joint pain,
constipation, diarrhea, and impotence (Hoehn and Marieb 2010, p. 612). Another common symptom that results from Graves’ disease is exophthalmos which is the protrusion of the eyeball(s). This symptom can be very serious and even irreversible if left untreated.

Thyroid imbalances pose significant problems and dysfunction within the body. “At any given time in the United States, more than 30 million people suffer from a thyroid disorder…and nearly 10 million people with thyroid imbalance remain undiagnosed. Some 500,000 new cases of thyroid imbalance occur each year” (Arem 2007, p. 4). Any type of thyroid abnormality can grossly affect the body. An abnormal thyroid can cause variety of symptoms and hinder several physiological processes. A healthy and properly active thyroid ultimately leads to normal body function.

THYROID TESTING

There are several testing devices used to detect an abnormal thyroid. “No one single laboratory test is 100% accurate in diagnosing all types of thyroid disease; however, a combination of two or more tests can usually detect even the slightest abnormality of thyroid function” (Norman 2010). Blood testing is one of the most commonly used procedures to identify a dysfunctional thyroid. Blood tests determine abnormal thyroid function by assessing the hormone level production of the thyroid and its related structures. Some of the hormones analyzed in blood tests include: thyrotropin-releasing hormone, thyrotropin-stimulating hormone, triiodothyronine, and thyroxine. Imbalanced levels of any of these hormones can indicate if the thyroid is not functioning normally or if the pituitary gland or hypothalamus is not working properly. A scan of the thyroid itself can also determine thyroid abnormality. Camera and computerized scans are both used to test thyroid size and function (Norman 2010). Thyroid scans and blood testing are used concurrently to accurately test and diagnose thyroid function.

NUCLEAR MEDICINE

Radioactive tracing is a useful mechanism used in diagnosing and treating disease. SNM Advancing Molecular Imaging and Therapy provides a brief overview of how nuclear medicine uses radiation in the medical field:

Nuclear medicine uses very small amounts of radioactive materials (radiopharmaceuticals) to diagnose and treat disease. In imaging, the radiopharmaceuticals are detected by special types of cameras that work with computers to provide very precise pictures about the area of the body being imaged. In treatment, the radiopharmaceuticals go directly to the organ being treated. The amount of radiation in a typical nuclear imaging procedure is comparable with that received during a diagnostic x-ray, and the amount received in a typical treatment procedure is kept within safe limits.

Nuclear medicine uses radioactive imaging and scanning to find dysfunction within the body. Thyroid scintigraphy or thyroid scanning is a branch of nuclear medicine that aids in finding abnormalities within the thyroid. Using radioactive tracing is a unique yet essential component in the diagnostic process of thyroid disease.

Nuclear medicine and radioactive imaging has been used in the medical field since the early twentieth century, shortly after radioactive rays were first discovered by Henri Becquerel in 1896. Becquerel’s discovery of radioactive rays was later confirmed by Marie and Pierre Currie.
They were all awarded the Nobel Prize in 1903 for their contribution to the field of physics. Since their findings, radiation has been used in a variety of ways within the medical community. Shortly after their discoveries, George von Hevesy began to study the use of radiation as an indicator on both organic and inorganic species. He was the first to use radioactive isotopes as a tracer on animals in 1924. The discovery of radiation influenced scientists and doctors to explore its affects it could have on thyroid disease. In 1938, John Livingood and Glenn Seaborg discovered a radioactive form of iodine, I-131, that is used today as an iodine tracer. In 1951, “Benedict Cassen, Lawrence Curtis, Clifton Reed and Raymond Libby automated a scintillation detector to ‘scan’ the distribution of radiiodine within the thyroid gland” (SNM 2012). This radioactive scanning process, scintigraphy, is widely used by the medical community and is an important component of nuclear medicine today, especially in the area of thyroid disease.

RADIOACTIVITY

In order to fully understand the effectiveness of nuclear medicine, a basic understanding of radioactivity must first be investigated. An atom’s nucleus is composed of protons and neutrons. The forces between these particles determine whether or not an element is stable. Coulomb’s Law explains that an electromagnetic force resides between two charged particles: similar charged particles repel one another and dissimilar charged particles attract one another. Since protons contain positive charges, they continually repel one another inside the nucleus. If electromagnetic force was the only natural force present, all atoms would be unstable because the nucleus would disintegrate as similar-charged protons would repel one another. As a result, nuclear stability is in need of a stronger force to supersede electromagnetic force. Strong nuclear force is the strongest force in nature and therefore allows elements to be stable despite the presence of electromagnetic forces. Serway and Vuille (2012, p. 989) explain how this process works: “The strong force is responsible for the tight binding of quarks to form neutrons and protons and for the nuclear force, a sort of residual strong force, binding neutrons and protons into nuclei. This force represents the ‘glue’ that holds the nucleons together and is the strongest of all the fundamental forces.” The presence of this strong force allows the protons and neutrons to reside in the nucleus despite its density. As a result, the nucleus remains intact and elements can be stable.

As the number of protons increase within the nucleus, the electromagnetic force between protons also increases. When an element contains too many protons, the strong nuclear force is unable to overcome the repulsive electromagnetic force between protons. As a result, the atom begins to decay or disintegrate. As this occurs, the atom in considered unstable and thus radioactive. An element can also become radioactive if there is an increase in the amount of neutrons within the nucleus. As the electromagnetic force increases between protons, the number of neutrons within the nucleus also increases in attempt to keep the atom stable. However, when an element becomes too large in mass, the short-distanced strong nuclear force is overcome by the longer electromagnetic force. As a result, the element becomes unstable.

As unstable elements begin to disintegrate and decay, they emit radiation. There are three types of radiation that elements can produce as they being to decay: (1) alpha particles, (2) beta particles, and (3) gamma rays. Alpha decay occurs when an atom contains too many protons. As a result, the unstable atom emits two protons and two electrons, or the nuclei of Helium, in attempt to decrease the electromagnetic force within the nucleus. Beta decay can
occur when the nucleus’ neutron-proton ratio is either too large or too small. If the nucleus contains too many neutrons, a neutron converts into a proton and an electron. The electron is then emitted as a beta particle. If the nucleus contains a small neutron-proton ratio, a proton transforms into a neutron and a positron, a positively charged electron. The positron is then emitted as a beta particle. Gamma decay occurs when the nucleus is in a high-energy or excited state. If an element is undergoing radioactive decay, the energy state of the nucleus can increase. In order to decrease or get rid of the excess energy, the nucleus emits high-energy particles called photons. These emitted photons create a type of radiation called gamma rays. These three types of radiation all differ in their penetrating powers. Alpha particles are the least penetrable and are unable to infiltrate the skin. Beta particles have a higher penetrating ability than alpha particles and are able to breach the skin but not the internal organs. Gamma rays are the most penetrable and are able to access the internal organs (Davis et al. 2012, p. 940). The Oracle Foundation illustrates each radiation decay process in the figure above.

RADIOACTIVE TRACERS

Unstable elements are not the only atoms that can emit radiation. Both natural and artificial isotopes can also be classified as radioactive. “Atoms of an element that contain the same number of protons, but different numbers of neutrons, are called isotopes of the element” (Nuclear Science). Many artificial isotopes are specifically designed to emit radiation for medical purposes. Radioactive isotopes of iodine are specifically used to trace and find thyroid imbalances. Radioactive isotopes are commonly used as iodine tracers to measure iodine uptake within the thyroid. As explained earlier, iodine plays an integral part in the production of thyroid hormone, specifically triiodothyronine and thyroxine. In order to monitor and examine the uptake of iodine within the thyroid, scientists have created several artificial isotopes of iodine to use as tracers such as I-123, I-124, I-125 and I-131. Many of these radioisotopes are also used to treat thyroid disease by emitting gamma radiation.

Radioactive tracers or radiopharmaceuticals can be very effective in measuring the thyroid’s uptake of iodine. If a doctor suspects that there may be an imbalance within the thyroid, he or she may use radioactive iodine tracers to measure the thyroid’s efficiency. In order to evaluate the performance of the thyroid gland, a patient is required to drink a small amount of radioactive sodium iodine. Since iodine is collected and processed in the thyroid, the radiopharmaceutical iodine will make its way to the thyroid gland, and within a few hours the amount of iodine in the thyroid gland is determined by measuring the radiation intensity in the neck area (Serway and Vuille 2012, p. 975). Central Chapter – Society of Nuclear Medicine briefly describes how radiopharmaceuticals are tracked once digested: “Once in the body the radioactive tracer gives off energy in the form of gamma rays. This energy is detected by equipment called a gamma camera or an uptake probe. This specialized equipment works in
conjunction with a computer to measure the amount of radiotracer absorbed in your body as well as detect how things are functioning."

Not only are doctors able to determine the size and shape of a patient's thyroid through radioactive testing but they are also able to determine the activity of the thyroid. As the gamma camera or probe detects the energy emitted by the radioactive tracer, it is able to produce an image of thyroid function. If the thyroid promptly absorbs the radioactive iodine, the thyroid image appears very active. The New York Thyroid Center provides an example of an overactive thyroid scan in the figure shown to the left. Absorption of excessive amounts of the tracer could lead to a diagnosis of hyperthyroidism. If the gland does not readily receive the tracer, the image appears to be underactive. A lack of absorption could conclude that the patient has hypothyroidism. While these tests can be helpful, it is essential to incorporate other testing procedures such as blood tests and other thyroid scans to affirm any type of diagnosis.

Radioactive iodine is not only a helpful diagnostic tool but it can also be used as an effective treatment option for thyroid disease. In fact, Iodine-131 is commonly used to fight thyroid cancer and help combat hyperthyroidism. The New York Thyroid Center boldly states: "Since radioactive iodine (RAI) targets thyroid cells only, it is a safe and effective way to treat Graves disease and thyroid cancer and to test thyroid function and monitor recurrence of thyroid cancer." Radiation is a proven helper in not only the diagnostic realm of thyroid imbalance but also an effective remedy for thyroid disease.

CONCLUSION

The thyroid is an integral part of the endocrine system and an essential component within the body. Abnormalities and thyroid dysfunction can cause several physiological processes to not function properly. Over thirty million documented patients suffer from a type of thyroid imbalance. Thyroid dysfunction is an all too common disease process that can affect all types of people. In order to find and treat thyroid imbalances, several tests can be used as diagnostic tools. Radiation, specifically the use of radioactive tracers, is utilized copiously within the medical community. Iodine radioisotopes are commonly employed to find thyroid abnormalities. Radiation and technology continue to work hand in hand to promptly diagnose and effectively treat several thyroid imbalances and disease processes.


ANGRY BIRDS

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Dr. Casey Durandet

April 17, 2012

PHY 111 TR 33640
Abstract

A game that has taken the world by storm is to be explored and uncovered in this essay. From the various laws and sub laws of physics that it uses, mainly categorized within Newton’s second law of motion. This essay also intends to provide a level of humor making it acceptable and intelligible to readers high school and up. This essay aims to show that there are actual constants to the game.

Written Report

In 2009, Rovio Entertainment Ltd. (later known as Rovio) released a game for the Apple iOS devices (Kee 2011). In less than three years, the game became one of the most popular games on the planet via internet and merchandise being sold in the stores. The reason it had such widespread success was because to the untrained brain, the game was simple, pull back your object and fire away at your target, creating as much carnage as possible to move on to the next level. But to the trained mind, there is more to the game than meets the eye. This game that changed the scope of time consumption pitted two unlikely foes against each other, swine and avian. After the years of designing and ensuring that they had carried all of their ones and rounded correctly, Rovio Entertainment Ltd. released Angry Birds in the Apple App Store (Kee 2011).

If you have played this game before then you know how it works. You begin a level where you need to “get rid of” all the green pigs by shooting birds at the pigs via slingshot.
Although there is something odd regarding the gameplay, these angry birds aren’t penguins. Why do they need a slingshot to soar through the air? The slingshot is one of the mechanisms that the designers used to draw players into the game. Thanks to the touch capabilities that the Apple iOS devices possess, players feel as though they are physically pulling back the bird, enhancing the experience when the bird is released and makes contact with the structure that the pigs are hiding in. But, that still doesn’t explain why the birds can’t fly like their avian counterpart can in *Tiny Wings*.

When the original idea of *Angry Birds* was presented, there was a picture of a large bird, with furrowed eyebrows, no legs, and no wings. There was nothing else on the screen. No slingshots and no green pigs. But for some reason, the members at the meeting liked the idea. They liked it so much that they decided to create a game around the image (Malik 2010). Pigs were chosen as the enemy because around that time H1N1, was popular, in the media and in hospitals, making it simple for H1N1 to be portrayed as the enemy (Malik 2010). Although, without the essence of flight, how would the game be interesting? In what way could the game draw in players to the extent that their noses are pressed up against the tiny screens? Aside from the “violence” in the game, Rovio still had to make the game family friendly. Thus the idea of making the birds crash into structures was put into effect. The slingshot answered the question regarding the birds’ incapability of flight, making every player smile each time contact was made.

Projectile motion is always fun right? Throwing something in the air and watching it come crashing into something else. No matter how many “childish” things you may have outgrown, you still laugh a little inside. Quite possibly being one of the first properties of physics

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1 Hemagglutinin 1 Neuraminidase 1 (also known as Swine Flu)
that we learn subconsciously as children, aside from “the bigger they are, the harder they fall.” Projectile motion is the vehicle that was chosen to ensure that the birds can hit their targets that are a distance away. But there are still rules and laws that must be abided by to ensure that all is well and cohesive, right? Yes. Those rules are the Kinematic Equations of Motion. Essentially the grand jury responsible for ensuring that motion is sustained in X and Y.

In everyday life, these kinematic equations help determine what will happen when we release something into the air, if we neglect air resistance:

These equations are used to determine the different aspects of an object’s flight or course of motion (Serway and Faughn and Vuille 2011). The reason that it is different from what life actually presents is the fact that the game is in a vacuum, where there is no air resistance or terminal velocity or any other factors to alter the flight path of the bird and how much velocity and acceleration it can have. If there were air

**Motion in X:**

\[ v_{xf} = v_{xi} + a_x T_x \]

\[ \Delta x = (1/2)(v_{xi} + v_{xf})T \]

\[ \Delta x = v_{xi} T + (1/2)a_x T^2 \]

\[ v_{xf}^2 = v_{xi}^2 + 2a_x \Delta x \]

**Motion in Y:**

\[ v_{yi} = v_{yi} - g T_y \]

\[ \Delta y = (1/2)(v_{yi} + v_{yd})T \]

\[ \Delta y = v_{yi} T - (1/2)a_y T^2 \]

\[ v_{yi}^2 = v_{yi}^2 - 2g \Delta y \]

(Serway and Faughn and Vuille 2011)
**Motion in X:**

\[ V_{xf} = V_{x_i} + a_x T_x - F_{air} \]

\[ \Delta x = \left( \frac{1}{2} \right) (V_{x_i} + V_{xf}) T - F_{air} \]

\[ \Delta x = V_{xi} T - F_{air} + \left( \frac{1}{2} \right) a_x T^2 \]

\[ V_{xf}^2 = V_{xi}^2 - F_{air} + 2 a_x \Delta x \]

While it's much more common to see the equations as one. They have been split up into their respective X and Y components (Serway and Faughn and Vuille 2011). Each variable in the equations represent a value that completes the equation:

<table>
<thead>
<tr>
<th>V</th>
<th>Velocity (m/s)</th>
</tr>
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<tbody>
<tr>
<td>T</td>
<td>Time (s)</td>
</tr>
<tr>
<td>a</td>
<td>Acceleration (m/s^2)</td>
</tr>
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<td>i</td>
<td>Initial</td>
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<td>f</td>
<td>Final</td>
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<tr>
<td>\Delta</td>
<td>Delta or “Change in”</td>
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<tr>
<td>g</td>
<td>Acceleration due to gravity (9.8 m/s^2)</td>
</tr>
<tr>
<td>F_{air}</td>
<td>Force of Air Resistance</td>
</tr>
</tbody>
</table>

(Serway and Faughn and Vuille 2011)

\[ F_{air} = \frac{1}{2} \int [v, y, \alpha(t)] dv \] (Mohazzabi and Lerro 2006)
Yet, the kinematic equations could not have miraculously appeared in the minds of the designers. It had to have come from somewhere else in time, or else that would mean that everyone would have been observing and playing with an unnamed property of physics. No. The kinematic equations of motion actually originate from Sir Isaac Newton's second law of motion. The second law states that "the acceleration of an object is directly proportional to the net force acting on it and inversely proportional to its mass." The equation of the law is $F=ma^3$. The Kinematic equations can be used to find the acceleration portion of the equation for its units are meters per second per second, also known as the change in velocity over time (Serway and Faughn and Vuille 2011).

Although, Newton was the first to come up with the law of motion, André-Marie Ampère was a French physicist who came up with the term "cinématique" in his book *Essai sur La Philosophie des Sciences* (Essay on the philosophy of the sciences) in 1834 (Ampère 1834). When translated to English, cinématique does not mean cinematic (i.e. cinematic experience), but it comes out as kinematic. Isaac Newton didn't exactly come up with the idea of kinematics like he did Calculus, he was trying to come up with an explanation as to why things work the way that they do in this world of ours. But the presence of the kinematics still isn't everything that Angry Birds has to offer. Understanding kinematics is the beginning to realizing just how much thought went into this game.

Kinetic and Potential energy have a large effect in the game. Kinetic energy represents the amount of energy that an object has due to its motion. Potential energy represents the amount of stored energy that an object possesses at the given instant. The interesting thing about kinetic and potential energy is that they are inversely proportional on an extreme scale. In regards to the game the energy is conserved, meaning that the potential energy at the beginning must match

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$F=ma$ / Force equals mass multiplied by acceleration
how much kinetic energy the bird has at the point of contact with the structure (Jain 2009). The equation for kinetic energy is $^4KE=(1/2)mv^2$ (Jain 2009). While the equation for potential energy is $^5PE=mgh$ (Jain 2009). The interesting thing is that the relationship between the two, for an object, is extremely obvious. Similar to parabolic trajectory the system is split into two parts. In theory there is motion in the x-direction, as well as motion in the y-direction. Motion in the y-direction would be Potential energy, for it needs a measurement of distance for the height. When the bird is at the maximum height value for its parabolic trajectory, that is actually the point where there is the most potential energy. At the initial point, the slingshot, and at the ending collision, the bird possesses no potential energy. But the conservation of mechanical energy is still in effect, for this is a system where no outside force (such as air resistance) is acting on the object in motion. The equation for the conservation of mechanical energy is, $(1/2)mv_f^2 + mgh_f = (1/2)mv_i^2 + mgh_i$ (Serway and Faughn and Vuille 2011). Where KE$_i$ and PE$_i$ are set equal to PE$_f$ and KE$_f$. The Kinetic Energy would take place in the x-direction. The component vector that combines both KE and PE, would be able to tell what the velocity of the object is in the direction that it is moving in.

This game caused a stir among the members in the world of physics, that a known physics explorer decided to give the game a try. Rhett Allain, an Associate Professor of Physics at Southeastern Louisiana University, had recently finished exploring the physics behind the popular desk toy: Newton’s Cradle, when he gathered together the $0.99 required for the game and began to play (Oullette 2011). When Rovio paired up with Google and released Angry Birds as an app in the Internet browser, Mr. Allain jumped on the opportunity to use the computing power available to go into full effect. By using TrackerVideo analysis (a motion capturing

$^4$ KE= (1/2)mv$^2$ / Kinetic Energy equals one-half the mass multiplied by the squared velocity
$^5$ PE=mgh / Potential Energy equals mass multiplied by the acceleration due to gravity multiplied by the height
program) and the Angry Birds game in Chrome, he was bale to conduct the experiment where he plotted the path of the bird.

Imbedded into the game are different attributes that each bird possesses, in particular, the yellow angry bird has one of the weirdest that you receive in the beginning of the game. When the screen is tapped on, after the bird takes flight, there is an additional acceleration applied to the bird. This extra boost give it the power to smash into the pigs with a greater force than the regular red bird can. Reason being, let’s say that the masses of the yellow bird and the red bird are identical, according to Newton’s second law, F=ma. With equal masses, the only way that the yellow bird can have a larger force is if it accelerates much faster than the red bird, which it does once the screen is tapped. Acceleration is defined as distance traveled over time over time. Velocity is defined as distance traveled over time. Using TrackerVideo analysis, Mr. Allain was able to see that the average velocity of the bird is estimated around 30m/s after the screen is tapped.

It appears that when you tap the angry yellow bird, two things can happen. First, it increases its speed to 30 m/s (in the same direction that it was going). Second, if its velocity is greater than 20°; below the horizontal the vertical acceleration will be lower than 9.8 m/s² (Allain 2011)

It is actually an accurate estimation, for if you launched a yellow bird straight up into the air, and then tap the screen at the moment it has reached the “zero point,” you see that the bird seems to go just as fast as it did when launched. If you have played far enough into the game to get the white bird, you realize that it drops an egg when the screen is tapped and flies away. Rhett Allain also found that the egg drops straight down regardless of the horizontal velocity (Goudarzi 2011). When in real life, it is known that the egg would move horizontally a little bit as well as

\(^6\) Highest point in parabola
straight down, because it is leaving its “container.” Very similar to when something is tossed out of a moving car, or dropped from a plane or helicopter.

This game possesses the ability to teach students more about the natural world than originally expected. If I were a physics teacher, and I needed to teach my students about kinematic equations I would completely use this game. It offers so much to both the trained and untrained eye, that it provides hours and hours of class time to be filled. Even if I’m not lecturing that day I could just engage all the students by putting the game up on the projector and having them figure out how to get the highest points possible on each level. Obviously, I wouldn’t kill an entire week doing it, but maybe three days if class was about one hour long. Several physics teachers from across the nation use Angry Birds to teach their students. Primarily high school physics teachers do it, but regardless it is a wonderful tool to use. Frank Noschese, a physics teacher at John Jay High School in New York said, “Angry Birds has good physics” (Matthews 2012). He believed that it is a useful tool, and in addition to the fact that Rovio has had over 500 million downloads it would appear to be extremely popular. Another physics teacher from Bettendorf High School, Chris Like, said, “If you don’t engage students, you lose them and it’s getting harder and harder to engage them” (Matthews 2012). Not only does this game pack in the joy of slingshots, but it also allows for multiple class use. The way that the immersion between the game and learning the equations would happen, is that I would have the bird hover in the slingshot until all the equations have been written on the board, then I would ask the students to tell me what to do to play the game, for I have “never played it before.” This process would continue until we begin drawing vector plots off of the bird and attempting to calculate every aspect of it while in motion. Once we finish, I would tell the students that it is actually a video, and I would play it, watching to see if they are correct in their calculations or not. We would then
proceed to try it again, only with the game running. On the final day, I may do something similar to what the MIT seniors did, by bringing the game to life entirely and submerging the students into the experience (Brown 2011).

Angry Birds doesn’t just lend itself to physics though. If I were a history teacher I would show kids a video of someone playing Angry Birds, and listen to their reactions to the shots, then I would have the video mesh into another involving a war scene from a movie that takes place in the middle ages. I might even show a few clips from Lord of the Rings, but then I would stop the video and ask the students to tell me what is similar about the two. They would state the physical properties to their hearts content, but I would tell them that they are both similar because they are both old forms of long range warfare. Crossbows, long bows, catapults, and trebuchets would not be spared from the lecture at all. I would then have the students see through history how they continued to change in shape, but they still kept the same properties.

Since the release of the game in 2009, Rovio has been busy. They haven’t stopped creating newer and newer versions of their smash hit, the newest being Angry Birds Space. In it, the birds experience the thrill of microgravity and they adventure to reclaim what was stole from them by the pigs. The original Angry Birds took the world by storm and has been subconsciously teaching individuals about parabolic trajectory and forces. Similar to how individuals who play Mario Kart may subconsciously react to a skid, more and more objects are hitting their targets, whether it be on a firing range or in a classroom (Adee 2011). From a fluke that became a stroke of luck, Rovio became the link from video games to education, educating the world with each feather lost.

Angry Birds is not just a game, nor is it just a school lesson in the waiting. It is an avenue for multi-platform education. From it’s conception to the implementation in the world, it isn’t
uncommon to be able to recognize the large avian head and talk about the stresses of each level in the game. But it also has been able to solidify in the minds of all the more than 500 million players, just how much an affect physics has on everyday life. Although, it is a good thing that the birds stay in their own world on our portable devices, for if they were real, we would be dealing with extremely large birds with some bad attitudes.
Bibliography


When Foods and Drugs Collide

By
Amanda Al-Said
March 6, 2012
Abstract

Comprehending mechanisms in Organic Chemistry is important to understand the mechanisms and reactions of pharmaceutical practices. Medications may cause good or bad interactions with food. This paper will include the most common food and drug interaction mechanisms and facts that you probably never thought of. Not all drugs interact with food, but there are some that do, and they must be recognized in order for a medication to accurately work and be effective without harm or interactions with other drugs and foods.

Dietitians, physicians, and pharmacists have long known that some drugs are absorbed well on an empty stomach and others with food. They also know that the calcium in dairy products can interfere with the availability of some antibiotics. But thanks to the discovery a little more than a decade ago that grapefruit juice contains powerful natural compounds that interfere with the cytochrome P450 enzyme system, or enzymes in the liver responsible for metabolizing about 50% of drugs currently prescribed, food-drug interactions have been garnering more attention!

A food-drug interaction is the alteration of a drug’s pharmacokinetics or pharmacodynamics when certain foods or beverages are consumed at the same time.

“A food effect can be positive or negative, and it can be quite significant” says Sophie Galloway, Midwestern University Pharmacy student. Generally, foods can either interfere with the body’s ability to absorb a medication, reducing the dose actually received, or they can increase absorption, which can improve availability of the drug or pose the risk of toxicity.

While grapefruit juice and the compounds it contains are among the most extensively studied foods and beverages for their effects on the metabolism and action of prescription drugs, recent research has found that other foods, including pomegranates, Seville oranges, black pepper, cranberry juice, grape juice, black tea, beer, cruciferous vegetables, kava, licorice root, wine, and olive oil, contain compounds that modulate P450 activity and can affect drug metabolism.

Just as each individual has a unique fingerprint and DNA profile, each drug has a unique P450 profile. So the effect these foods have on drug metabolism varies greatly among people.

One of the most medically consequential and well-recognized food-drug interactions is that of vitamin K-rich foods such as broccoli and spinach, and Coumadin (warfarin), an anticoagulant prescribed to thin the blood and prevent clots. If someone taking warfarin also consumes a great amount of foods rich in vitamin K, a known blood-clotting factor, the blood-thinning effect can be cancelled out and the results can ultimately be life threatening.
Another well known food-drug interaction is that of foods containing the substance tyramine, including chocolate, beer, wine, avocados, some aged cheeses, and some processed meats, and monoamine oxidase (MAO) inhibitors, a type of antidepressant. Tyramine slows the metabolism of these drugs and can result in a dangerous rise in blood pressure.

The most well-publicized food-drug interaction of late has certainly been that of grapefruit juice and a virtual pharmacopeia of drugs. Drinking just a glassful of grapefruit juice per day can lead to dangerous increases in the blood levels of some drugs, such as the cholesterol-lowering drugs Lipitor (atorvastatin) and Zocor. Researchers have discovered that the molecule bergamottin found in grapefruit juice inactivates drug-metabolizing enzymes in the liver, allowing drug levels to build up in the bloodstream. It can take up to four days for the body to metabolize the offending chemical and for the effects of a single glass of grapefruit juice to wear off. The juice can also interact to cause higher blood levels of the antianxiety medicine Buspar (buspirone), the antimalaria drugs Quinerva or Quinite (quinine), and Halcion (triazolam), a medication used to treat insomnia. Other drugs that grapefruit juice may also affect include calcium channel blockers, immunosuppressants, sedatives, antidepressants, and drugs for erectile dysfunction.

Natural licorice, which contains the compound glycyrrhizin, can reduce the effectiveness of blood pressure medications and diuretics such as Aldactone (spironolactone). It can also increase the risk of Lanoxin (digoxin) toxicity. (Lanoxin is used to treat congestive heart failure and abnormal heart rhythms.)

The estimated 20 million Americans taking statins for high cholesterol who want to drink grapefruit juice may have the option of switching to Pravachol (pravastatin), which doesn’t involve the P450 enzyme system in its metabolism and so is unaffected by the juice. But that is an option patients must discuss with their physicians.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Food</th>
<th>Increase Drug Effect</th>
<th>Decrease Drug Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some statins (Lipitor, Zocor, Mevacor, Advacor)</td>
<td>Grapefruit, pomegranate, cranberry juices</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Antidepressants (MAO inhibitors)</td>
<td>Chocolate and other foods containing tyramine</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Allergy medications (Allegra)</td>
<td>Black pepper</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Food</td>
<td>Increase Drug Effect</td>
<td>Decrease Drug Effect</td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
<td>--------------------</td>
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<td>----------------------</td>
</tr>
<tr>
<td>Potentially all drugs metabolized by P450 liver enzymes</td>
<td>Black Tea</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Cancer Drugs (Tamoxifen)</td>
<td>Beer</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Anti-clotting agents (Plavix)</td>
<td>Fatty fish</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers (hypertension medications)</td>
<td>Meat</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Blood thinners (Coumadin)</td>
<td>Leafy greens</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers (hypertension medications)</td>
<td>Natural licorice</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Antibiotics (Cipro, tetracycline)</td>
<td>Milk and calcium-fortified juices</td>
<td>***</td>
<td></td>
</tr>
</tbody>
</table>

Risk for food-drug and drug-nutrient interactions can be affected by many factors such as:

- age
- gender
- medical history
- body composition
- nutritional status
- number of medications used

**How Drugs React in the Body**

Pharmacokinetics is defined as the study of the movement of a drug through the body during the following phases: absorption, distribution, metabolism, and excretion. In order to understand food/drug and drug/nutrient interactions, it's important to understand how drugs work in the body. There are four stages of drug action for medicines taken by mouth:

1.) **Absorption** refers to the amount of medication that enters the bloodstream.
2.) **Distribution**: Once absorbed into the bloodstream, medication either leaves the bloodstream and enters the tissues, including but not limited to the site of action, or it remains in the blood, bound to protein components.

3.) **Metabolism**: The breakdown and elimination of drugs from the body occurs by metabolism and excretion. The metabolism of medication is the breakdown of medication in the body. Here, the drug molecule is altered in some way to create a secondary molecule called a metabolite. Some drug molecules are not susceptible to metabolic breakdown, and may travel directly to the kidneys to be excreted. The liver is the major organ in which drugs metabolism occurs, although significant metabolism can occur in the small intestine. Very little metabolism occurs in other organs, such as kidneys and lungs. Metabolism is most often accomplished by protein substances called enzymes. The most common enzymes that metabolize drugs belong to a family of enzymes called the cytochrome P450 system. These enzymes are very reactive in converting a drug to its metabolites.

4.) **Excretion** refers to the irreversible removal of a drug or metabolite from a body fluid.

   Drugs can compete with other drugs for metabolism within the system or alter the metabolic system all together, resulting in drug interactions. A drug interaction is defined as the impact of a drug or food product on the amount of activity of another drug in the body. The food-drug interaction can result in enhanced, reduced, or new activity of the drug in the body. The most common cause of drug interactions is altered drug metabolism in the liver. For example, some medications, foods and herbal products can inhibit enzyme activity, which results in reduced drug metabolism of the medication. Conversely, some drugs can induce the metabolism of other medications. These two mechanisms are the most common forms of drug interactions. Thus, knowing the metabolic effects of each medication dispensed to a patient can help if a drug interaction is likely to exist.

   Not all medications are taken by mouth. Still, they are all transported to the site of action. Effects of drug/nutrient and food/drug interactions vary according to:

   - type of medication
   - form of drug (pill, liquid, etc.)
   - dosage
   - site of absorption (mouth, stomach, intestine)
   - route of administration (oral, intravenous, etc.).

**Food-Drug Interactions**

   Foods can interfere with the stages of drug action in a number of ways. The most common effect is for foods to interfere with drug absorption. This can make a drug less effective
because less gets into the blood and to the site of action. Second, nutrients or other chemicals in foods can affect how a drug is used in the body. Third, excretion of drugs from the body may be affected by foods, nutrients, or other substances.

With some drugs, it's important to avoid taking food and medication together because the food can make the drug less effective. For other drugs, it may be good to take the drug with food to prevent stomach irritation.

The Different Groups of Medicines

Drugs are grouped into classes based on illnesses for which they are prescribed. They can also be grouped in other ways, such as their chemical make-up or actions in the body. Different foods can interact with more than one class of drugs.

Analgesic

Analgesics are drugs that relieve pain. Analgesics often cause stomach irritation. It's a good idea to take analgesics, like aspirin, with food. A full stomach lowers the risk for stomach irritation.

Antacid, Acid Blocker

Antacids neutralize stomach acid, and acid blockers reduce stomach acid production. Long term use of these drugs may lead to certain nutrient deficiencies. This is because stomach acid is important in the digestion and/or absorption of nutrients.

Antibiotic

Antibiotics are used to treat bacterial infections. There are many different types of antibiotics. Some antibiotics decrease the synthesis of vitamin K by the bacteria normally found in our intestines. Vitamin K is important for normal blood clotting.

Tetracycline antibiotics bind to calcium found in dairy products. This can decrease the absorption of the antibiotic.

Other drugs like penicillin and erythromycin are most effective when taken on an empty stomach. This is because they may be partially destroyed by stomach acid when taken with food.

Anticoagulant- Anticoagulants slow the process of blood clotting. This can decrease risk of strokes in patients whose blood tends to clot too easily. These drugs, like warfarin (Coumadin), work by interfering with the use of vitamin K in blood clotting.
People taking these anticoagulants should be consistent in the amount of vitamin K they get from foods. It's very important to avoid eating large amounts of foods high in vitamin K. Rich sources of vitamin K include liver, and green vegetables such as broccoli, spinach, and other leafy greens.

**Anticonvulsant**

Anticonvulsant drugs help control seizures. Phenytoin (Dilantin), phenobarbital, and primidone may cause diarrhea and a decrease in appetite. This can decrease the availability of many nutrients.

**Antihistamine**

Antihistamines are used to treat allergies. Many of these drugs often cause drowsiness. They may also increase the appetite, which can lead to weight gain. Increased physical activity can help reduce weight gain. Alcohol can cause an even greater increase in drowsiness caused by antihistamines like diphenhydramine (Benadryl), chlorpheniramine (Chlor-Trimeton), and other over-the-counter drugs containing antihistamines.

**Anti-inflammatory**

Anti-inflammatory medication is prescribed to patients for a number of problems such as chronic joint pain, headaches, and arthritis. Long-term use may lead to stomach irritation and eventually ulcers. These medications should be taken with food.

**Blood Pressure Lowering Drugs**

Antihypertensives are used to control high blood pressure.

**Cancer Drugs**- Antineoplastic agents are used to treat different forms of cancer. These drugs can irritate the cells lining the mouth, stomach, and intestines. Many cause nausea, vomiting, and/or diarrhea. All of these can affect nutrient status.

Methotrexate reduces availability of the B vitamin folic acid. Supplementation of folate may be recommended for people taking this drug, but ask your doctor before starting folic acid.

**Diuretic**

Diuretics cause the body to excrete more urine and are often used to treat high blood pressure.

**Laxative**- Laxatives speed up the movement of materials through the digestive tract. This reduces the time for nutrient absorption. Excessive use of laxatives can deplete vitamins and minerals needed for normal body function. Laxatives also increase fluid losses. This may lead to dehydration.
Lipid Lowering Drugs

Lipid lowering drugs, also called Antihyperlipemic drugs, reduce blood cholesterol levels. Mental Health Drugs

Psychotherapeutic drugs treat depression, anxiety, and other mental health conditions. Some of these drugs increase appetite while others decrease it. Either effect can impact

MAO Inhibitors - These drugs decrease the body’s use of compounds called monoamines. MAO inhibitors can also react with tyramine found in foods. This reaction can cause a dangerous rise in blood pressure. If not treated, this can cause death. Some aged and fermented foods are high in tyramine. They should be avoided by people taking MAO inhibitors.

<table>
<thead>
<tr>
<th>Food-Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Class</strong></td>
</tr>
<tr>
<td>Analgesic acetaminophen (Tylenol)</td>
</tr>
<tr>
<td>Antibiotic</td>
</tr>
<tr>
<td>→tetracyclines</td>
</tr>
<tr>
<td>→amoxicillin, penicillin, zithromax, erythromycin</td>
</tr>
<tr>
<td>→nitrofurantoin (Macrobid)</td>
</tr>
<tr>
<td>Anticoagulant warfarin (Coumadin)</td>
</tr>
<tr>
<td>Medication Type</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Anticonvulsant</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Antifungal</td>
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<tr>
<td>Antihistamine</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Antihyperlipemic</td>
</tr>
<tr>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Drug Class</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
</tr>
<tr>
<td>naproxen (Naprosyn), ibuprofen (Motrin)</td>
</tr>
<tr>
<td>spironolactone (Aldactone)</td>
</tr>
<tr>
<td>Psychotherapeutic</td>
</tr>
<tr>
<td>MAO inhibitors: isocarboxazid (Marplan), tranylcypromine (Parnate), phenelzine (Nardil)</td>
</tr>
<tr>
<td>Drug/Nutrient Interactions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Food that Interacts</th>
<th>Effect of the Food</th>
<th>What to Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid Blocker</td>
<td>Vitamin B&lt;sub&gt;12&lt;/sub&gt;</td>
<td>Decrease vitamin absorption</td>
<td>Consult your physician regarding B&lt;sub&gt;12&lt;/sub&gt; supplementation</td>
</tr>
<tr>
<td><strong>Antihyperlipidemic</strong></td>
<td><strong>Fat soluble vitamins</strong> (A, D, E, K)</td>
<td><strong>Decreases vitamin absorption</strong></td>
<td><strong>Include rich sources of these vitamins in the diet</strong></td>
</tr>
<tr>
<td>------------------------</td>
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<td>---------------------------------</td>
<td>-----------------------------------------------------</td>
</tr>
<tr>
<td>cholestyramine (Questran), colestipol (Colestid)</td>
<td>Folic acid, vitamin B₁₂</td>
<td>Decreases vitamin absorption</td>
<td>Consult your physician regarding supplementation</td>
</tr>
<tr>
<td><strong>Antineoplastic</strong></td>
<td><strong>Many minerals</strong></td>
<td><strong>Increases mineral loss in urine</strong></td>
<td><strong>Include fresh fruits and vegetables in the diet</strong></td>
</tr>
<tr>
<td>methotrexate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>furosemide (Lasix), hydrochlorothiazide (HCTZ)</td>
<td>Vitamins and minerals</td>
<td>Decreases nutrient absorption</td>
<td>Consult your physician regarding supplementation</td>
</tr>
<tr>
<td><strong>Laxative</strong></td>
<td>( \text{fibercon, Mitrolan} )</td>
<td></td>
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</tr>
</tbody>
</table>

**What Is a Food-Drug Interaction?**

Any time that a food or beverage changes the effects of a drug, the change is considered a food-drug interaction. Food-drug interactions can occur with prescription drugs, over-the-counter drugs, herbal products, and dietary supplements.

**What Are Some Common Food-Drug Interactions?**

Tyramine and MAO inhibitors: Foods that contain the substance tyramine (including beer, wine, avocados, some cheeses, and some processed meats) slow down enzymes that metabolize MAO inhibitors (a type of antidepressant medication) and can cause dangerously high blood pressure.

Calcium and antibiotics: if you drink a glass of milk when taking the prescription antibiotic tetracycline, the calcium in the milk will bind to the tetracycline, making a compound that is impossible for your body to absorb. Therefore, the desired effect of the tetracycline (as well as the benefits of calcium) will not occur.

Vitamin C and iron: Drinking a glass of citrus juice at the same time that you take an iron supplement is beneficial because the vitamin C in the citrus juice increases the absorption of iron.

**Warfarin**
\[
\begin{align*}
\text{Acetaminophen} & \xleftarrow{\text{P450 (enzyme)}} \text{N-acetyl-p-aminophenol} \\
\text{N-acetyl-p-aminophenol} & \xrightarrow{\text{enzyme}} \text{P450} \\
\text{P450} & \xrightarrow{\text{GSH}} \text{Iminoquinone} \\
\text{Iminoquinone} & \xrightarrow{\text{GSH}} \text{GSH} \\
\end{align*}
\]
Consistency is the key with warfarin in all circumstances. The most notorious food-drug interaction regarding warfarin occurs with “green, leafy vegetables” due to their rich vitamin K content. Warfarin, by its mechanism of action, interferes with the synthesis of vitamin-K-derived clotting factors. Increasing vitamin K intake will result in more clotting factors, reducing the efficiency of warfarin. Some people erroneously believe that warfarin recipients cannot eat any green, leafy vegetables. However, if patients remain consistent with vitamin K intake, taking their medication as directed, the interaction is not substantial. Soy milk, char grilled foods, and sushi containing seaweed may also decrease the effect of warfarin. Cranberry juice in contrast, can potentiate the anticoagulant effects of warfarin.

The Most Commonly Misunderstood Interaction: Grapefruit Juice

The fact is that although some medications may interact with grapefruit juice, most do not. Also, it is believed to be safe to consume grapefruit juice while taking any over-the-counter medication.

Over a decade ago, scientists discovered that a substance in grapefruit juice interferes with certain prescription drugs. Since then, many scientists have focused on the effects of grapefruit and have discovered specific drug interactions that may be dangerous in some instances. As a result, media reports have exaggerated the risks of grapefruit juice, leading many people to believe that grapefruit juice must be avoided when taking any medication. However, dozens of drugs that have no interaction with grapefruit juice may be used to treat the same condition.

The interactions seen with grapefruit juice occur because grapefruit juice changes the actions of enzymes in your intestine. Only medications that are metabolized by these enzymes will be affected by grapefruit juice.

Components in grapefruit juice include the two common bergamottin and 6,7-dihydroxybergamottin. Both irreversibly inhibit cytochrome P450 isoenzymes in the intestinal
wall, decreasing the pre-systemic metabolism of affected drugs taken 72 hours after grapefruit consumption.

**What Is a Food-Drug Interaction?**

Any time that a food or beverage changes the effects of a drug, the change is considered a food-drug interaction. Such interactions are not uncommon. But not all medications are affected by food, and some are affected only by certain foods. Food-drug interactions can occur with prescription drugs, over-the-counter drugs, herbal products, and dietary supplements. Although some interactions are harmful or even fatal in rare cases, others can be beneficial, and the majority will not cause noticeable changes in your health.

**How Do Foods and Drugs Interact?**

Foods and drugs can interact in many different ways. Often, a specific compound in the food causes the effect. Other changes can be caused by the amount of protein in your diet, or even the way food is prepared.

One of the most common ways foods affect drugs is by changing the way drugs are broken down (metabolized) by your body. Proteins called enzymes metabolize many drugs. Some foods can make these enzymes work faster or slower, either shortening or lengthening the time that the drug spends in your body. If the food speeds up the enzyme, the drug will spend a shorter time in your body and may be less effective. If the food slows the enzyme, the drug will spend a longer time in your body and may cause unwanted side effects.

**What Are Some Common Food-Drug Interactions?**

Foods that contain the substance tyramine (including beer, wine, avocados, some cheeses, and some processed meats) slow down enzymes that metabolize MAO inhibitors (a type of antidepressant medication) and can cause hazardous effects, including dangerously high blood pressure.

Some foods can prevent certain drugs from being absorbed after you swallow them, and others can increase absorption. For example, if you drink a glass of milk when taking the prescription antibiotic tetracycline, the calcium in the milk will bind to the tetracycline, making a compound that is impossible for your body to absorb. Therefore, the desired effect of the tetracycline (as well as the benefits of calcium) will not occur. On the other hand, drinking a glass of citrus juice at the same time that you take an iron supplement is beneficial because the vitamin C in the citrus juice increases the absorption of iron.

Finally, some foods can actually interfere with the intended effect of the medication. For example, people who use the blood-thinning drug warfarin should not also eat foods that have a lot of vitamin K in them, such as broccoli or spinach. Vitamin K helps make blood clot, therefore reversing the effect of warfarin. The opposite can happen with vitamin E, onions, and garlic.
because they all produce effects that are similar to those of warfarin. Large amounts of these foods can make the effects of warfarin too powerful.

**MEDICATIONS THAT SHOULD BE AVOIDED WITH GRAPEFRUIT JUICE:**

- amiodarone (Cordarone)
- astemizole (Hismanal)
- atorvastatin (Lipitor)
- budesonide (Entocot)
- buspirone (Buspar)
- cerivastatin (Baycol)
- cilostazol (Pletal)
- cisapride (Prepulsid, Propulsid)
- colchicine
- eletriptan (Relpax)
- etoposide (Vepesid)
- halofantrine (Halfan)
- lovastatin (Mevacor)
- mifepristone (Mifeprex)
- pimozide (Orap)
- quinidine (Quinaglute, Quinidex)
sildenafil (Viagra)
simvastatin (Zocor)
sirolimus (Rapamune)
terfenadine (Seldane)
ziprasidone (Geodon)

HOW BIG A PROBLEM ARE DRUG INTERACTIONS?

- Americans over age 65 comprise 12% of the population, but they consume about 30% of all prescription drugs and 40% OTC drugs.

- When 2 to 4 different drugs are taken, the potential for interaction is 6%, but the risk increases to 50% with 5 drugs and almost 100% with 8 drugs!

- The average older person takes 4 to 5 drugs daily.

- Drug interactions are responsible for 3% to 10% of admissions of older patients to the hospital, which costs an estimated $20 million annually in the United States.

Now that pharmacy records and prescription order-entry are computerized, doctors have come to rely on software to prevent drug interactions. In many systems a warning box appears when, for example, a patient on warfarin is prescribed an antibiotic like ciprofloxacin. Preventing potentially deadly drug interactions is one of the nice things about practicing in the 21st century.

Although less common than drug-drug interactions, food-drug and supplement-drug couplings can cause significant harm. Food can alter the pharmacokinetics (how a drug is absorbed and distributed) or pharmacodynamics (physiologic effect) of drugs. Some foods can reduce the bioavailability of certain drugs, while other foods can increase the effect. Conversely, drugs can alter or compromise the nutritional status of some patients, particularly the elderly.

The most common food-drug interaction is the limited intestinal absorption of a drug if taken with food. Limited absorption can lead to incomplete benefit from the drug or even treatment failure. Common drugs that should be taken on an empty stomach include captopril, most antihistamines and several antibiotics, including ampicillin and amoxicillin, cephalosporins (except cefuroxime), ciprofloxacin, doxycycline, and tetracycline. A high-protein meal can decrease the absorption of carbidopa-levodopa and can be partially responsible for the variability of effect in Parkinson's patients. High-fiber foods speed transit times and may reduce absorption
of metformin and other medications. Thyroxine is particularly problematic with meals and supplements.

Taking levothyroxine with any food can reduce absorption, and the drug should never be taken with other supplements, such as iron or multivitamins with minerals. Two other drugs, ciprofloxacin and levofloxacin, are also rendered almost ineffective if taken with calcium.

Some medications are better absorbed when taken with food. Eating stimulates gastric and intestinal secretions that improve the dissolution and absorption of many drugs. Fatty foods, for example, stimulate bile salts that facilitate uptake of lipophilic drugs. Drugs that are better absorbed with food include cefuroxime, erythromycin, ethylsuccinate, statins, and lithium. The antifungal griseofulvin is significantly better absorbed if taken with a fatty meal. Protein can facilitate some drugs as well, including propranolol, which is 50% more bioavailable if taken with a high-protein meal.

Grapefruit juice causes one of the more interesting drug-food interactions. In 1989, three Canadian researchers studying the effects of alcohol on absorption of felodipine attempted to blind the study participants to alcohol consumption by using grapefruit juice as both the alcohol mixer and the control. They found little effect from alcohol, but the double-strength grapefruit juice approximately tripled the plasma felodipine peak concentration and area under the curve (AUC).

One of the investigators even went to the extent of testing himself, taking felodipine with water and then grapefruit juice. His blood concentrations were fivefold higher when he took felodipine with grapefruit juice, and he experienced significant side effects. Subsequent investigations showed that even regular-strength grapefruit juice augments felodipine AUC to nearly the same extent as double-strength grapefruit juice.

Grapefruit juice inhibits cytochrome P450 3A4 (CYP3A4), both in the intestine (which increases the absorption of some drugs) and in the liver (which inhibits metabolism). A single glass of grapefruit juice can block CYP3A4 for up to 24 hours, so delaying taking medications for a few hours after drinking grapefruit juice is of no value.

Many drugs are affected by grapefruit juice, but the most common are the statins lovastatin, simvastatin and atorvastatin. Other statins are not metabolized via the same pathways, and are not affected. Other drugs affected by grapefruit juice include dihydropyridine calcium channel antagonists as well as the non-dihydropyridine agent verapamil. Phosphodiesterase inhibitors used for erectile dysfunction may also be affected by grapefruit juice, although the interaction is less pronounced and more variable. Benzodiazepines, especially diazepam and temazepam, may have increased blood levels and augmented effects when taken with grapefruit juice, especially in the elderly. The transplant drug cyclosporine is also strongly affected by grapefruit juice, so much so that researchers are looking at the combination as a way to increase the beneficial effect of the drug.
Now that pharmacy records and prescription order-entry are computerized, doctors have come to rely on software to prevent drug interactions. In many systems a warning box appears when, for example, a patient on warfarin is prescribed an antibiotic like ciprofloxacin. Preventing potentially deadly drug interactions is one of the nice things about practicing in the 21st century.
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Asthma and Bronchospasm Management with Albuterol vs. Xopenex

Tennille Allen

4/14/12
Abstract

The purpose of this paper is to provide an overview of the clinical presentation, diagnosis, and management of Asthma and Bronchospasm. A case study will be presented for a patient experiencing exercise induced bronchospasm. The use of Albuterol vs. Xopenex for management are effective treatment regimens that produce similar outcomes with different side effects. The pathophysiology, biological application, reactions and stereochemistry will be explored and expanded upon throughout. Various images will be further demonstrated.

Overview

Asthma is a chronic inflammatory disease of the airways where there is typically a temporary blockage or narrowing that occurs producing an array of secondary symptoms. It is estimated that nearly 20 million people in the United States have Asthma and despite the availability of treatment, it remains poorly controlled by many. Asthma can be caused by allergic or non-allergic triggers. Some types of triggers include, but are not limited to, allergens, cold and dry air, smoke, exercise and viruses. Despite the cause, the two secondary symptoms that are produced are very similar. The inflamed airways cause the bronchi to become very reactive and highly sensitive to all kinds of triggers and the ability of the lungs to produce effective airway exchange is compromised. Along with airway swelling, mucous clogs the airways and the muscles tighten producing spasms. Asthma often acts up at night, for reasons not known. Asthma also has a hereditary component that often predispose a person to developing the disease. Common symptoms can include cough, shortness of breath, wheezing and chest tightness.

Diagnosis and treatment of asthma is key to avoid potentially life threatening complications and enable patients to live full and active lives. Common diagnostic tests include: personal and medical history, physical exam, pulmonary functions tests, trigger tests, chest x-ray, gastrointestinal reflux testing, sputum analysis, sinus x-rays and allergy testing. The personal and medical history focuses on family history, medications, lifestyle, history of allergies or smoking, physical symptoms experienced, past medical history and skin conditions such as eczema that may predispose one to asthma. The physical exam is focused on the skin, respiratory, ear, nose throat and cardiovascular systems. Pulmonary function testing can include spirometry and peak flows. Spirometry is the recommended test for confirming the diagnosis of asthma whereas peak flows are a simple and quick test to assess air flow. Treatment of asthma involves prevention and management with long acting and short acting medications. Long acting medications prevent or reverse airway inflammation making the airways less sensitive to triggers. Types of long term medications include: inhaled cromolyn, inhaled corticosteroids, oral steroids, leukotriene modifiers, long acting inhaled beta agonists and anti-IgE therapy. Short acting medications provide quick relief during asthmatic attacks and episodes such as bronchospasm.
Bronchospasm is a frightening acute event that results in an abnormal smooth muscle contraction of the bronchi causing a narrowing and obstruction of the airways. The bronchospasm is usually temporary and causes cough, shortness of breath and wheezing. The smooth muscle contraction and relaxation is involuntarily controlled by the autonomic nervous system. The most common cause of bronchospasm is asthma. During bronchospasm, the bronchial muscles go into a state of tight constant contraction which narrows the diameter of the bronchus. The mucosa becomes swollen and inflamed, the bronchial glands produce excessive amounts of sticky mucous that may form plugs, which further decrease the bronchial diameter and reduce airflow. The excess mucus is irritating, often triggering cough, and a greater respiratory and muscular effort is needed to aerate the lungs. The causes for bronchospasm are similar as for asthma, such as allergies, exercise, emotions, upper respiratory infections and irritants.

Diagnosis and treatment of bronchospasm must be immediately and acutely managed to prevent further respiratory distress. Diagnosis is made based upon clinical exam revealing cough, shortness of breath and wheezing, usually presenting in an acute persistent manner. Treatment is the primary focus. Treatment consists of an inhaled short acting beta2-agonist such as Albuterol or Xopenex. These medications are often referred to as bronchodilators and they work to relax airway smooth muscle surrounding the walls of the bronchioles while modulating the release of mast cells and basophils. Mast cells and basophils mediate the inflammatory response that is stimulated during an asthma attack, or bronchospasm.
Case Study

Up to 90% of patients with asthma are reported to have exercise induced asthma (EIA) or exercise induced bronchospasm (EIB), and as many as 12-15% of patients without asthma may develop EIB usually during or within 20 minutes of moderate to vigorous exercise. Rather than seeking medical diagnosis and management, individuals with asthma or EIB may decide not to participate in exercise, leaving them at higher risk for other conditions, such as obesity, which may impact their overall health and lifestyle further. The widespread incidence of asthma and EIB suggests that healthcare providers will encounter these patients on a daily basis.

Although the pathogenesis of EIB is not fully understood, it is likely caused by exercise induced hyperventilation and corresponding changes in in airway pathophysiology. A history of cough, shortness of breath, chest tightness and wheezing, or endurance problems during exercise, can be used, as discussed earlier, to assist in diagnosis of asthma and bronchospasm. Typically a 10-15% decrease in peak flows, or forced expiratory volumes (FEV₁), is compatible with EIB. The EIB Landmark Survey was an initiative to obtain an objective understanding of the impact of exercise related respiratory symptoms. It demonstrated the under diagnosis and treatment of EIA and EIB. A majority of the adults surveyed (65%), who experienced respiratory symptoms during or shortly after exercise had never been diagnosed with EIA or EIB. Treatment of EIB is well documented and found that prophylactic treatment with a short acting beta2 agonist inhaler, such as Albuterol or Xopenex, before starting exercise, is highly effective in 80-95% of patients. However, in the EIB Landmark Survey, less than 25% of asthma patients use this recommended prophylactic treatment thus fail to effectively manage EIB. Furthermore, 96% of healthcare providers and 57% of patients, agreed that these short acting beta2 agonist inhalers should be used before exercise to reduce the chances of EIB. This is a very interesting find. One can conclude that providers need to educate patients more effectively and regularly on this treatment protocol, while also screening more patients regularly for symptoms of EIA and or EIB.

The case study focuses on a patient with EIB without underlying asthma, illustrating the impact EIB can have when not managed effectively. A 34 year old female visits her nurse practitioner (NP) with complaints of fatigue and lethargy. She is overweight, with a body mass index of 28, and has a history of depression, for which she has been taking an antidepressant (SSRI) for since the birth of her child 5 years ago. Her blood pressure is 140/80 and routine labs reveal elevated cholesterol levels. She has no other remarkable history, including no history of asthma, recurrent bronchitis or smoking. She denies cough, chest pain, palpitations, peripheral edema, and nocturnal awakening with respiratory symptoms. Additional questioning reveals that she has been avoiding recreational activity since adolescence because it often left her out of breath, with mild wheezing, and unable to keep up with her peers. She has gained 40 pounds since the birth of her second child, which she feels has slowed her down more. A review of her medical history reveals she has recently started to become more active in an attempt to get back into shape. She has started a walking program but becomes short of breath within 5-8 minutes of
exertion. If she continues walking, she experiences chest tightness and wheezing when she exhales. Her symptoms resolve when she rests or drinks coffee. Her physical exam was unremarkable. Differential diagnosis considered were asthma, other pulmonary disease, cardiovascular disease, vocal cord dysfunction, obesity, poor conditioning and anemia.

Diagnostic testing included a chest x-ray, complete blood count and electrocardiogram, all of which were normal. An exercise challenge revealed an oxygen saturation of 99% at rest and 98% after 3 minutes of jumping jacks. Pulmonary function testing revealed normal lung volumes and FEV₁. Her baseline spirometry was normal, but after the exercise challenge, revealed a significant 15% decrease in her FEV₁. A presumptive diagnosis of EIB was made. The next step in diagnosis of EIB is to administer pulmonary function testing before and after giving a short acting inhaled beta2 agonist, such as Albuterol or Xopenex. A decrease of 10% in the FEV₁ after exercise is sufficient to diagnose EIB, especially if the patient is symptomatic. A diagnosis of asthma can be made after 15 minutes of using the short acting inhaler, if the FEV₁ improves by 12%.

Treatment of EIB, as discussed previously, would be to administer 2 puffs of a short acting beta2 agonist inhaler, such as Albuterol or Xopenex, just before exercise. This has been found to be effective in 80% of cases. Use of long acting inhalers is discouraged for EIB as it can disguise poorly controlled persistent asthma. Long acting inhalers should be used in conjunction with inhaled corticosteroids for asthma management only. Leukotriene inhalers, such as Advair, can be used with asthmatics, as well as patients with EIB who only use short acting inhalers, to attenuate EIB in up to 50% of patients.

This case study patient was diagnosed with EIB and managed with a short acting beta2 agonist inhaler, Albuterol. The patient was educated on inhaler use and that there is no need to avoid physical activity. The patient was also instructed on other warm up activities to reduce the degree of EIB, such as placing her hands over her mouth to attenuate the cold air introduced into her lungs. An exercise program was discussed that included 30 minutes of moderate to vigorous walking 5 times a week and a complemented nutritional program to follow. Goals set for her follow up visit in 3 weeks included a decrease in weight, decrease in blood pressure, diminished respiratory symptoms, feeling more energetic and positive, and further formal follow up with an asthma specialist. The patient followed up 4 weeks later, all goals were accomplished.

This case study highlights the implications of under managed EIB and the possible consequences of a sedentary lifestyle. It is important that EIB not limit physical activity. Inhaled short acting beta2 agonists attenuate EIB in 80-95% of patients with asthma and are effective 2-3 hours during exercise. Guidelines for the diagnosis and management of asthma indicate that patients with EIB should be monitored regularly to ensure their symptoms are well controlled and not representative of uncontrolled asthma. Referral to an asthma specialist for further evaluation and treatment is a recommended and standard practice. Patient education is essential in achieving positive patient outcomes.
Albuterol vs. Xopenex

Albuterol sulfate is the generic name for Proventil, or salbutamol sulfate, and is a sympathomimetic amine\textsuperscript{12}. The molecular weight is 576.7 and the empirical formula is (C\textsubscript{13}H\textsubscript{21}NO\textsubscript{3})\textsubscript{2} H\textsubscript{2}SO\textsubscript{4}\textsuperscript{12}. Albuterol sulfate is a white to off white crystalline solid that is soluble in water and slightly soluble in ethanol\textsuperscript{12}. The inhalation aerosol is a pressurized metered dose that delivers 90mcg per dose\textsuperscript{12}. The recommended dosing is 2 puffs every 4-6 hours, as needed. Each canister provides 200 doses. This is a short acting beta2 agonist inhaler. Beta adrenergic agonists affect BOTH beta1 and beta2 smooth muscle receptors in the body. Beta1 affects the heart in a stimulating way producing tachycardia, elevated blood pressure and excitability. The Beta1 effects 10-50\% of cardiac beta adrenergic receptors\textsuperscript{12}. Beta 2 affects the lungs by relaxing the smooth muscle and dilating the bronchioles. Activation of Beta2 adrenergic receptors on airway smooth muscle leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic -3', 5'- adenosine monophosphate (cyclic AMP)\textsuperscript{12}. This increase in cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation\textsuperscript{12}. Albuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Albuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges\textsuperscript{12}. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway\textsuperscript{12}.

Xopenex is the brand name for levalbuterol hydrochloride\textsuperscript{13}. The molecular weight is 275.8 and the empirical formula is C\textsubscript{13}H\textsubscript{21}NO\textsubscript{3} HCl\textsuperscript{13}. Xopenex is a white to off white crystalline solid and the inhalation is a clear colorless preservative free solution of the HCl salt of levalbuterol, the (R)-enantiomer of the drug substance racemic albuterol\textsuperscript{13}. The inhalation aerosol is a pressurized metered dose that delivers 45mcg per dose\textsuperscript{13}. The recommended dosing is 2 puffs every 4-6 hours, as needed. This is a short acting beta2 agonist inhaler that SELECTIVELY stimulates ONLY beta2 adrenergic receptors thereby relaxing airway smooth muscle without the stimulation of beta1 receptors. Activation of Beta2 adrenergic receptors on airway smooth muscle leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic -3', 5'- adenosine monophosphate (cyclic AMP)\textsuperscript{12}. This increase in cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation\textsuperscript{12}. Xopenex relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Xopenex acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges\textsuperscript{12}. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway\textsuperscript{12}.

Studies show that a single dose, 45mcg of Xopenex vs. a single dose, 90mcg of Albuterol was more effective at relaxing smooth muscles of the airways, longer lasting, metabolized through the gastrointestinal tract as opposed to the renal system with Albuterol, and had little to
no effect on the beta1 adrenergic receptors thereby hardly affecting the cardiovascular system\textsuperscript{19}. In clinical practice, Albuterol is commonly used, despite this information. Xopenex is a far superior medication when used to manage AIB and or EIB. The reason for this discrepancy... cost. Xopenex is very expensive and often not covered, or covered at a very high cost to the patient, therefore it is not commonly used.

\textbf{Xopenex}

\hspace{3em} S-albuterol \hspace{3em} R-albuterol

\hspace{3em} Ball-and-stick model of the (R)-albuterol (top) and (S)-albuterol

\textbf{Patient’s Instructions for Use}

\textbf{Figure 1}

\textbf{Figure 2}
Conclusion

Asthma is a chronic inflammatory disease of the airways where there is typically a temporary blockage or narrowing that occurs producing and array of secondary symptoms\(^1\). Bronchospasm is a frightening acute event that results in an abnormal smooth muscle contraction of the bronchi causing a narrowing and obstruction of the airways\(^2\). Millions of people suffer from asthma and bronchospasm. These conditions are often under diagnosed and under or improperly treated. Exercise induced bronchospasm resulting from asthma or otherwise, can be effectively treated, once recognized, with short acting beta\(2\) agonist inhalers. Although Xopenex is a far superior medication choice to Albuterol, limiting factors such as cost preclude its use. These inhalers are most effective at decreasing respiratory symptoms and improving exercise tolerance if used just prior to exercise. The case study presented implications for a sedentary lifestyle, recognition and treatment of EIB followed by the therapeutic outcomes as a result. The images used helped to demonstrate these point further.
1. http://www.aafa.org/display.cfm?id=8&cont=5
   +images&hl=en&client=safari&rls=en&prmd=imvns&tbo=u&source=univ&sa=X&ei=LJyKT9u7AdTViALxm8zlCw&ved=0CDMQsAQ&biw=1875&bih=1506
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Aspartame

*The Infamous Sweetener*

April 20, 2012
Dr. Mancini
Organic Chemistry 2

Ted Amble
Abstract

Aspartame, an artificial sweetener, is a common ingredient found in thousands of products. More commonly known as nutrasweet or equal, aspartame is an FDA approved, synthetic, calorie free sweetener that has been linked to cancer, anxiety, obesity, and liver damage, among dozens of other symptoms. Aspartame provides no nutritional value and is approximately 200 times sweeter than sucrose. Some common items that contain aspartame include soft drinks, yogurt, mints and bubblegum, puddings, and snacks.

Origins and Approval by FDA

In 1965, James Schlatter, a scientist for G.D. Searle, was working on an anti-ulcer drug. During a certain stage of development, he inadvertently spilled some powder onto his finger. Against wiser judgement, he licked his finger to easier pick up a piece of paper and noticed an intensely sweet sensation in his mouth. This is universally believed to be the first known creation of aspartame. Fast forward to 1970, A report published by Cloninger and Baldwin in Science compared the relative sweetness of aspartame to sugar, saccharin, and cyclamate. The report proposed aspartame could be used as an artificial sweetener.

Aspartame gained FDA approval in 1974, however, the agency rescinded their decision when evidence was presented that aspartame may be linked to malignant brain tumors in animals. Around the same period, an FDA scientist noticed an irregularity in a test conducted by G.D. Searle on the drug Flagyl, which then made the agency suspicious of the quality and validity of numerous other tests; One of which included aspartame. A special investigation task force was set up to investigate these irregularities. Two studies that involved aspartame were discovered to contain serious errors within the study.

In January, 1970, the FDA set up a grand jury hearing into the investigation of G.D. Searle for failing to make required reports to the FDA, concealing material facts, and making false statements. Ultimately no charges were ever filed. Further investigations on aspartame were conducted shortly thereafter, however these investigations brought only more questions and fewer answers.

The FDA decided that, in spite of unanswered questions and shady laboratory practices conducted by G.D. Searle, their data was reliable. The resulting decision led to the studies being submitted to a public board of inquiry in 1980. The board was to determine whether or not aspartame was linked to brain cancer, brain damage, and endocrine dysfunction. The board of inquiry agreed that more tests on aspartame were needed. Despite these recommendations, The then-FDA-commissioner Arthur Hull Hayes approved aspartame’s use in dry foods in 1981. Two years later, he approved its use in soft drinks. In 1996, Aspartame was approved as a general purpose sweetener in all food and drinks.
Chemical Composition

Aspartame is classified as a methyl ester of a peptide composed of aspartic acid and phenylalanine. Aspartame exists in two forms; an alpha and beta form. The alpha form bears the sweetness characteristics unlike its beta counterpart. Aspartame is a white, odorless, crystalline powder. Aspartame lacks the bitter, metallic aftertaste characteristic of saccharin. Aspartame is not recommended for use in baked or fried food products due to degradation upon exposure to high temperatures.(1)

Manufacturing Process of Aspartame

Aspartame is manufactured by the coupling of the amino acids L-phenylalanine methyl ester and L-aspartic acid to produce the dipeptide methyl ester. If the coupling is done chemically, both the sweet alpha form and the non-sweet beta form of aspartame are produced, requiring separation to obtain only the alpha form. The process illustrated at right shows esterified L-phenylalanine (Phe) reacted with N-protected L-aspartic anhydride (Asp) to form N-protected alpha-aspartame. After the coupling reaction, a series of steps of protection removal, crystallization, decolorization, filtration, sterilization, fine crystallization, and drying, the final product aspartame (L-aspartyl-L-phenylalanine methyl ester) is obtained.(1)
Chemical Components of Aspartame

Upon ingestion of aspartame, it is hydrolyzed in the intestinal lumen into its components aspartic acid, phenylalanine, and methanol. These components are then absorbed into the bloodstream and each is metabolized further.\(^{(3)}\)

**Methanol**

Methanol oxidizes within the liver to form formaldehyde. Formaldehyde further oxidizes to form formic acid by formaldehyde dehydrogenase. Formic acid eventually converts into water and CO\(_2\).\(^{(1)}\) The actual amount of methanol expected to be consumed from a typical diet soda is estimated to be 55 milligrams of methanol per liter. It must be noted that methanol is found naturally in food and the amount of methanol created from one liter of diet soda is vastly less than amounts found in other food products. For example, fruit juice contains up to 680 mg/L of methanol.\(^{(4)}\)

**Aspartic Acid**

Aspartic acid, a nonessential acid amino acid, is produced naturally within the human body whether or not food that is consumed contains it. Aspartic acid plays a role in hormone production and release, as well as nervous system function. It is found within beef, eggs, salmon, milk, and shrimp.\(^{(4)}\) In general, aspartic acid is consumed in far greater quantity found in meat and dairy than is consumed from aspartame.

**Phenylalanine**

Phenylalanine is an essential amino acid that the body is not capable of producing on its own. It is found in three forms: L-phenylalanine, the natural form found in proteins, D-phenylalanine, an identical copy of L-phenylalanine created in laboratory, and DL-phenylalanine, a combination of the two forms.\(^{(5)}\)
Consumption of Aspartame estimates

It is difficult to accurately determine the average consumption of aspartame, per person, per day in the USA. A study in 1989 estimated that based on the amount of aspartame sold to food and beverage processors, aspartame replaced 15 of the approximately 132 pounds of total sweeteners consumed per person per year. This would be equivalent to 38 grams per person per year. This is further calculated to be 108 mg per person per day.(1) Further studies have shown that aspartame sales in 2005 totaled approximately 8000 tons. In 2002, this number climbed to 10,100 tons. By the most current estimations, 18,000 tons are produced globally with 9600 tons being consumed within the US in 2006.(1)

The most common product containing aspartame is the Diet carbonated soft drink segment. It is estimated that 5.55 ounces of aspartame containing soda were consumed per person per day per year in 2004. (1)

![U.S. per capita consumption of diet soft drinks](image)

Rats

Due to the components that Aspartame breaks down into inside the human body, there have been many studies conducted to ascertain evidence whether or not aspartame does indeed have an adverse effect on the body. Most notably, there have been experiments conducted on rats given a steady diet of aspartame containing diets while monitoring the results. In 2005, two experiments (of approximately 150 rats each) were conducted by feeding rats varying doses of aspartame containing diets. In the first report, the notable results were reduction of weight gain, reduced food consumption, and a greater incidence of the combined incidence of lymphomas and
leukemia’s in the treated animals. Food consumption decreased significantly with increasing concentrations of aspartame. The second report noted increases in lymphomas and leukemia’s, significant increase of cell carcinomas of the renal pelvis and ureter and their precursors in females, increased incidence of malignant schwannomas of peripheral nerves with a positive trend in males, significant positive trend of increased incidence of hyperplasia of the olfactory epithelium in both sexes, and increased incidence of malignant tumor bearing animals with a positive trend in males and females.

As a result of these studies, several food safety authorities requested additional information regarding the testing of these animals to evaluate on their own whether this data was valuable. The organizations requesting this information stated the claims of these reports were made in an over diagnosed manner.

![Graph showing incidence of lymphoma + leukemia with aspartame concentration](image)

**Weight Loss**

The American dream may be owning a home, but America’s obsession is weight loss. Artificial Sweeteners give society the satisfying sweet sensations of sugar without the caloric splurge that often accompany sugar laden foods. It is no surprise, then, that society loves sugar free foods. Aspartame is used in over 6000 different products worldwide and it is the primary sweetening agent found in many diet soft drinks.

Dieters who consume aspartame containing products have been the target of studies pertaining to both weight loss, weight maintenance, and level of energy. Multiple studies have been conducted to determine the effect of aspartame as an effective dietary supplement in weight loss.

In the analysis of 16 studies, 15 studies reported energy reduction intake when subjects drank aspartame sweetened beverages instead of sucrose containing beverages. This can likely be contributed to the lack of caloric value that aspartame provides when compared to sucrose. Nine of the sixteen studies had pertinent weight loss data (Smaller group sizes had inconclusive
The analysis was conducted in three stages. The first stage involved all weight outcomes including follow-up weights. The second stage excluded studies in which the control group gained weight and the third study excluded follow-up periods. A significant reduction in weight was seen in all three stages of analysis. There was a roughly 3% reduction in body-weight noted. Weight maintenance was better in men who consumed more aspartame products over follow-up but there was no difference in women. Weight regain was noticed to be significantly less for those consuming aspartame sweetened products over those who were not. This analysis determined that consuming aspartame sweetened products reduced both body weight and energy level of participants. (6)

Not all reports agree with these results. Aspartame has been linked to an increase in carbohydrate cravings(7), as well as increased hunger and food consumption.(1) Furthermore, aspartame consumption has been linked to increased waist sizes in elderly, and increased glucose levels in diabetic prone mice.(8)

A human study of 474 participants conducted by the San Antonio Longitudinal Study of Aging showed that during the course of three follow up exams over a 10 year period, participants who consumed artificially sweetened beverages saw a 178 percent greater increase in waist circumference compared to those who did not. (8) Those who consumed two or more artificially sweetened beverages saw a 500 percent increase in waist circumference. A similar study published in Epidemiology, 2008 looked at the relationship between consumption of artificially sweetened beverages and weight gain among subjects aged 25 to 64 years of age. This analysis showed that those who consumed artificially sweetened drinks nearly doubled their risk for obesity over the next seven to eight years. (8)

**Phenylalanine**

Phenylalanine, a component of aspartame, can be hazardous to anyone affected by phenylketonuria. Individuals born with phenylketonuria must avoid the amino acid phenylalanine. Individuals afflicted are missing the enzyme that the body employs to use phenylalanine. Today, Phenylketonuria is tested on newborns within 48 - 72 hours of birth. If phenylketonuria isn’t treated by 3 weeks of age, it can cause irreversible mental retardation. Those afflicted with phenylketonuria must take tyrosine supplements to have optimum brain development and growth.(5)
Methanol - Formaldehyde

Methanol, another component of aspartame, breaks down into formaldehyde during metabolism. Formaldehyde is rapidly metabolized into formic acid. Formaldehyde is a constituent of many foods and is produced in the body during the endogenous demethylation of many compounds. It is estimated that more than 50,000 mg of formaldehyde is produced and metabolized in an adult human body daily and that an adult liver can metabolize 22 mg of formaldehyde per minute. Any amount of formaldehyde consumed from aspartame is believed to be negligible in this respect. (1)

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<td>Inner layer</td>
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<td>Outer layer</td>
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*Calabrian sausage, smoked pork fat, speck, hard, Hungarian salami, pursen: NR = not reported.
FDA Complaints concerning Aspartame

Eye:
blindness in one or both eyes
decreased vision and/or other eye problems such as:
blurring, bright flashes, squiggly lines, tunnel vision, decreased night vision
pain in one or both eyes
decreased tears
trouble with contact lenses
bulging eyes

Ear:
tinnitus - ringing or buzzing sound
severe intolerance of noise
marked hearing impairment

Neurological:
epileptic seizures
headaches, migraines and (some severe)
dizziness, unsteadiness, both confusion, memory loss, both severe drowsiness and sleepiness
paresthesia or numbness of the limbs
severe slurring of speech
severe hyperactivity and restless legs
atypical facial pain
severe tremors

Psychological/Psychiatric:
severe depression, irritability, aggression, anxiety, personality changes, insomnia, phobias

Chest:
palpitations, tachycardia, shortness of breath, recent high blood pressure

Gastrointestinal:
nausea, diarrhea, sometimes with blood in stools, abdominal pain, pain when swallowing
Skin and Allergies:
itching without a rash, lip and mouth reactions, hives, aggravated respiratory allergies such as asthma

Endocrine and Metabolic:
loss of control of diabetes, menstrual changes, marked thinning or loss of hair, marked weight loss, gradual weight gain, aggravated low blood sugar (hypoglycemia), severe PMS

Other:
frequency of voiding and burning during urination
excessive thirst, fluid retention, leg swelling, and bloating, increased susceptibility to infection

Additional Symptoms of Aspartame Toxicity:
death, irreversible brain damage, birth defects, including mental retardation, peptic ulcers, aspartame addiction and increased craving for sweets, hyperactivity in children, severe depression, aggressive behavior, suicidal tendencies

Aspartame may trigger, mimic, or cause the following illnesses:
Chronic Fatigue Syndrome, Epstein-Barr, Post-Polio Syndrome, Lyme Disease, Grave’s Disease, Meniere’s Disease, Alzheimer’s Disease, ALS, Epilepsy, Multiple Sclerosis (MS), EMS, Hypothyroidism, Mercury sensitivity from Amalgam fillings, Fibromyalgia, Lupus, non-Hodgkin's, Lymphoma, Attention Deficit Disorder (ADD) (9)

My opinion

I work in grocery retail. I see every day what people are buying. While my views may be region specific to the area I work in, I believe that my observations are likely pretty consistent throughout the USA. I see people buy a lot of diet soda. I do mean a lot. I estimate that diet soda outsells regular soda 4 to 1. Diet Coke is our number one seller, followed by Coke Zero, followed by Diet Pepsi, and so on. I also have noticed that we are getting new diet sodas that aren’t sweetened with aspartame. It is my belief that food companies are catching on to the swirling controversy that surrounds aspartame and other artificial sweeteners and are producing dietary products with the new crop of “all natural” sweeteners like stevia and truvia. Truly, for every one report that claims aspartame is dangerous, another crops up that claims it is safe. If something is so controversial, proven or not, I try to avoid them. The more society becomes educated on such topics the more I think people will act the same. In 2005, Coke released Diet Coke with splenda instead of aspartame. Clearly, Coke is listening to its consumers, as well as the health reports. I predict that within 10 years aspartame will not be common and only found in the very cheapest generic labeled foods.
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Deficiency in Vitamin B12

Kalthoum Baiz 20 April 2012
ABSTRACT

Vitamin B12 is a complex water-soluble vitamin. This vitamin is more than likely deficient to be in people who are vegetarian, vegan, older adults, and alcoholics. The cause, symptoms, diagnosis, and nutrition are briefly discussed in the text. Vitamin B12 is essential in the everyday life of a human's body. It plays many key roles in the brain, nervous system, and formation of blood. Long time deficiency of vitamin B12 is irreversible.

INTRODUCTION

Basic Structure of Vitamin B12
(C63H88CoN14O14P)

"Vitamin B12 (a.k.a. cyanocobalamin) and its derivatives are corrinoids, or cobalt corrin complexes (corrin is the planar tetrapyrrrole ring). Corrinoids are synthesized exclusively by microorganisms (especially anaerobes) and have been shown to mediate the reductive dechlorination of PCE and TCE in several bacteria (1)." Figure 1- shows the molecular structure of vitamin B12.

CAUSES AND EPIDEMIOLOGY

Vitamin B12 deficiency is a widespread problem. Among the population groups at risk are older people, vegetarians, pregnant women, and patients with renal or intestinal diseases. The neurological symptoms of vitamin B12 deficiency can be irreversible. Since the problems that come with deficiency of vitamin B12 are irreversible, early diagnosis is essential for the population effected by it. Vitamin B12 deficiency is the common cause of macrocytic anemia (2)

The main causes of vitamin B12 deficiency are malabsorption from food, dietary deficiency, postsurgical malabsorption, and pemicious anemia. In older adults, atrophic gastritis, a condition that affects 10%-30% of the older adult population. Atrophic gastritis decreases secretion of hydrochloric acid in the stomach (2). When that happens, it results in decreased absorption of vitamin B12.

Strict vegetarians and vegans are another group that is at great risk of developing vitamin B12 deficiency. The majority of vitamin B12 source comes from foods that contain animal meat. Some fortified breakfast cereals are several of the few sources that contain vitamin B12, and that can be used as a dietary source for strict vegetarians and vegans.
Common Symptoms of Vitamin B12 Deficiency

The symptoms of vitamin B12 have been reported for decades now. The symptoms are fatigue, constipation, weakness, weight loss, and loss of appetite. The more severe symptoms of vitamin B12 deficiency include poor memory, confusion, depression, dementia, difficulty maintain balance, and soreness of the tongue or mouth. Symptoms of vitamin B12 are irreversible and can cause damage to the nerve system. Early diagnosis and intervention is important to prevent irreversible damage (3).

Neurologic symptoms

The Neurologic symptoms of vitamin B12 are as followed, numbness and tingling of limbs (it is more common in the legs). When there is tingling in the limbs especially in the legs, patients have reported that they have a hard time walking. Vitamin B12 plays a role in neuron transmitters, when a patient is vitamin B12 deficient they have memory loss, and that is why dementia is a neurologic symptom. Progression of neurologic complication is a slow process and often the symptoms are not reversible especially if that patient has been vitamin B12 deficient for a long time. Vitamin B12 deficiency is known to damage the sheath covering the spinal, cranial, and peripheral nerves (4).

Diagnosis

Generally, serum vitamin B12 can be broken down into 3 values:

- Likely vitamin B12 deficiency: <148 picomols/L (<200 picograms/mL)
- Possible vitamin B12 deficiency: 148 to 258 picomols/L (201 to 350 picograms/mL)
- Unlikely vitamin B12 deficiency: >258 picomols/L (>350 picograms/mL).

Homocysteine is the name of the test for people who are “thought” to be vitamin B12 deficient. Physicians run this test for patients, who are malnourished, elderly, vegetarian, alcoholics, etc. The doctor can order both urine and blood homocysteine form, and that is to help diagnosis vitamin B12 deficiency. A gene test can be ordered to test for one or more of the most common genetic mutation, if a family member has been diagnosed with homocystinuria, then for sure the patient should be tested because it was found in a family member (5).

Nutrition

Vitamin B12 is naturally found in animal products (fish, meat, poultry, eggs, milk, and milk product). Large amount of B12 is found in sea food. 8 ounces of Steamed clams (about the size of a deck of cards) has about 84mcg (4). In general, vitamin B12 is not found in plant good,
but it can be found in cereals because they are fortified in the cereal. In dietary supplements, vitamin B12 is most likely in the form of cyanocobalamin, and then the body converts it to its active forms methylcobalamin and 5-deoxyadenosylcobalamin (5).

The graph below shows the Recommended Dietary Allowance for vitamin B12. It splits the recommended amount for each age group and sex:

Figure 2: Recommended Dietary Allowances (RDAs) for Vitamin B12 (4)

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months*</td>
<td>0.4 mcg</td>
<td>0.4 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7–12 months*</td>
<td>0.5 mcg</td>
<td>0.5 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 years</td>
<td>0.9 mcg</td>
<td>0.9 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>1.2 mcg</td>
<td>1.2 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>1.8 mcg</td>
<td>1.8 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14+ years</td>
<td>2.4 mcg</td>
<td>2.4 mcg</td>
<td>2.6 mcg</td>
<td>2.8 mcg</td>
</tr>
</tbody>
</table>

* Adequate Intake

**Metabolic Function of Vitamin B12**

Vitamin B12 found in food is chemically broken down in the stomach by pepsin and gastric acid. The gastric acid and enzymes found in the stomach help separate vitamin B12 from food and that allows vitamin B12 to bind with proteins called R-binder. Vitamin B12 binds to the R-binder called (haptocorrins), and then is transferred to the intrinsic factor in the intestinal lumen by means of pH dependent process of 2.

"In the terminal ileum, the intrinsic factor-vitamin B12 complex binds with intrinsic factor receptor on the membrane surface of enterocytes and it is then transferred from the terminal ileum to the ileum membrane." In the alkaline environment of the small intestine, R proteins are degraded by pancreatic enzymes, freeing vitamin B12 to bind to intrinsic factor (IF) (4).

Finally, vitamin B12 is slowly released in the enterocytes and transferred into transcobalamin II. In (figure 3), holotranscobalamin shortened as (holoTC), is vitamin B12 bind to transcobalamin II. When vitamin B12- transcobalamin II becomes holotranscobalamin, it arrives in the blood circulation and keeps circulating until a cells takes it in. Vitamin B12 plays an important role in DNA synthesis, and it also helps with the formation and maintenance of myelin sheaths. Vitamin B12 also plays a huge role in neurotransmitters and erythropoiesis (2).
Normal Absorption of Vitamin B12

Methylmalonic acid

\[
\text{Methylmalonyl-CoA} \quad \text{Homocysteine} + \text{folic acid}
\]

\[
\text{Succinyl-CoA} \quad \text{B}_{12} \quad \text{Methionine}
\]

(Figure 3) shows the process of vitamin B12 transforming from food to chemical in the body, and how it is being absorbed in the body (cellular absorption of vitamin B12) (2).

The illustration above shows that there are two enzymatic reactions are known to be dependent on vitamin B12. The first one shown is methylmalonic acid. Methylmalonic acid is
known as a carboxylic acid, and helps with the body break down of certain proteins and fats. Methylmalonic acid is converted to succinyl-CoA using Vitamin B12 as a cofactor of this reaction. Succinyl-CoA helps in the process of breaking down fat in the body. Therefore, vitamin B12 deficiency can lead to increased levels of serum methylmalonic acid in the blood (6).

Methylmalonic + Vitamin B12 \rightarrow \text{Succinyl-CoA}

Homocysteine is the second reaction shown in the illustration above. Homocysteine is an amino acid found in the blood plasma. Homocysteine is converted to methionine using vitamin B12 and folic acid as a cofactor. Methionine is an amino acid group that contains sulfur, and is a powerful anti-oxidant and assist in the breakdown of fats. Therefore, deficiency in vitamin B12 may lead to increased homocysteine levels in the blood (6).

Homocysteine + Vitamin B12 + Folic Acid \rightarrow \text{Methionine}

**Biochemistry**

"The first type of Vitamin B12 to be isolated had a cyanide group attached to the cobalt; this was picked up during the purification of the vitamin, and is the form which is still referred to as "Vitamin B12". The commercial form of the vitamin is usually obtained as the cyanide, it metabolizes easily to the coenzyme."(7)

The most common enzymatic form of Vitamin B12 is 5-deoxyadenosylcobalamin. The momentous feature of this molecule is the cobalt-carbon bond between the 5 carbon of the 5-deoxyadenosyl moiety (the sugar part) and the cobalt of cobalamin. In Vitamin B12 as it is extracted, cyanide replaces this sugar link. This occurs during the final purification with active charcoal. "Aquocobalamin and hydroxycobalamin, with water and hydroxide are also known, as is the methylated form, methylcobalamin. A number of other cobalt-carbon bonded have been prepared synthetically, but are not known to occur in vivo."(7)

**Model Complexes**

"The simplest form of vitamin B12 is the [MeCo(CN)5]3- ion, and an early observation was that this complex group will transfer its methyl group to a mercury(II), generating the highly poisonous [MeHg+] moiety" (7).

The principle models used for Vitamin B12 are the alkylcobalt (III) dimethylglyoxinates, also called alkylcobaloximes, which have the advantages of easy preparation and simplicity.
methyl complex photolyses readily to form ethane and the methyl radicals can be trapped with spin-traps such as PBN. Reaction with mercury(II) forms the highly toxic MeHg(II) ion, modeling what happens when Hg(II) attacks methyl Vitamin B12. Of course none of these will ever provide substitutes for Vitamin B12, but they do provide platforms on which various aspects of the mechanisms of the Vitamin B12 catalyzed reactions can be studied (7).

**Cyanocobalamin- C63H88CoN14O14P**

Vitamin B12 is essential for the human body; it plays key roles in growth, blood formation, cell reproduction, protein synthesis, and tissue synthesis. Cyanocobalamin is a manmade form of vitamin B12 and it is developed in a lab for treating patients who are vitamin B12 deficient (8). People who are allergic to cobalt should not use this product. Cobalt (chemical symbol Co) is a metal that may be stable (non-radioactive, as found in nature), or unstable (radioactive, man-made) (9). The most common radioactive isotope of cobalt is cobalt-60.

Cyanocobalamin comes in a shot form and people who are vitamin B12 have to use this product for the rest of their life to help prevent them from any irreversible nerve damage in the spinal cord. To get the correct dosage of cyanocobalamin, the doctor will have to run a blood test every three to six months. That will help the physician determine the correct amount of dosage and this will determine if the shot is improving the health of the patient (10).

**Supplements of Vitamin B12**

Cyanocobalamin and methylcobalamin are forms of vitamin B12. They are found and available in supplements. Cyanocobalamin in a stronger form is injected in the body as a shots or nasal spray, and that needs a prescription for a physician (8). Over-the-counter medication that contains cyanocobalamin is found in multivitamin, vitamin B-complex, and vitamin B12 supplements (11). These supplements do not need a prescription, and they are taken orally. Since vitamin B12 is a water-soluble vitamin, it will be removed in the urine. That is why people who are deficient are recommended by their physician to take it in the injection form, so the body will absorb and store it longer (4).

**Cofactor for methionine synthase**

Vitamin B12 is a very unique and complex vitamin. It contains the metal ion, cobalt. As discussed in the “Metabolic Function in Vitamin B12”, vitamin B12 takes the form of methylcobalamin and 5-deoxyadenosyl cobalamin in the human body, so it can be used in the body to boost up the metabolic function and other important jobs. Methylcobalamin enzyme is required for synthesis of methionine, amino acid, from homocysteine. Methionine in turn is required for the synthesis of S-adenosylmethionine, a methyl group donor used in many biological methylation reactions, including the methylation of a number of sites within DNA and RNA. Methylation of DNA may be important in cancer prevention. Inadequate function of
methionine synthase can lead to an accumulation of homocysteine, which has been associated with an increased risk of cardiovascular diseases (4).

**Cofactor for L-methylmalonyl-CoA mutase**

5-Deoxyadenosylcobalamin is required by the enzyme that catalyzes the conversion of L-methylmalonyl-CoA to succinyl-CoA. This biochemical reaction plays an important role in the production of energy from fats and proteins. Succinyl CoA is also required for the synthesis of hemoglobin, the oxygen carrying pigment in red blood cells. 5-Deoxyadenosylcobalamin is extremely important in the human body because this chemical structure helps with the metabolic function. This is what gives the human body the boost of energy (4).

**Conclusion**

Vitamin B12 can take many different forms as it process in the body. When Vitamin B12 reacts in the stomach and intestines and changes it form to holotranscobalamin which is vitamin B12 and protein receptors bind together. When this form happens then it can be absorbed in the cell. People who are vitamin B12 deficient are putting their bodies through damage that cannot be irreversible and they will have to be on Cyanocobalamin (manmade vitamin B12) shots for the rest of their lives. Older adults, vegetarian, vegans, and alcoholics should check their blood to make sure they are not deficient in vitamin B12. During this research, I have how important vitamin B12 is in the absorption of the body. It helps the metabolism metabolize different types of proteins and fats. Overall, people who are in the risk group should talk to their physicians on different diet and supplements they can take.
BIBLIOGRAPHY


Adderall: The "Study Drug"

By: Rita Balyan
Organic Chemistry 236
Dr. Hank Mancini
Paradise Valley Community College
April 20, 2012
Abstract

The subject matter of this paper is aimed at the psychostimulant drug called, Adderall (Dextroamphetamine and Amphetamine). Adderall is a prescription medication prescribed most commonly to patients diagnosed with attention-deficit/hyperactivity disorder (ADHD). The history, development and synthesis, treatment uses, side effects and the abuse of the prescription drug will be discussed thoroughly.

History

Amphetamine was first synthesized at the University of Berlin in 1887 by Lazar Edeleanu, and its generic name came from a contraction of α-methyl-phenethyl-amine. This was one of the series of the compounds that were related to the plant derivative Ephedrine. Psychopharmacologist Gordon Alles, who was part of a group of researchers looking for a substitute for Ephedrine, resynthesized the compound in 1927. It was first marketed with pharmacological use as a Benzedrine inhaler in 1932 for treatment of asthma and congestion. In 1935 dextroamphetamine (Dexedrine) was marketed for treatment of narcolepsy.

Amphetamines became popular in the use of many of the worlds militaries, predominantly in the air force to aid in fighting fatigue and increasing alertness in their pilots. The German military was notorious for their use of methamphetamine (a derivative) in World War II. After decades of reported abuse, the FDA banned Benzedrine inhalers, and limited amphetamines to prescription use in 1959, but illegal use became common. The use of amphetamines is the United States is only prohibited by prescription and is considered a Schedule 2 drug. It was made a Schedule 2 drug in the 1960's when the U.S began to recognize abuse potential for amphetamines, and by 1970, 10 billion amphetamine pills were produced in USA per year at least 10% of USA population > 14 years old had used some form of this drug.

Many of the brands of amphetamines, such as Biphentamine (known as black beauties) were discontinued in the 90’s in the U.S because of growing abuse of them. Although many brands were discontinued due to abuse there still remains a constant problem of abuse with the remaining few amphetamines prescribed today, especially with the most common and popular brand, Adderall.

Attention-deficit/hyperactivity disorder (ADHD)

In order to have a better understanding the function and necessity of Adderall, it is necessary to understand the disorder that it treats. Attention-deficit/hyperactivity disorder, also known as ADHD for short, is a behavioral disorder characterized by impulsivity, inattention, and hyperactivity. By the age of 7 the symptom of hyperactivity may be the only one that is distinguishable to parents, although when children continue elementary school the symptom of inattention will become more obvious. ADHD has 3 subtypes:

- **Predominantly hyperactive-impulsive**
  - Most symptoms, hyperactivity-impulsivity (6 or more)
  - Inattention may be present, less than 6 symptoms

- **Predominantly inattentive**
  - Most symptoms are inattention, (6 or more).
- Fewer than 6 hyperactive-impulsive symptoms
- Children with this subtype are quieter and less likely to act out. 

• **Hyperactive-impulsive and inattentive**
  - The subtype most children have
  - Six or more symptoms of hyperactive-impulsive and inattention

These symptoms are usually recognized in children at a young age and the disorder follows most of them throughout their adulthood. The cause of ADHD is still unknown, although most researchers suggest that there could be a combination of factors to the disorder. In addition to genetics, there may be non-genetic environmental factors that could have been part of the cause. Studies show alcohol and tobacco use in pregnant women could be a potential link of the disorder. 

The functions impaired by the disorder are not those that can be learned or exercised. These impairments are of natural activities of complex neural networks of the brain. Adderall is used to treat and control the chemicals and nerves in the brain that contribute to hyperactivity, inattention and impulse control.

**Chemistry**

Adderall is a mixture of four S(+) and R(-) amphetamine salts and is a phenylalkylamine. The chemists J.H. Biel and B.A. Bopp (1978) state the definitive structural features of AMPH as (1) an unsubstituted phenyl ring, (2) a two-carbon side chain between the phenyl ring and nitrogen, (3) an a-methyl group, and (4) a primary amino group.

![Chemical structures of Adderall components](image)

Its effects are very similar to those of recreational drugs because its structure resembles drugs like methamphetamine (also known as crystal meth) and MDMA (3,4-Methylenedioxymethamphetamine) (also known as ecstasy). Most people don’t realize that amphetamine and methamphetamine have the same effects, in regards to dopamine release in the
striatum, rates of elimination, or other pharmacokinetic properties. There is no distinguishing equal doses of both drugs in human discrimination studies.¹ This is why Adderall is very carefully distributed and monitored by the government.

The two types of amphetamine salt mixtures are Adderall and Adderall XR, which is an extended release. These salts are crystalline compounds that are manufactured synthetic substances that consist of elements, carbon, nitrogen and hydrogen. The salts are 4 mixtures of amphetamine and dextroamphetamine. The difference between amphetamine and dextroamphetamine is that, dextroamphetamine has a few molecules of dextrose, which is a type of sugar.² "Dextroamphetamine saccharate, amphetamine aspartate monohydrate, dextroamphetamine sulfate and amphetamine sulfate tablets contain d-amphetamine and l-amphetamine salts in a 3:1 ratio of isomers."³ The d- and l-isomers of amphetamines have been studied by in vitro and microdialysis which demonstrated the effects of the isomers on extracellular levels, uptake, and release of monoamines.

**Adderall and Adderall XR are powerful blends of four amphetamines that includes Dexedrine and Benzedrine.**

**Each contains:**⁴

<table>
<thead>
<tr>
<th>EACH ADDERALL TABLET CONTAINS:</th>
<th>5 mg</th>
<th>7.5 mg</th>
<th>10 mg</th>
<th>15 mg</th>
<th>20 mg</th>
<th>30 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine Aspartate</td>
<td>1.25 mg</td>
<td>1.875 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
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<td>Dextroamphetamine Sulfate USP</td>
<td>1.25 mg</td>
<td>1.875 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>7.5 mg</td>
</tr>
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<td>1.875 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Dextroamphetamine Saccharate</td>
<td>1.25 mg</td>
<td>1.875 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>TOTAL AMPHETAMINES</td>
<td>3.1 mg</td>
<td>4.7 mg</td>
<td>6.3 mg</td>
<td>9.4 mg</td>
<td>12.6 mg</td>
<td>18.8 mg</td>
</tr>
</tbody>
</table>

[Fig 2]⁹

<table>
<thead>
<tr>
<th>EACH ADDERALL XR CAPSULE CONTAINS:</th>
<th>5 mg</th>
<th>10 mg</th>
<th>15 mg</th>
<th>20 mg</th>
<th>25 mg</th>
<th>30 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine Aspartate</td>
<td>1.25 mg</td>
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<td>3.75 mg</td>
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<td>6.25 mg</td>
<td>7.5 mg</td>
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<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
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<tr>
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<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
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<tr>
<td>Dextroamphetamine Saccharate</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>TOTAL AMPHETAMINES</td>
<td>3.1 mg</td>
<td>6.3 mg</td>
<td>9.4 mg</td>
<td>12.5 mg</td>
<td>15.6 mg</td>
<td>18.8 mg</td>
</tr>
</tbody>
</table>

[Fig 3]⁹
How it works

Adderall is used to bring patients to a normal baseline of stimulation in the brain where they need it. When patients with ADHD take Adderall they initially become understimulated for a few minutes and then the medication gradually increases stimulation to a normal baseline. Dopamine, epinephrine, and norepinephrine, are catecholamine neurotransmitters that are partly responsible for activating certain sensory regions throughout the brain. There are adjoining receptors that are sensitive to certain specific neurotransmitters and these chemicals in the brain manage communication from one neuron to another. Adderall is able to mimic the actions of these catecholamine neurotransmitters.

The nucleus accumbens in the mid-brain, is most responsible for stimulation from drugs and is abundant in dopamine receptors. Dopamine has been carefully researched and there have been findings that people with ADHD have a deficiency in dopamine. Dopamine is involved in many functions of the brain such as reward-seeking behavior, control of motor skills, pituitary hormone secretion, sexual behavior, and also memory functions. The isomer that is more potent in the reuptake and release of dopamine is the d-isomer, having twice the potency of the l-isomer in the striatum. The l-isomer is more potent than the d-isomer with norepinephrine release in the cortex. It is crucial to have a balance of norepinephrine and dopamine in ADHD treatment and normal frontal lobe function. The central nervous system is affected when the amphetamines in Adderall bind to dopamine receptor sites and are able to release these and other neurotransmitters in the brain that can result in different emotional responses. Some of these emotional responses include euphoria, anxiety, alertness, and sometimes psychosis. In addition to emotional responses, the bonding of amphetamine compounds to catecholamine neurotransmitters can cause physical responses in the peripheral nervous system, such as the vasoconstriction of blood vessels, tachycardia, and hypertension.

Not only does Adderall release catecholamines but it also inhibits the function of monoamine transporters. The job of these transporters is to remove the neurotransmitters from the synapse to stop the signal, in a process called “reuptake”. For example, when dopamine is released and does its job by stimulating another neuron, it becomes recycled in order for it to be able to be released again. The amphetamines in Adderall block this process and the dopamine is not able to be used again, which results in lower amounts of dopamine in each neuron, even though the brain is receiving stimulation from the Adderall to release more.
Side effects and Addiction

Just like any other medication, Adderall also has its side effects. Some of the common side effects experienced by those who take the prescription are dry mouth, nervousness, addiction, insomnia, headache, jitteriness, stomach aches, anxiety and irritability. Less common side effects include high blood pressure, depression, paranoia, tolerance (higher dose needed to achieve same effect) and hallucinations. There is a growing problem with abuse of psychostimulant’s and along with that come the more severe overdose symptoms that would be in need of immediate medical assistance such as personality changes, seizures, vomiting, erectile disorder, dehydration, unexplained muscle pain, lower abdomen pain and psychosis.

One of the best documented problems that is caused by stimulants that are prescribed by physicians to treat ADHD, such as Adderall is growth in children, indicated by recent work. The National Institute of Mental Health did a study with 579 children, that involved ADHD treatments in 2007. The study compared 7 to 10 year olds that were medicated and those that were not medicated over a 3 year period. The medicated children compared to the un-medicated children grew 2 fewer centimeters in height and weighed less by 2.7 kilograms. “Although this growth-stunting effect came to a halt by the third year, the kids on the meds never caught up to their counterparts.”

The abuse of Adderall worldwide has become more common than ever. The severe side effects of the prescription are usually brought on by abusers of the medication. The dangerous part about the drug is it is a Schedule 2 drug and acts just like methamphetamines in the body which makes it a very high risk drug for dependence and addiction. Addiction is an unusual disease in that it is not a consequence of cellular dysfunction: addictive drugs “hijack” normal learning processes to reinforce their own acquisition.” Addictive drugs share a common trait in which they seem to each enhance dopamine neurotransmission by means that alter it from its normal drive. The 3 major factors that are driven by dopamine levels are, neuronal firing, reuptake by the dopamine plasma membrane uptake transporter, and the state of the pre-synaptic terminal which is in charge of controlling the responses to neuronal activity. Therefore, addictive drugs possibly do the opposite of these functions by, enhancing neuronal firing beyond what is normal, inhibiting the reuptake of dopamine, and altering release probability from the pre-synaptic terminal. Amphetamines themselves are less predictable and release dopamine via reversal of the plasma membrane uptake transporter.
The “Study Drug”

Very common abusers and addicts of Adderall are college students. The stimulant has grown in popularity and has become known as the “study drug”. According to the National Survey on Drug Use and Health (NSDUH), “that 15% of college students have admitted to using some form of psychotherapeutic drugs for non-medical use. Of those 15%, 7% have claimed to use Adderall to either increase attention span, party, or improve grades”. The number of prescriptions for Adderall tripled between 1993-2003 and only 2% percent of the students who possess it actually were prescribed it by a physician. This does not mean that obtaining a prescription for the narcotic is difficult. There are a series of questions Physicians and Psychiatrists ask to patients to diagnose them with ADHD. The questions are fairly straightforward and it wouldn’t take much for someone to be able to know what the right answers were to give to win them a prescription. An example of such a question could be, “How well do you do in your college courses?” a very simple question with a obvious answer. According to USCIence Review, there was a study done where 95% of students “were able to obtain a false diagnosis of ADHD by faking symptoms on one of the most commonly used self-reporting scales”.

Students do not realize that taking this medication comes with a price. A study was conducted with 175 students in 2007 concerning Adderall. The students were undergrads that viewed Adderall as harmless and morally acceptable. They all had similar reasons for believing this myth. One reason is that unlike methamphetamine and cocaine, Adderall is not an illegal drug, therefore it must be harmless and if used in moderation there will be no potential danger to health. Another reason is that many students are aware of the symptoms of ADHD and begin to self-diagnose themselves if they find themselves sometimes unable to concentrate or catch themselves day-dreaming and when they take the medication they realize that they are able to focus. A common belief of many students is that prescription drugs have low risk factors. The Partnership for Drug-Free America did a study and found that “40% of teens believed that prescription drugs are "much safer" to use than illegal drugs; 31% viewed "nothing wrong" with occasionally using a drug without a prescription; and 29% believed that prescription medications are not addictive.”

The Truth about Adderall

Medical professionals have recognized the dangerous effects of Adderall not only for people who do not have ADHD but also for patients who have been diagnosed with ADHD and legally have it prescribed by their physician. Between the years 2000 and 2005, the FDA found that 1000 patients that were taking Adderall and other stimulants were having hallucinations and caused psychosis and mania. The FDA has informed physicians to give patients that are prescribed the medication a medication guide that describes the risks and dangers of the Adderall and were told to prescribe it sparingly.
What is most likely believed by students is that if they stop use of the drug then they can always return to their normal brain function and lifestyle which is not the case, in fact on the contrary studies show the misuse of the medication can have permanent and long-term damage to the brain. The prevention of reuptake of catecholamine's back into the pre-synaptic neuron causes dopamine to remain in the synapse, increasing activation of the post-synaptic neuron receptors. Reuptake doesn’t occur so the dopamine doesn’t get metabolized and recycled but gets washed away, resulting in lower concentrations of this catecholamine in neural system. Fallon Schulz, a licensed clinical social worker from New Jersey said its like Adderall "tricks the brain that it doesn't need to make dopamine, and dopamine is the only chemical in the brain that once it is damaged, you never get it back." Dopamine is what controls a person’s emotions so less of it results in depression and irregular moods which in turn has caused “high rates of aggression, psychosis, and suicide for many long-term users of Adderall, as shown by studies at UCLA”.6

Unfortunately there have been much worse tragedies due to Adderall. Adderall XR was pulled off the shelf in Canada after it was linked to 20 sudden deaths and 12 strokes. Fourteen of the fatalities were children and 2 of the strokes were children. It was reported that the adverse reactions were not of misuse or overdose of the medications. The U.S Food and Drug Administration reviewed the reports and didn't think it warranted pulling the drug off the market in the United States.9

**Conclusion:**

To conclude, there are many pro’s and con’s to prescription amphetamines such as Adderall. It is a very useful medication for patients suffering with symptoms of ADHD and can be helpful to them in their everyday life, giving them the ability to focus and function, just like those without the disorder. It is unfortunate that with the blessing there is a price. The long-term effects of the drug can in some opinions outweigh the good it does. In my opinion the pro’s outweigh the con’s for ADHD patients as long as they are not misdiagnosed with the disorder. My biggest problem with the drug is the millions of young people prematurely destroying their bodies and brains while becoming addicted to the narcotic without having the correct knowledge of its harmful effects. I feel the drug is still not prescribed as sparingly as it should be and many are taking the medication that have very minor symptoms of ADHD, or none at all.
Bibliography


Eczema

Jessica Barnes
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Eczema

Abstract

This research discusses the skin condition Eczema. There are many different forms of Eczema, all in which exhibit different symptoms and are triggered by different causes. Depending on the severity of the Eczema condition, different levels of potency in topical corticosteroid are prescribed and non-medication treatments are available as an alternative as well.

Introduction

The skin is the largest organ within the human body. This organ serves many vital functions to the human body such as providing a protective barrier against harmful pathogens, and chemicals. Not only does the skin serve to protect the internal fragile organs, but the skin also plays a role in regulating the human body temperature. The skin is composed of three main layers: Epidermis, dermis, and subcutaneous tissue.

The epidermis is the most outer layer of the skin, the dermis is the middle layer, and the subcutaneous tissue is the inner layer. Within the epidermis layer of the skin, cells called Keratinocyte are found. The Keratinocytes cells serve to protect the skin against environmental damage. When the skin is exposed to substances or chemicals that trigger irritation, the Keratinocyte cell send out chemicals, called proinflammatory mediators, which causes the skin to swell. Within the Epidermis layers, cells called Langerhans are also found, these dendritic cells transport the harmful antigens that come into contact within the skin to the immune system. The immune system ultimately determines whether or not the antigen the skin came into contact with is harmful. If the antigen is determined as harmful, then the Langerhans cells are transferred to the lymph nodes where inflammatory cells are sent out to the affected skin area. The dermis layer also contains cells called Fibroblast and mast cells. The Fibroblast cells produce collagen, and also play a role in wound healing. The Mast cells controls the redness, swelling, and itchiness of inflammation. The mast cell also informs and calls other cells to action. The cells that are called to action are: basophils, eosinophils, and most importantly T cell lymphocytes. T cell lymphocytes are responsible for regulating the body’s immune responses against infected cells. Correct functioning of the immune responses helps protect the body from potential harmful
substances. Improper functioning of the immune responses can lead to a skin condition called Eczema. Improper functioning of the immune responses is called dysregulation and with this condition the body will defend itself from normal foreign substances outside of the body.\(^1\) An example of this condition can be seen with the hands soaking in water for too long; the body begins to defend the epidermis layer from the water damage by producing anti-inflammatory cells. The problem comes when there are too many anti-inflammatory cells at the site of the skin, and causes the itchy-like symptoms of Eczema.

Eczema is a skin condition characterized by excessive itching, and inflammation. This skin condition affects 15 million individuals in America.\(^2\) Eczema is non-contagious and can affect individuals of any age, although, eczema is more commonly seen with infants. The term Eczema is derived from the latin word “zein”, which means to boil out. Often times individuals with Eczema will experience symptoms such as inflammation, which looks like the skin is “boiling or popping out”. Other symptoms that individuals can experience depend on their severity of Eczema. Mild symptoms include dry, reddened, itchy skin. More serious symptoms include blistering, oozing lesions, intensive itching, and thickened, scaly skin surface.

Types of Eczema

When addressing the skin condition Eczema, most often individuals use the term Eczema and Atopic Dermatitis interchangeably. Atopic is actually a common form of Eczema. There are many forms of Eczema that exist. The many forms of Eczema are: Atopic Dermatitis, Contact Dermatitis, Seborrheic Eczema, Nummular Eczema, Neurodermatitis, Stasis Dermatitis, and Dyshidrotic Eczema.
Atopic Dermatitis:

Atopic Dermatitis is also commonly called Dermatitis or Eczema. This skin condition is characterized by chronic itching. These chronic itches are reoccurring and can come and go the following day. Since Atopic Dermatitis is chronic, the skin condition requires daily care and maintenance. If left untreated, Atopic Dermatitis has the potential to become more severe producing symptoms such as swelling of the skin, or a condition called “weeping”, in which a clear blister like sac develops on the skin and clear fluid oozes out of the sac. About 10% to 20% of the world population has Atopic Dermatitis. The exact causes of this condition cannot be pinpointed but there are certain conditions that may increase the chances of developing Atopic Dermatitis. An individual’s risk of having this skin condition will be more likely if their family has had a history of having Atopic Dermatitis, asthma, or hay fever. Also individuals who live in well developed countries where high levels of air pollution are more prevalent can have a higher risk of developing Atopic Dermatitis.

Contact Dermatitis:

Contact Dermatitis is defined as an itching outbreak or irritation of the skin occurring when an individual comes into contact with a particular substance. The most common types of substances that may cause an individual to develop irritation of the skin or an allergic reaction are shampoo, detergent, jewelry, gluten, clothing, and perfume. Repeated exposure to substances that cause irritation to the skin will enhance the chances of developing contact dermatitis. Also individuals who work in occupations such as hair dresser, janitors, mechanics, and health care workers have a higher chance of contracting contact dermatitis due to the chemicals, and latex gloves that these workers come into contact with.

Seborrheic Eczema:

Seborrheic Eczema also commonly called dandruff, cradle cap, and seborrhea occurs in the scalp region and can sometimes spread to the face, or the entire body in severe cases. This skin condition appears oily, and waxy on the skin. Red discoloration, inflammation, dry patches of skin can also occur. Common places that Seborrhea can occur is within the scalp, hairline, upper lip, beneath eyebrows, ears, eyelids, nose, and other areas that have oil producing glands called sebaceous glands. Seborrhea tends to develop during infancy, puberty, or middle-aged adults. Possible factors that lead to Seborrhea is having: oily skin, family history of Eczema, acne, or Rosacea.

Nummular Eczema:

Nummular Eczema is characterized by a ring or coin shaped lesion around the skin. Often times they are mistaken for a ring worm infection because of their round, and clear appearance around the skin. Some symptoms for this condition are swelling of the skin region in which produces a blister-like appearance. These round, blister-like patches weep fluid in the beginning and then dry out and become crusty. The infected area also itches, and itching tends to aggregate during the night time. Possible causes of this skin disorder are exposure to mercury found within dental fillings, exposure to nickel, or exposure to formaldehyde. Having a family
history of Eczema, or living in low humidity areas can increase the chances of developing nummular eczema.

Neurodermatitis:

Neurodermatitis is commonly called scratch dermatitis and is a skin condition that is distinguished by chronic itching. This condition begins with a small, dry patch of skin that itches and the individual scratches the region, but the scratching causes the region to itch more, which accumulates more scratching produced by the individual. Constant scratching can cause the infected skin area to appear very dry, leathery, and scaly looking. The infected area that itches is usually limited to one area. Some causes of this skin condition are: stress, anxiety, tight clothing that rubs onto skin, wool fabric, or insect bites. Possible factors that increase the risk of developing neurodermatitis is having a family history of skin conditions, being middle to late age, and being female.

Stasis Dermatitis:

Stasis Dermatitis is also known as venous eczema, and Gravitational eczema. This skin condition is characterized by swelling of the leg, and open sores within swollen leg areas. The swelling of the legs are caused by poor blood circulation. Often these swollen areas around the leg will appear discolored and will be thin and inflamed. Individuals will often experience an itching sensation within this area. Stasis Dermatitis more commonly affects elderly individuals over the age of fifty. This risk of developing this skin condition increases with advancing age, varicose veins, blood clots, high blood pressure, obesity, and heart conditions. Treating Stasis Dermatitis is different from treating other Eczema forms because not only does the skin region need treatment, but the circulatory problem requires a separate treatment as well.

Dyshidrotic Eczema

Dyshidrotic Eczema is commonly called Pompholyx or hand eczema. This skin condition is identified by the blisters that form within palms of hands, sides of fingers, and soles of feet. Symptoms of this skin condition are itchiness, burning, and inflammation of skin. Small blisters on fingers can also form, and skin can feel thin and raw from excessive scratching. If left untreated, these itchy skin regions can become infected and ooze out from the blisters. Individuals ranging from ages 20-40 yrs old are more likely to develop this condition, and children will rarely develop this condition. Excessive sweating is linked to the cause of Dyshidrotic Eczema. Stress and weather can contribute to the outbreak of this skin condition also. Having a family history of skin condition or having a skin infection or contact dermatitis in the past will increase the chance of developing this skin condition.

Diagnosis

Physicians will use physical examination, and questionnaires to diagnose Eczema. With the physical examination, the physicians will look at the affected skin area to notice any symptoms associated with Eczema such as scaly skin, blisters, and itchiness. The physician will also ask questions to determine the type of Eczema. Some questions asked will refer to when the
patient noticed the problematic skin development, if any changes within the patient’s environment occurred, or if the patient came into contact with certain materials. The physician may also use an allergy test or a patch test if the physician suspects that the patient has allergic contact dermatitis. If the symptoms are too vague, or show resemblance to other skin conditions, the physician may resort to skin biopsy to diagnose the patient’s skin condition.

Treatment

There is no cure to Eczema, however there are treatments used to prevent eczema outbreaks, and worsening of the condition. In conjunction to using treatments, patients may have to make lifestyle changes as well to prevent eczema symptoms from reoccurring. The course of treatment for Eczema depends on the severity of the symptoms. Corticosteroid creams are usually prescribed to reduce inflammatory reaction. The potency of corticosteroid creams range from mild, medium to high and are prescribed depending on severity of the eczema condition. For mild cases, topical steroids that contain 0.5-2.5% Hydrocortisone are prescribed. These ingredients can be found in over the counter drugs such as Cortaid. For more severe symptoms, a very potent form of corticosteroid may be prescribed. An example of this is Clobetasol propionate, also known as Dermol.

Chemical structure of Cortaid and Dermol:

Other medications available for controlling Eczema symptoms are topical (creams). These topical medications are Tacrolimus (Protopic), and Primecomilus (Elidel). These topical steroids both belong to the immune suppressant drug class. They inhibit the enzyme that produces T-cells, which contribute to the immune response system.

Chemical structure of Tacrolimus and Primecomilus
For severe itching symptoms of Eczema, oral antihistamines are prescribed to control the itch. Antihistamines are drugs that fight off the histamine released during an allergic reaction by blocking the histamine from triggering an inflammatory response on the tissue.\textsuperscript{4} Antihistamine drugs include Benadryl, Atarax, Vistaril, and Cyproheptadine.

\textit{Diagram of Histamine Allergic Reaction}

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\end{center}

\textit{Alternative therapies}

There are other therapies that help control Eczema flare ups as well. Some individuals feel more comfortable with utilizing alternative therapies, because they do not want to experience the drowsiness produced by antihistamine side effects, or atrophy (thinning of the skin region) produced by using corticosteroid creams for long term. Chamomile is a plant that is used to help heal Eczema. The chamomile plant itself is applied to the skin, or if the plant is not available chamomile tea compresses, or chamomile essential oil provide the same benefits. The properties in Chamomile are anti-inflammatory and anti-itch. In a study consisting of 161 patients suffering from rashes on their hands, forearms, and lower legs, researchers compared the effects of chamomile cream vs. steroidal and non-steroidal skin products. Over the course of three to four weeks, the chamomile cream showed similar efficacy to hydrocortisone and it actually worked better than the non-steroidal anti-inflammatory agent and the steroid preparation.\textsuperscript{6} Another effective way of controlling Eczema flare ups is utilizing ultraviolet light therapy, also known as phototherapy. Phototherapy involves subjecting the part of the skin infected by eczema to ultraviolet light of a controlled intensity and frequency range. Phototherapy prevents the exaggerated immune response that causes inflammation. One study conducted in Germany investigated the effects of phototherapy on severe Atopic Dermatitis. Investigators found more than 80\% of the patients with Atopic Dermatitis who were treated with phototherapy showed significant improvement, and in some cases, complete clearance within three weeks.\textsuperscript{7}
Prevention

Lifestyle changes are the first steps of controlling Eczema. Regardless of how severe the Eczema symptoms are, physicians will often times recommend a change in lifestyle in conjunction with taking medication. Lifestyle changes can help reduce the severity of eczema outbreaks or symptoms. The guidelines of daily maintenance of Eczema are: keeping the skin moisturized as much as possible, limiting contact with substances that may cause irritation, avoiding activities that cause sweating or overheating, avoiding extreme heat or cold weather, keeping finger nails short to prevent infection from scratching, dressing in loose cotton clothing or other “breathable” fabrics, reducing stress, double washing clothes in plain water to prevent irritation caused by detergents, and to follow the treatment plan if it is prescribed by the physician.

Conclusion

Eczema is a skin condition that affects many individuals. Improper functioning of the immune response causes an overproduction of anti-inflammatory cells, which causes problematic itchy, inflammation, and blister-like symptoms of Eczema. The severity of symptoms will depend on the form of eczema. The many forms of Eczema are: Atopic Dermatitis, Contact Dermatitis, Seborrheic Eczema, Nummular Eczema, Neurodermatitis, Stasis Dermatitis, and Dyshidrotic Eczema. Atopic Dermatitis is characterized by chronic itching symptoms that can come and go. Contact Dermatitis is characterized by coming into contact with a substance that causes irritation or allergic responses. Seborrheic Eczema is characterized by dry patches of skin within the scalp and oil producing gland regions. Nummular Eczema is characterized by a ring or coin shaped lesion around the skin. Neurodermatitis is characterized by an itch that itches more when scratching is accumulated. Stasis Dermatitis is characterized by itchy patches on swollen regions of the leg. Dyshidrotic Eczema is characterized by the itchy, blister-like sacs that form on sides of fingers, and soles of feet. There are no cures to these eczema forms, but there are treatments that can control the flare ups of the eczema symptoms. Physicians may prescribe Corticosteroid, Antihistamine, or topical medications depending on how severe the symptoms of Eczema are. Other alternatives that do not use medication are chamomile, and light therapy. Using treatment to control Eczema flare ups also require lifestyle changes which will maximize the healing process.
Bibliography

Scorpion: Menace or Miracle?

Jill Berger
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Abstract

Scorpions are one of the oldest creatures on this planet, having existed for millions of years, nearly unchanged. Scorpions are non-aggressive creatures that use their venom for hunting and as a means of defense when absolutely necessary. There are only a few species of scorpions that pose any real threat to humans, with only one of those being found in the United States. Scorpion venom possibly holds the key to a number of medical and industrial problems, making them far more of an asset to society than as the little monster most people believe them to be.

History

Scorpions have existed on this planet nearly unchanged for over 400 million years. These venomous arthropods of the class Arachnida, are one of the oldest living land animals. They actually predate the dinosaurs by more than 200 million years (1, 2, 3). Today, there are approximately 1500 species of scorpions found throughout the world on every continent except Antarctica. They are well adapted to live in a wide variety of habitats from deserts to tropical rain forests. Some are even found on snow-covered mountains at elevations of over 12,000 feet (4, 5). These extremely hardy creatures can survive days fully submerged in water, weeks of freezing, and as long as 2 years without food or water. Their average lifespan is 3-7 years, but some species can live up to 25 years (2, 6).

Although giant aquatic scorpions of the past may have reached close to 2 meters in length, modern day scorpions range in size of 1-21 cm (7, 8). Scorpions have flat elongated bodies with 4 pairs of legs, 2-5 pairs of eyes, and a pair of pedipalps with pincher-like claws. Their abdomen is divided into 12 segments, the last 5 of which form their signature “tail” called the metasoma. The bulb shaped structure at the end of the abdomen is called a telson. It contains the venom glands and is tipped with a sharp curved stinger for venom delivery (1). On the underside of the abdomen, scorpions have 2 feathery sensory organs called the pectines that hang down and trail on the ground. These are used to sense the texture and vibrations of surfaces, alerting them of nearby prey as well as being chemoreceptors for pheromones, alerting them to potential mates (1, 9).
**Scorpion Venom**

Scorpions use their venom for mating, subduing prey, and most often as a means of defense. They are primarily ambush hunters, sitting and waiting for their prey to approach. They first grasp their prey with their pincers, which for many larger scorpions does the job. Prey that can't be killed with pincers alone is stung with the scorpion's hypodermic needle like barb one or more times paralyzing or killing it (3). This more often occurs with smaller scorpions or those with weaker pincers, but there is a catch. It can take up to two weeks to regenerate the venom, leaving them somewhat defenseless (10). Therefore, most scorpions try to rely on their pincers and limit the use of their venom on prey as much as possible, saving their venom for self-defense. In general, scorpions are not aggressive towards non-prey such as humans. They are nocturnal creatures that primarily hunt at night and hide from the sun during the day. Most human stings occur when someone accidentally disturbs a scorpion in their daytime hiding place (8). Although painful, scorpion stings are rarely worse than that of a wasp or a bee. Similarly to bees, a person that is allergic to the venom, may experience a life threatening reaction to species otherwise considered non-threatening (5).

Although all scorpions are venomous to insects and other small creatures they prey upon, only about 25 species are potentially dangerous to humans with less than a dozen being linked to serious envenomation or death (5,6). With the exception of the *Hemiscorpius lepturus* species, found in Iran and Iraq, they all belong to the family of *Buthidae*. The thing that distinguishes members of the *Buthidae* family from those in the other 5 families is their triangular-shaped sternum. The other distinguishing characteristics shared by most potentially dangerous scorpions are weak-looking pincers, thin bodies, and thick tails (8). Only one member of this "club" is found in the United States, *Centruroides sculpturatus* (1). It is commonly referred to as the Arizona bark scorpion.
Scorpion Venom and the Human Body

There are multiple things to take into consideration when discussing the toxicity of scorpion venom in humans. The first thing is the potency of the venom itself. In general it is inversely proportional to the size of the pinchers (7). Species with smaller more delicate pedipalps usually have larger stronger tails with more potent venom. This has probably lead to the belief that the smaller scorpions are the most dangerous, something that isn’t entirely accurate, especially because they have less venom available. According to Chippaux and Goyffon, “any species exceeding 5 cm must be considered potentially dangerous to humans” (5). Thus, the next thing that needs to be taken into consideration is the quantity of venom injected. Thanks to a striated muscular layer surrounding the venom glands, the amount of venom released is under voluntary control. They usually inject between 0.1-0.6 mg of venom, but in the case of a “white” or “dry” sting, no venom is injected at all. This at least partially explains the variability in severity of symptoms with all other conditions being similar (3, 5). The third and fourth things to consider are the general health and the size of the victim. Rarely is hospitalization or anti-venom necessary for anyone other than infants or small children, mainly due to their small size. Basically, the larger the ratio of venom to body weight, the more severe the reaction will be (8). Technically, if simply considering toxicity by weight, some scorpion venoms are among the deadliest of all animal poisons, but rarely can a scorpion inject enough venom to produce a lethal reaction in a healthy adult (5). Pre-existing conditions, such as heart problems, hypertension, or pneumonia can also turn an otherwise minor reaction to something much more severe (3).

When it comes to venom composition and potency, there is a large variation amongst species. Scorpion venom is a water-soluble, antigenic, heterogenous mixture that may contain multiple toxins and other compounds, most of which have not been investigated. The venom from an individual scorpion may contain varying concentrations of neurotoxin, cytotoxin, cardiotoxin, nephrotoxin, hemolytic toxin histamine, serotonin, enzymes, enzyme inhibitors, mucous, various salts, peptides, nucleotides, amino acids, as well as other unidentified compounds (3,8). Clinically speaking, the most important effects of envenomation are neuromuscular, neuroautonomic, or localized tissue effects.

It is hypothesized that certain components of scorpion venom causing nothing more than localized pain or discomfort evolved solely for defensive purposes. This aspect of the venom is similar to that of bees. Like bees, some scorpions contain the enzyme phospholipase A and histamine causing the dilation of blood vessels resulting in redness and swelling around the site of the sting (3,11). In contrast, serotonin, another
component of scorpion venom, actually causes blood vessel constriction, often leading to pain. Some researchers have found that the serotonin in scorpion venom has lead to spontaneous abortions (miscarriages) in rats by inducing uterine contractions. This suggests that serotonin may be what’s responsible for the miscarriages in woman stung during their first trimester (3).

![Histamine (vasodilator) and Serotonin (vasoconstrictor)]

Venom toxins are the cause of the most severe and potentially life threatening effects. Their primary targets are voltage-dependent ion channels. Alterations in the normal activity caused by scorpion venom may lead to excessive neuronal activity. This can then cause a chain reaction, resulting in secondary end-organ effects. The most potent of these toxins, as well as the most researched, is the neurotoxin (3,11).

Neurotoxins

Neurotoxins are poisons that target the body’s nervous system, specifically, the victim’s excitable nerve cells, or neurons. Neurotoxins disrupt the signals that allow neurons to communicate effectively by interfering with membrane proteins and ion channels (3, 12, 13). Most of the neurotoxins found in scorpion venom target the voltage-dependent sodium and potassium ion channels, with one medically significant exception, chlorotoxin, which inhibits the conduction of chloride channels.

These changes alter the neuron’s firing pattern through prolonged action potential and/or repetitive firing, leading to the build up of sodium or calcium ions within the cell (3). Not only does this cause autonomic and neuromuscular overexcitation symptoms, it also prevents the transmission of normal nerve impulses (11). The end result is the massive release of neurotransmitters, such as acetylcholine, glutamate, aspartate, and the “fight or flight” catecholamines, epinephrine and norepinephrine. Unfortunately, the effects cascade throughout the body as additional tissues become affected by the neurotransmitters. Interestingly enough, the scorpion venom itself isn’t the cause of the most severe symptoms, instead the neurotoxins essentially cause the victim to use it’s built in communication system against itself (3, 11).

![Epinephrine and Norepinephrine]
Neurotoxin Research

One of the most interesting aspects of the numerous neurotoxins found in scorpion venom is its extreme selectivity. Professor Michael Gurevitz of Tel Aviv University has developed a way to isolate key neurotoxins in scorpion venom. The venom is a potential treasure chest of active components having survived millions of years of evolutionary selection. Some toxins have evolved that recognize and affect sodium channels of specific invertebrates such as insects, whereas others affect only the channels of mammals (14). Often the toxins even have the ability to target specific sites on the nerve cell itself (3). According to Gurevitz, this idea of an evolutionary deviation in specificity can be viewed as a "lesson of how toxins may be manipulated at will by genetic engineering" (14).

Many scorpions show this type of selectivity, but Gurevitz chose to focus his attention on one of the most potent scorpions in the world, *Leiurus quinquestratus*. The venom of this scorpion, often referred to as the death stalker or the Israeli yellow scorpion, contains more than 300 peptides, most of which have yet to be studied. In order to better investigate how certain toxins act against insects and mammals, Professor Gurevitz, developed methods for producing and manipulating them in the lab using bacteria. His research, over the past two decades, has helped pave the way for the potential in both the agricultural industry as a safe pesticide and in the pharmaceutical industry as a safe, non-addictive alternate to Morphine (14, 15). "Instead of running the risk of addiction, this venom-derived drug, mimicking the small peptide toxin, would do what it needs to do and then pass from the body with no traces or side-effects," Professor Gurevitz says (14).

Another important neurotoxin isolated from the death stalker scorpion is chlorotoxin or CTX. Unlike most of the other scorpion toxins that affect the potassium and/or sodium channels, this 36 amino acid peptide has a high affinity for binding to calcium-activated chloride channels (16). As luck would have it, this type of channel is over-expressed in many types of tumors, including gliomas, a particularly aggressive and often deadly form of brain cancer. Researchers at the University of Washington found they could cut the spread of cancerous cells by 45 percent with chlorotoxin alone, but combined with nanoparticles of iron oxide, they were able to cut the spread by 98 percent. CTX also slows the spread of cancer by binding to the MMP-2 proteins on the cell’s surface. When CTX enters the cell, it draws the MMP-2 protein inside as well. It is believed that MMP-2 help cancer cells break down the extracellular matrix surrounding them, effectively granting them access to the rest of the body (see the image on the following page). Tests
were done with CTX and nanoparticles alone and it was found that not only did the combination reach more cancer cells, but it also prevented the cells from elongating, something that only occurred when the two were combined. If a cell can no longer change shape, it’s ability to slip through the body is inhibited (17).

a) Diagram of chlorotoxin (CTX) attached to a nanoparticle. b) Each nanoparticle complex can simultaneously latch on to many MMP-2s, which are thought to help tumor cells migrate through the body. c) Over time nanoparticles draw more of the MMP-2s into the cell, slowing the spread of the tumor.

Similar research has been done at Ceders-Sinai Medical Center in Los Angeles where a drug, TM-601, was created using a synthetic version of chlorotoxin bound to the radioactive isotope iodine-131. TM-601 was designed to target the small amounts of cancer cells that are inevitably left behind after brain tumors are surgically removed. It delivers a highly-localized dose of radiation directly to brain cancer cells without harming other tissue. In the first trial, patients tolerated the treatment well with very few adverse side effects and showed very promising results in terms of effectiveness (18).

Chlorotoxin (CTX)
Another peptide, GaTxl, from the death stalker, is showing promise in the treatment of secretory diseases such as cystic fibrosis. There is limited understanding about the structure and mechanisms of the chloride channels crucial for secretion in many epithelial tissues. The opening of these channels to allow the flow of chloride ions creates the osmotic gradient needed to allow the flow of water. Those affected by cystic fibrosis have a lack of water flow in airway cells that stem from a mutated CFTR protein containing the critically important chloride channels. The body's quality control system, chaperone proteins, bind to the misfolded CFTR protein and they are thus discarded from the cell. Without the CFTR channels, there is no water flow causing abnormally thick, sticky mucous to build up leading to blockages that can obstruct the airway. GaTxl binds to the same site as the chaperone proteins, effectively preventing the loss of the CFTR proteins. They would still be mutated and unable to function at full capacity, but researchers at the Georgia Institute of Technology think that they would probably be able to function at about 50 percent. This would allow ions and water to flow from the cells thinning the mucous and hopefully preventing blockages. GaTxl may also be able to inhibit the channels and thus treat secretory diseases that have the reverse effect. If the CFTR channels are overactive, there is nothing to stop the flow. Diarrheal diseases, such as cholera and secretory diarrhea, cause thousands of deaths each year (19).

The potential medical significance of scorpion venom is constantly growing. There has been evidence to suggest that other components in the venom may one day be used to treat diabetes, by aiding in the regulation of insulin (4). Promising studies have been done in the area of halting the loss of teeth and the bones that keep them in place. The researchers involved feel this could be adapted to help those with arthritis and other bone destructive disorders (20). The sting of the Brazilian scorpion, Tityus serrulatus, often results in pancreatitis (inflammation of the pancreas). An enzyme within the venom removes the ability of the pancreas to absorb or release components. Researchers at NC State University are using it to better understand the pathology of pancreatitis, hopefully resulting a better treatment (21). One additional area of research is in the development of anti-venom.

Anascorp

Antivenom is only used to treat severe envenomations, primarily seen in small children. Last summer, the FDA approved Anascorp, the first specific treatment for Centruroides scorpion stings in the United States. It has been available for years in Mexico, but without the approval of the FDA, it couldn't be used by hospitals in the US. Prior to the availability of Anascorp, infants often ended up in the ICU from a severe sting. In most cases, the children can now be treated solely in the ER, usually going home in hours as opposed to days. Unfortunately, it's not all 'unicorns and rainbows.' Anascorp may cause delayed allergic reactions in people sensitive to horse protein because it is made
from the plasma of horses immunized with scorpion venom. Also, because Anscorp comes from a biological source, there is a risk of virus transmission from the plasma itself (22).

As with most things these days, cost is also a major factor. Anscorp is readily available in Mexico for $100 a unit. In the US, the very same drug goes for as much as $12,000 a unit. Most patients requiring 3-5 units per sting, therefore, Anscorp comes with quite a price tag. According the Jenny Gold of Kaiser Health News, the increased cost comes partially from the company that funded the clinical trials who sells it for “$3500 to another firm that provides it to Arizona hospitals for about $3,780. Hospitals mark up the drug to cover other costs, including the expenses of patients who are uninsured and the heavy discounts it gives to insurers” (23). Unless something is done, this means only the sickest of patients are likely to ever receive anti-venom in the United States.

Conclusion

After spending more than a decade making movie monsters into reality, I will openly bare a little of the blame for helping to make creatures such as scorpions, into the loathsome monsters most believe them to be. We have invaded their world, not the other way around. Scorpions have been on this planet far longer than man and will most likely out live our fragile species. These little guys can survive in nearly any climate under the harshest of conditions, the human species can’t dream of saying the same.

We as a society need to recognize the wonders that exist all around us. We need to acknowledge the connection we share with the many other creatures on this planet and try to embrace them rather than to shy away from things that appear menacing, when in truth, we simply do not understand them. We have barely scratched the surface of the mysteries that lie within these amazing little creatures. As we learn more about how scorpion toxins work, we will inevitably be lead to a deeper understanding of ourselves. I just hope that the research continues to be funded and people are open to the possibilities. The miracles we seek are often right in front of us, if we are willing to open our eyes and look.
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Sexual Cannibalism:
Different Hypotheses and the Role of Pheromones

Elisabeth Binkley
April 16, 2012
Abstract: This paper will discuss sexual cannibalism and the two major hypotheses that explain this behavior. Aggressive spillover and behavioral syndromes are considered to be the most prominent explanations. The role of pheromones will also be discussed in relation to how they may explain the male’s behavior.

The subject of sexual cannibalism is one that continues to leave researchers scratching their heads with many unanswered questions. To begin to understand more about this occurrence, we first must ask ‘what is sexual cannibalism?’ Sexual cannibalism is a form of sexual conflict in which the female organism kills and consumes a male of the same species before, during, or after copulation. This intersexual conflict poses various questions to researchers, one of them being ‘how is this behavior adaptive’? When first looking into this extreme behavior, we see that there are multiple possible benefits for the female in the situation but seemingly none for the male. So the question remains, how is this behavior adaptive? In order to try to pose an answer to this question, researchers have begun to explore two very different hypotheses as to why the female in this situation behaves in such an aggressive manner. The two main hypotheses that have been discussed by researchers are the adaptive foraging hypothesis, and the aggressive spillover hypothesis. In addition to these two hypotheses, there is emerging evidence that suggests that females may be tricking males into this situation by the use of pheromones. These three possible explanations will be discussed in further detail as we explore this puzzling, yet fascinating topic.

Now that we know what sexual cannibalism is, before we begin to explore this topic we must know what kinds of species take part in such an act. Sexual cannibalism is extremely rare and only occurs in a handful of species. Since this event is so uncommon, there is much more interest in why these species are partaking in such a behavior. Today, sexual cannibalism has only been observed and recorded in arachnids, insects, and amphipods, or in simpler terms, spiders, bugs, and crustaceans. In order to learn more about sexual cannibalism, more research has been done on arachnids and insects since they are easier to control and observe. All three of these species are capable of utilizing pheromones; therefore, their behavior may be able to be explained as a whole by shared use of this common invisible communication tool. Later, we will discuss pheromones and how they may be the underlying reason why sexual cannibalism happens in the first place.

The adaptive foraging hypothesis has been the leading hypothesis as an explanation to precopulatory sexual cannibalism by females. The adaptive foraging hypothesis suggests that sexual cannibalism offers adult females direct, material benefits. This hypothesis uses an economic model to demonstrate that sexual cannibalism can be explained as a result of adaptive tradeoffs, these tradeoffs being the nutrients provided by cannibalizing the male versus the fertility benefits of mating with the male. In order for the adaptive foraging hypothesis to be valid, it must be shown that sexual cannibalism has adaptive benefits. This leads us to our next
hypothesis— the aggressive spillover hypothesis. Sexual cannibalism may be the result of a spillover of aggression from previous life stages. Unlike the adaptive foraging hypothesis that requires an adaptive benefit, the aggressive spillover hypothesis suggests that sexual cannibalism may be a non-adaptive by-product of a general syndrome of voracity, or aggression towards prey. This hypothesis demonstrates an example of how a behavioral syndrome may produce behaviors that may appear suboptimal when observed in an isolated context (1). This second hypothesis allows for the fact that high levels of aggression may be selectively advantageous in juveniles because higher levels of aggression give juveniles a greater ability to hunt and consume more prey which will allow them to grow much more rapidly. If this high level of aggression continues throughout maturity and into adulthood, this is where we see the aggression manifest as sexual cannibalism and hinder the ability to mate.

Since the aggressive spillover hypothesis seems to indicate that it is not adaptive it has become somewhat controversial in the world of animal behavior. The idea that the answer to why sexual cannibalism occurs is not always adaptive is very anti-Alcock. As shown consistently throughout John Alcock’s Animal Behavior, animals are always thought to be engaging in optimal adaptive behavior in order to have their absolute best chance at survival (2). But is this always possible? Are animals always behaving in a manner that is most advantageous to them and their survival? This does not seem likely. To make this clearer, we can think of fitness as a mountain. Not all organisms are able to be at the top of the mountain, and on their way to the top of the mountain it is possible to get stuck in a “valley” where they are not improving their fitness. Organisms are unable to travel down this mountain of fitness, so they are kept in these valleys until natural selection acts upon various elements and “push” the organisms out of the valley and up the mountain. Could it be that the aggressive spillover hypothesis explains one of these valleys, the valley being the behavioral syndrome of aggression? This aggressive spillover hypothesis is becoming increasingly popular due to the fact that optimal behavior is not always so black and white.

In Johnson’s 2001 paper, “Sexual cannibalism in fishing spiders (Dolomedes triton): an evaluation of two explanations for female aggression towards potential mates,” both the adaptive foraging and aggressive spillover hypotheses are tested (3). Results from the tests performed provided support for both of these hypotheses as well. First, in support of the adaptive foraging hypothesis it was shown that increased adult food availability produced nonsignificant fecundity benefits in the female’s first egg sac and highly significant fecundity benefits in the female’s second egg sac. The results also revealed that consumption of a male did increase the probability of a female being able to successfully hatch her egg sac however it did not increase the amount of offspring produced. The mating trials from the experiment yielded mixed support for the adaptive foraging hypothesis. The results demonstrated that mated females did tend to attack courting males more frequently than virgin females. As for the aggressive spillover hypothesis, one example of support was that for juveniles, food availability had a considerable positive effect on fecundity and fixed female size. This specific finding was supportive of the aggressive
spillover’s claim that strong fecundity selection acts on juvenile feeding and fixed adult size. These findings stated above are of great importance since this was the first study on fishing spiders that manipulated juvenile food availability, which ultimately documented the link between juvenile food, fixed size, and fecundity. It is important to note that under experimental conditions, females were unable to translate fixed adult size into fecundity benefits. It is equally important to state that it was shown that juvenile and adult food appeared to both be main factors that determine fecundity. This is supported by the idea that intense fecundity selection acts on juvenile female fishing spiders to secure prey items and maximize fixed adult size. This then leads us to the likelihood of cannibalism. The results illustrated that females may act aggressively towards all males, regardless of their size and only the large ones survive. The paper also stated that female mating status is indeed an excellent predictor of the likelihood of sexual cannibalism.

In this paper, there were multiple suggestions of future work to be done. Previously we discussed the fact that for juveniles, food availability had a significant positive impact on fixed female size and fecundity. Johnson proposes that there needs to be further work done to determine whether these factors offer early maturing females a selective advantage. Next, it has been documented that there are varying sex ratios throughout the breeding season for these fishing spiders. It is advised that future empirical and theoretical work focus on the temporal patterns of male abundance and female aggression towards males throughout the breeding season. Next, juvenile voracity remains to be worked on. In this study, juvenile voracity was not measured and fixed size was artificially enhanced. For future studies that were being conducted while this paper was proposed, it was important to test whether the most voracious juveniles would be the most likely to attack their mates. In addition, in order to achieve a better approximation of the costs of aggression to female fertilization rates future field surveys of egg sac fertilization rates along with experimental manipulations of available males should be conducted. Finally, it is necessary to look into whether the male being eaten is a qualitative addition to the female’s diet.

The next paper to be discussed, “Precopulatory sexual cannibalism in fishing spiders (Dolomedes triton): a role for behavioral syndromes,” is also written by Johnson (1) and picks up where the previous paper left off. This paper is significant since it is the first in-depth test of the aggressive spillover hypothesis. In this particular study, support was found for 3 characteristics of the aggressive spillover hypothesis. It was discovered that increased fecundity, large adult size, and high feeding rates resulted from voracity towards hetero-specific prey. Next, it was shown that juvenile and adult voracity are positively correlated. And third, precopulatory sexual cannibalism is positively correlated with voracity towards hetero-specific prey. In addition, upon further investigation antipredator behavior revealed positive correlations between boldness towards predators, voracity, and precopulatory sexual cannibalism. After putting all of these results together, it was shown that precopulatory sexual cannibalism is a part of a behavioral syndrome that covers at least three key contexts: foraging, predator avoidance, and mating. In
systems characterized by precopulatory sexual cannibalism mating, foraging, and predator-prey issues are distinctively inseparable. This is because males are potential mates while also being prey items, and females are potential mates while being predators too (4). These suites of associated behaviors or behavioral syndromes seem to be having an effect on the sexual selection of precopulatory cannibalism. It is possible that natural selection is attempting to remove this behavior since it appears to be maladaptive, but the constraints by these behavioral syndromes are slowing down, or impeding the process. In order to test these behavioral syndromes, hunger was not controlled during the experiment. By not controlling hunger, a syndrome of voracity was tested for in spite of hunger differences rather than in the absence of hunger differences. The results from this support the idea that precopulatory sexual cannibalism is indicative of a spillover of aggression from a broader syndrome of correlations. As shown, this paper provided multiple pieces of support for the aggressive spillover hypothesis, but showed no support in favor of the adaptive foraging hypothesis. So what does this mean if one shows support for both, and another shows support for just one? The results from both of these papers tell us that none of the evidence for or against either hypothesis can mutually exclude the other. It is also very possible that each hypothesis explains sexual cannibalism at different stages of the mating sequence (3). Yet again, there is still much work to be done to reveal more answers to this puzzling form of mating behavior.

This paper informs us that there is still a vast amount of work to be done in order to understand sexual cannibalism and how natural selection is acting up it. The first place to start in this field would be to try to document voracity correlations across the entire juvenile life cycle, rather than just part of it. There could be a link throughout this period that we’re missing that could possibly lead us to some more answers. More ongoing work should be concerned with whether or not voracity in the mating context involves fertility costs. Next, there are some more costs and benefits that need to be weighed. We need to look into whether the feeding benefits can outweigh the costs of unsuitably elevated levels of boldness towards predators. Another way in which we may learn more about sexual cannibalism is to look at the same individuals in various developmental and behavioral contexts. Finally, another possible constraint that is mentioned in addition to behavior syndromes is the genetic constraints. These genetic constraints limit the variety of behavioral flexibility in aggressiveness so that some individuals tend to be highly aggressive while others continue to be less aggressive (4). There could be an explanation to this precopulatory sexually cannibalistic behavior lying in the genes. More work should be done to see if there is any one gene in particular that constrains the flexibility of aggressive behavior.

While both of these papers present excellent data to explain possible reasons for sexual cannibalism and whether or not it is adaptive, they both fail to adequately explain why the males allow this to happen. As we previously discussed, males are both potential mates and prey while females are both potential mates and predators. If there is even a chance of a female being a predator instead of a mate, why would a male risk his life to find out? Could it be that he is willing to make such a great sacrifice in order to ensure that his genes will live on for another
generation and possibly more? Does the male rarely encounter females and deems it a worthy opportunity to mate? Or could there be another explanation that would make the male’s behavior much more understandable to those who are dedicating time to find an answer to the perplexing phenomenon.

This is where the idea that pheromones are controlling some of this behavior comes into play. But first, what are pheromones? Pheromones are a chemical produced by organisms that signal its presence to other members of the same species (5). In the insect world, pheromones are used to signal many different things. For example, queen bees are capable of emitting a pheromone that affects the development of worker bees, ants are able to recruit other members of their colony to a food source, and aphids can emit an alarm pheromone that tells other aphids nearby to flee from a nearby predator. Pheromones are also known to be of particular importance in sexual behavior for these organisms. This powerful scent is what many males and females use in order to attract mates. It should be stated that insects’ responses to pheromones are automatic; therefore, they have no control over whether they respond to them or not (6). This is the reason why many pest control companies use an insect’s own pheromones against them to lure them to the poison that will in fact kill them. The insects have no choice but to be led to their own deaths. Is it possible that many sexually cannibalistic organisms are doing the same thing? If in fact female insects, arachnids, and amphipods are using a sexual pheromone to lure males to their death, this whole act of sexual cannibalism would seem much less confusing. This knowledge would allow us to see that the males are not sacrificing themselves, but are rather being tricked instead.

If in fact males are being lured to their deaths by females so easily how have they not evolved a way to prevent their imminent deaths? We know there is an evolutionary arms race between and amongst species, with each one trying to outdo the other. In these cases specifically it is males versus females. So if there is a way for males to evolve to act against this sexual cannibalism, what is taking so long? There are many possible explanations to this. It could be that the males are in fact currently evolving a way to prevent themselves from falling victim to these sexually cannibalistic traps, but we know that evolution takes an incredible amount of time so we just might not be able to see it taking place. It could also be that females and males were previously having such a hard time mating that this was the best evolutionary option. Is this the way things are supposed to be, or is another shift in the sexual cannibalism dynamic going to occur? These are questions that must remain unanswered for the time being, as we do not know the true nature behind this evolutionary process and we do not know how long this evolution may take place.

In conclusion, scientists still are not certain as to why females sexually cannibalize males, or why males allow themselves to be sexually cannibalized. There are two front-running plausible explanations for this occurrence which have both been supported by scientific data. It could very well be that both the aggressive spillover hypothesis and the adaptive foraging hypothesis are related to one another and are both responsible for this exceptional phenomenon.
What future researchers now need to do is focus on the role that pheromones play in this picture. It is very clear that pheromones could possibly have a large role in this whole occurrence. We know need to learn exactly how pheromones are used in this event and if they are the main or only reason why males are susceptible to this sexual cannibalism. Once this mystery of why the males allow this to happen is solved, the whole situation is going to take on a whole new perspective. If proven, scientists can then stop looking into why this behavior is adaptive to the males, and instead see that they are purely not in control of the situation and have no choice but to become sacrifices. Although we may develop more insight to this perplexing event, we still may never know the true reason why sexual cannibalism originated and why it occurs still today.

![General hydrocarbon chain - basis for all organic compounds, including pheromones](image)

<table>
<thead>
<tr>
<th>Chemical Group</th>
<th>Chemical Structure</th>
<th>Pheromone example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td><img src="image1" alt="Chemical structure" /> OH</td>
<td>Attractant for tea torrix moth, sunflower moth, and cotton bollworm</td>
</tr>
<tr>
<td>Aldehydes</td>
<td><img src="image2" alt="Chemical structure" /> O</td>
<td>Tobacco budworm pheromone</td>
</tr>
<tr>
<td>Carboxylic Acid</td>
<td><img src="image3" alt="Chemical structure" /> O</td>
<td>Sex pheromone for Pacific coast wireworm</td>
</tr>
<tr>
<td>Acetates</td>
<td><img src="image4" alt="Chemical structure" /> OCOOHg</td>
<td>Peach teabugger</td>
</tr>
<tr>
<td>Ketones</td>
<td><img src="image5" alt="Chemical structure" /> O</td>
<td>Yellow-banded fireworm</td>
</tr>
<tr>
<td>Esters</td>
<td><img src="image6" alt="Chemical structure" /> O</td>
<td>Soybean looper</td>
</tr>
<tr>
<td>Epoxides</td>
<td><img src="image7" alt="Chemical structure" /> O</td>
<td>Gypsy Moth</td>
</tr>
</tbody>
</table>

Examples of different pheromones used by various insects and the chemical group they are derived from (7).
<table>
<thead>
<tr>
<th>Insect</th>
<th>Compound</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugar beet wireworm (Limonius californius)</td>
<td>Valeric acid</td>
<td><img src="#" alt="Valeric acid structure" /></td>
</tr>
<tr>
<td>Honeybee (Apis mellifera)</td>
<td>9-Keto-2-decenonic acid</td>
<td><img src="#" alt="9-Keto-2-decenonic acid structure" /></td>
</tr>
<tr>
<td>Cabbage looper (Trichoplusia ni)</td>
<td>cis-7-Dodecen-1-ol</td>
<td><img src="#" alt="cis-7-Dodecen-1-ol structure" /></td>
</tr>
<tr>
<td>Fall army worm (Laphygma frugiferda)</td>
<td>cis-9-Tetradecen-1-ol</td>
<td><img src="#" alt="cis-9-Tetradecen-1-ol structure" /></td>
</tr>
<tr>
<td>Black carpet beetle (Alticarus angustus)</td>
<td>trans-3-cis-5-Tetradecadienoic acid</td>
<td><img src="#" alt="trans-3-cis-5-Tetradecadienoic acid structure" /></td>
</tr>
<tr>
<td>Silk worm moth (Bombyx mori)</td>
<td>trans-10-cis-12-Hexadecadien-1-ol</td>
<td><img src="#" alt="trans-10-cis-12-Hexadecadien-1-ol structure" /></td>
</tr>
<tr>
<td>Gypsy moth (Porthetria dispar)</td>
<td>d-10-Acetoxy-cis-7-hexadecen-1-ol</td>
<td><img src="#" alt="d-10-Acetoxy-cis-7-hexadecen-1-ol structure" /></td>
</tr>
<tr>
<td>Male butterfly (Lycosa cures cures)</td>
<td>Cetyl acetate</td>
<td><img src="#" alt="Cetyl acetate structure" /></td>
</tr>
<tr>
<td>Male butterfly (Lycosa cures cures)</td>
<td>cis-Vaccenyl acetate</td>
<td><img src="#" alt="cis-Vaccenyl acetate structure" /></td>
</tr>
<tr>
<td>Pink bollworm (Pectinophora gossypiella)</td>
<td>10-Propyl-trans-5,9-tridecanol acetate</td>
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<tr>
<td>Male butterfly (Lycosa cures cures)</td>
<td>2,3-Dihydro-7-methyl-1 H-pyrolizidin-1-one</td>
<td><img src="#" alt="2,3-Dihydro-7-methyl-1 H-pyrolizidin-1-one structure" /></td>
</tr>
</tbody>
</table>

Examples of insect sex hormones (8).
Bibliography


The Effects of Plastic Containers on Food

Sara Blankemeyer
April 20, 2012
Abstract

Plastic has become a ubiquitous aspect of every day life. Due to modern advances in fabrication and wide spread utilization in food packaging. In the past few years, growing concern of plastics and health side effects have become a rising concern of the public.

All over the world in nearly every culture, plastic is used as a main component in everyday life. Its application permeates everything from medical equipment to baby bottles.

The first man-made plastic was created by Alexander Parkes who publicly demonstrated it at the 1862 Great International Exhibition in London. He called his material Parkesine\(^{(1)}\) was an organic material derived from cellulose that once heated could be molded, and retained its shape when cooled. The mixture was put on a heated rolling machine from which some of the solvent was then removed. While still in the plastic state the material was then shaped by dies or pressure.\(^{(1)}\) Over the years, many different types of plastics have emerged such as thermoplastic polymers. One type of thermoplastic polymers are polycarbonates. They are typically fashioned into food containers.

Plastics in food packaging help keep food fresh and safe, and protects against spoilage. Plastic packaging provides a hygienic and safe environment for foods and medicine by protecting against contamination while keeping foods fresh throughout use. It also often provides tamper-evident features (shrink bands, tear strips, etc.) for food and medicine. A wide range of foods - from fresh produce to dairy products to beverages - can be transported over long distances and stored safely without compromising the quality of the product. This also helps prevent food waste. Polycarbonates are cheap and easy to manufacture, hence their popularity in many food containers. However, with the tradeoff of low cost manufacturing may cause health related problems associated with the degradation of the plastic.\(^{(1)(2)}\)

The main structure of polycarbonate material is produced by the reaction of bisphenol A \(\text{C}_{15}\text{H}_{16}\text{O}_2\) or \((\text{CH}_3)_2\text{C}(\text{C}_6\text{H}_4\text{O})\) and phosgene \(\text{COCl}_2\).\(^{(2)}\)

![Chemical structures of bisphenol A and phosgene](attachment:image.png)
Polycarbonate

Polycarbonates are created through the following mechanism. The first step in making a polycarbonate is treating the bisphenol A with NaOH. The hydroxyl group is going to take a proton away and deprotonate the bisphenol A. When this happens the hydroxyl group becomes a water molecule, and the bisphenol A, an alcohol, will then become a sodium salt. Then the same reaction happens again on the other alcohol group of bisphenol A. \(^{(3)}\)

The bisphenol A has become a salt and will react with the phosgene COCl\(_2\). The oxygen in the bisphenol A salt now has a negative charge on it. The negative charge can donate a pair of electrons to the carbon atom in the phosgene. When that carbon gets a new pair of electrons from the bisphenol A salt, it releases one of the pairs it had been sharing unequally with the carbonyl oxygen. This pair places itself on that oxygen giving it a negative charge. \(^{(3)}\)
The electrons on that oxygen will go back to the carbon, reforming the carbon-oxygen double bond. The carbon now has ten electrons and wants to get rid of them to satisfy its 8 electrons. The two electrons that leave are the pair the carbon has been sharing with one of the chlorine atoms. So the chlorine and its electrons get released from the molecule. The molecule left is called a chloroformate. The chloride ion will bond with the sodium ion to form NaCl. (3)

A repeated attack of the bisphenol A will attack the chloroformate similar to the phosgene did at the beginning of the reaction.
The molecules go through a similar intermediate and moving of electrons to get the carbonate containing species.\(^{(3)}\)

The salt group on the newly formed molecule will react with more phosgene and become polycarbonate.\(^{(3)}\)
The U.S. Food and Drug Administration (FDA) carefully reviews the safety of packaging food with plastics. New material is permitted for use only after the FDA is satisfied that the manufacturer's test data ensures it is safe to use with food. Currently there are seven classes of plastics used in packaging. Currently in the USA there are no regulation prohibiting certain types of plastics, which have been linked to health related problems, of which Bisphenol –A (BPA) has drawn the most interest.\(^1\)

In 1953, Dr. Hermann Schnell of Bayer in Germany and Dr. Dan Fox of General Electric in the United States independently developed manufacturing processes for a new plastic material, polycarbonate, using BPA as the starting material. The new polycarbonates had properties in which were shatter resistance high heat resistance and optical clarity which many plastics did not have prior to the 1950’s. The actual commercial production began in 1957 in the United States.\(^2\)

Bisphenol A (BPA): BPA is commonly used in the manufacturing of polycarbonates and epoxy resins which are found in food containers and linings of cans. BPA is formed by a strong acid, which is synthesized by the condensation of acetone with two identical phenol functional groups. The following reaction of acetone and phenol to make Bisphenol A is\(^3/4\)

\[
\begin{align*}
\text{HO} & \quad + \quad \text{O} \quad + \quad \text{OH} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \quad \text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{O} & \quad \text{H}^+ \quad \text{H}_2\text{O} \\
\text{HO} & \quad \text{HO}
\end{align*}
\]

BPA is an estrogen-like endocrine disruptor that is said to hydrolyze and leach into foods. The controversy lies within the event of hydrolysis (degradation by water, often referred to as leaching), which can releases bisphenol A. The chemical reaction of polycarbonates and the releasing of bisphenol A\(^5/6\)

\[
\frac{1}{n} \left[ \text{OC(OC}_6\text{H}_4)\text{CMe}_2 \right]_n + \text{H}_2\text{O} \rightarrow \left( \text{HOC}_6\text{H}_4 \right)\text{CMe}_2 + \text{CO}_2
\]

When a polycarbonate is placed under high heat or alkaline conditions the polymer breaks down into freeform BPA, which are linked to health concerns. Currently there is much research being done to show a link between exposure to BPA through
plastic food containers. Links such as cancer, heart disease, early childhood development, and altering the structure of DNA (mutagen) are some of the findings of the effects plastic containing BPA have on humans.

In a study from Kyushu University reveals that BPA was found to be a xenoestrogen. Xenoestrogens are compounds that mimic esterogenic substances found in the endocrine system but are made from different chemical structure. BPA binds to estrogen-related receptor gamma (EER gamma) but not to the estrogen receptor. Proving that BPA imitates estrogen and is an xenoestrogen. This does not change the internal structure of the ERR gamma. BPA binding to ERR-γ preserves its basal constitutive activity and protect it from deactivation. There is still much to be known about xenoestrogens, but these compounds lead to under developed genitals in mice fetuses and reproductive system under development and abnormalities.

Another research study, from the University of Cincinnati has shown a link in plastics to metabolic syndrome in human tissue. Once again bisphenol A was found as the initial cause of this health related problem. They found that exposing human tissues to BPA levels within the range of common human exposure resulted in suppression of a hormone that protects people from metabolic syndrome. Adiponectin is the hormone responsible to regulate insulin sensitivity in the body. BPA suppressed the hormone, adiponectin which create a higher risk for metabolic syndrome. Without this hormone, people have higher blood levels of sugar and lipids and a lower response to insulin. Overall, this syndrome can lead to health problems such as coronary artery disease, stroke and type 2 diabetes.

Many laboratory tests have confirmed that they do indeed cause harmful effects to many lab animals. An animal study using mice unveiled a link between environmental estrogens (BPA) and insulin resistance. This study also concluded that the higher exposure to BPA could lead to a higher risk of type 2 diabetes mellitus, hypertension and dyslipidemia. Unfortunately most studies are in animals and not actually on human research participants.

One survey conducted by the US Centers for Disease Control and Prevention detected BPA in the urine of 93% of people age 6 years and older. The full effects on humans are still unknown because of the complexities of the human body. The effects that can be seen in an organisms exposed to an endocrine disrupting chemical depends on which hormone system it targets. Further understanding of the endocrine system needs to be established before a full assessment of what true effects the BPA can have on an organism.

The growing concerns of BPA exposure has caused many government to take drastic measures. Countries like Canada have placed BPA on the "toxic substance" list and banned the use of BPA in baby bottles. The LA Times newspaper pointed out a finding that the FDA has spent over $30 million dollars to investigate the hazards of BPA on the body. Many of the studies conducted have been in the past ten years due to the rise of concern of BPA and advancing technologies. In 2011, it was reported that "almost all plastic products" sampled released chemicals with esterogenic activity, although the researchers identified plastics which did not leach chemicals with esterogenic activity. Many manufactures of plastic containers, Nalgene (a water bottle manufacture)
are taking out BPA from its plastic containers because of the growing concern about the chemical.\textsuperscript{10} However there are still no conclusive evidence linking BPA to cancers and other adverse health effects.\textsuperscript{11}

I believe that plastic will remain a staple in human life far into the future. The benefits of plastic in food packaging often outweigh the side effects, mainly due to costs and abundance of plastic. However, the side effects could one day outweigh the positive convenience that plastic affords us. The most alarming negative side effect of plastic is leaching of BPA. There is still much research to be done before a true conclusion of the plastic and its harmful effects on the body. As more research and awareness is being done, from a consumer stand point, purchasing products free from BPA will easier to obtain. Almost eliminating the negative side effects of plastic on foods.
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Physics of Electrical Stimulation in Physical Therapy

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Abstract:

Electrical stimulation being used in physical therapy not only has a medical component, but has a physics component as well. The physics components of electrical stimulation relates to the history of electrical stimulation, the circuit mechanism, what the circuits are composed of, different types of electrical stimulation, and the effects of current flow through the body. The physics of electrical stimulation are of great importance when the outcome is based on whether the circuits and currents are correctly operated.

What Electrical Stimulation Is Used For:

Electrical stimulation is a rehabilitation modality with a wide range of clinical applications. These applications include but are not limited to muscle strengthening, pain control, facilitating the healing of recalcitrant wounds, resolution of edema and inflammatory reactions following injury or surgery, increase tissue blood flow, destroy bacteria, and exercise for paralyzed or non-paralyzed muscles. There are many professionals who use this modality to assist them in their practices, most importantly physical therapists.

History:

Electrical currents date back all the way to 46 AD, but it was not until the late 18th and early 19th centuries when there was interest for electrical currents within the medical field. Galvani, in 1791, was the first person, who recorded muscle contractions when a frog’s leg was in contact with metal. A few years later, Volta constructed a precursor to the battery which was termed a “Galvanic current”. Next, Duchenne mapped out “motor points,” locations on the skin where electrical stimulation specifically caused muscles to contract. Following Duchenne, in the 1830’s Faraday discovered moving a magnet induced bidirectional currents, this was termed a “Faradic current”. By using the Faradic current, Lapicque in 1905 developed the “law of excitation” which involved the relationship between intensity and duration of a stimulus. This is the determining factor of whether or not a muscle would contract. During 1948, Alexander Mauro and Samuel Black conducted a neurophysiological investigation. The goal was to find a device that could control the duration and repetition rate of a volley of electrical current delivered to the tissue under observation. Later in the 1960’s Melzack and Wall developed the gate control theory of pain perception, which stated the use of electrical currents could control the severity of pain. As recorded, there were many individuals that contributed to the development of currents and relationships involved in electrical stimulation.

Components of an Electrical Stimulation Machine:

Mauro and Black’s investigation in 1948 on neurophysiology and a device to control the duration and repetition rate of a volley of electrical stimuli that delivered electrical stimuli to tissue brought about the first electronic circuit. Mauro and Black discovered that the circuit had three main components- the gating, pacemaker tubes, and a univibrator. The gating is a cathode tube that operates in a cut-off condition and is activated for the desired time interval by a positive square wave that is generated by the univibrator. The width of the pulse determines the duration of time that the stimulation current is allowed to pass through the tissue and is controlled by a resistor-capacitor combination. The pacemaker determines the rate at which the univibrator pulses and the positive pulse generated is used to activate the univibrator and the rate of
discharge is controlled by a variable resistor. The input stimulus can be derived either from a sine wave, square wave, or other voltage sources. The components can be easily modified by varying the resistor-capacitor combinations of the pacemaker and univibrator circuits. This was the first electrical stimulation machine ever designed and became a useful tool to many medical professionals.

Figure 1 – Circuit of Components for an Electrical Stimulation Machine

1 – Metal chassis, 11 x 7 x 2 inches
2 – Thorodson transformer, T-21F11
3 – 6SN7
4 – Bargewell 2508, 45 v.
5 – Bargewell M 16, 45 v.
6 – Bargewell 5740, 6 v.
7 – 500 K, 1 W resistor
8 – 50 K, 1 W resistor
9 – 25 K, 1 W resistor
10 – 10 K, 1 W resistor
11 – 2 K, 1 W resistor
12 – 50 K, 1 W resistor
13 – 1.2 K, 1 W resistor
14 – 1.1 K, 10 W resistor
15 – 5.3 M, 1 W resistor
16 – 1 M, 1 W potentiometer
17 – 5 M, 1 W potentiometer
18 – 1 mfd. capacitor
19 – 0.5 mfd. capacitor
20 – 0.1 mfd. capacitor
21 – 0.08 mfd. capacitor
22 – 0.04 mfd. capacitor
23 – 0.02 mfd. capacitor
24 – 0.001 mfd. capacitors
25 – Toggle switch (S1)
26 – Single pole, double throw switch (S2)
27 – Single pole, 3 position, rotary switch (S3)
Basic Physics and Principles of Electricity:

The basic foundation of electricity is important to understand when conducting and performing electrical stimulation. Electromagnetic force, potential difference, and voltage are a few terms used to explain electricity which is the force created by an imbalance in the number of electrons at two points or “poles”. The cathode is an area of high electron concentration and the anode is an area of low electron concentration. There are also two different types of circuits: closed and open. A closed circuit forms when there is a complete path between two poles, allowing the flow of electrons. An open circuit is when there is an interrupted or incomplete path blocking the flow of electrons.

Once the basics of electricity are known, it is now possible to learn about the multiple types of currents used in electrical stimulation.

Types of Currents Used in Electrical Stimulation:

There are multiple types of current used in electrical stimulation. The different types of current are a direct current (DC), an alternating current (AC), or a pulsed current. The terms “direct” and “alternating” refer to the uninterrupted flow of electrons, where “pulsed” refers to the electron flow being interrupted by time periods of no electron flow. When deciding which current to use, there are four distinct properties to consider: amplitude, isoelectric point, pulse duration, and pulse charge. Amplitude which is the maximum distance the pulse rises above or below the baseline. Isoelectric point is the baseline where the electric potential between two poles is equal and no current flow occurs. Pulse duration is the horizontal distance necessary to complete the wave. Pulse charge is the total area within the waveform which represents the amount of current the pulse contains. Within each type of current there are sub-classes of currents.

Direct Currents (DC):

Direct currents only have one class; this current is uninterrupted and has a unidirectional flow of electrons. DC has a basic pattern of a square wave and has continuous flow on ONLY one side of the baseline when electrons travel from the cathode to the anode. The direct current uses the term “galvanic” to express the current. An example of a direct current in physical therapy is the use of iontophoresis which uses a current to disperse medicine into the tissues.

Alternating Currents (AC):

Alternating currents have only one class; this current is uninterrupted and has bidirectional flow of electrons. Alternating currents have no positive or negative poles and the electrons shuffle back and forth between two electrodes, which alternate being positive and negative. The direction of flow alternates between positive and negative in a cyclical manner. In AC the cycle duration and frequency are important and inversely related, meaning that "as the duration of the cycles increases, fewer cycles per second can occur". An example of an alternating current in physical therapy is Interferential Stimulation for pain control and/or muscle contractions.
Pulsed Currents:

Pulsed currents have three different classes; Monophasic, Biphasic, and Asymmetrical. The first type is Monophasic currents which is a unidirectional flow of electrons with periods of non-current flow. Monophasic currents have one phase per pulse and remains on one side of the baseline. The polarities of the electrodes are known, with one being the cathode and the other being the anode. An example of a Monophasic current in physical therapy is High Voltage Pulsed Stimulation for muscle contractions and pain control.

The second type is Biphasic currents, they are symmetrical and each phase is a mirror image of the other. The two phases occur on either side of the baseline, meaning the electrode carries both positive and negative charges and are equal in current flow. The pulse is balanced because the positive and negative currents cancel each other out, so there is no electrical charge. Biphasic symmetrical currents have been researched to be the most comfortable during therapy because of the low number of charges per phase. An example of a Biphasic current in physical therapy is Neuromuscular Electrical Stimulation.

The third type is Asymmetrical currents which is when the two phases do not mirror each other. When an asymmetrical current is involved in therapy each phase needs to be considered separately because each phase has a different shape. There are two types of Asymmetrical currents: Balanced and Unbalanced.

Balanced currents have two phases that carry equal electrical charge and the shape of the pulse allows for greater anodal or cathodal effects, but the net electrical charge will be zero over time.

Unbalanced currents have two phases that carry unequal charges. Like the Balanced currents the shape of the pulse allows for greater anodal or cathodal effects, but unlike the Balanced currents over time there is a net electrical charge.

These are the three types of currents that make up different types of Electrical Stimulation.
Types of Electrical Stimulation:

Russian current stimulation, Interferential current stimulation, Transcutaneous Electrical Nerve Stimulation (TENS), and Iontophoresis (Ionto) are the four main types of electrical stimulation.\(^4\)

**Russian Current Stimulation:**

Russian current stimulation is performed by using a “2.5-kHz AC, applied in 50-Hz rectangular bursts with a burst duty cycle of 50%”. Meaning, the current will pulse on and off for the duration of the stimulation. The duration of the burst or pulse is 10 milliseconds at the 50-Hz. Most professionals use Russian current stimulation when conducting therapy because this stimulation is beneficial for muscle strengthening and poses lower risk for damaging tissues.\(^6\)

**Interferential Current Stimulation:**

Interferential current stimulation is performed by applying two pairs of electrodes diagonally to produce an interference effect on the targeted area.\(^6\)\(^7\) Interferential current stimulation is used during therapy because the high frequencies used to send current do not stimulate the nerves, only the muscles, so no pain is associated with this stimulation.\(^7\)

**Transcutaneous Electrical Nerve Stimulation:**

TENS has been the stimulation method used since the 1950’s because it was the first way that produced depth-efficient stimulation of nerve and muscle.\(^6\) The main reason professionals’ use TENS in their practice is for pain control of affected areas.\(^4\)

**Iontophoresis:**

Iontophoresis is conducted from a low-voltage direct current circuit. Ionto is used when medication needs to be administered through the skin to the affected area. Ionto is performed by generally using a form of Dexamethasone, generally Dexamethasone Phosphate due to the negative charge and solubility in water, depending on whether the medication is needed as an anti-inflammatory or for pain relief. Two electrodes are used by placing the electrode with medicine directly over the affected site and the other electrode 4-6 inches away, allowing enough distance for the medication to spread over the entire affected area.\(^4\) The purpose of the current is to direct and move the medication into the tissues.

Russian current stimulation, Interferential current stimulation, Transcutaneous Electrical Nerve Stimulation (TENS), and Iontophoresis (Ionto) are the four main types of electrical stimulation professionals’ use in their practice. The patient’s injury (type and location) determine which type of stimulation is used.

**How a Current Moves Through the Body:**

The human body is composed of water, which plays a significant role in human life, but is also necessary for an electrical current to flow through the body. Another important factor in allowing current to pass through the body is knowing the anatomy and physiology of the area being stimulated. Electrical stimulation has different effects on excitable cells (nerves, muscle fibers, cell membranes, etc) and non-excitable cells (bone, cartilage, tendons, adipose tissue, and
Excitable tissues are composed of 70-75% water content making these tissues easy contenders for electrical stimulation. Due to the composition of skin there is only one primary way for the current to enter the body and it is through a series circuit. Once the current passes into the tissues, it starts moving in a parallel circuit. The parallel circuit allows the current to follow the path of least resistance using the muscles, nerves, and blood to spread through the affected area.\textsuperscript{8}

![Diagram of electrical current flow](image)

**Figure 8 – Flow of Electrical Current\textsuperscript{8}**

The third factor allowing current to move through the body depends on the electrodes. Electrodes introduce current to the body. The electrodes are connected to the generator by electrode leads which transmit the electrons from the generator, to the electrodes, and then to the patients. Two electrode leads are required to make a complete and closed electrical path for the electrons to travel. To ensure the circuit is closed, one electrode from each output must be firmly attached to the patient's skin. The placement of the electrodes on the skin creates a capacitor between the electrode and the excitable tissues; the passing of ions into the skin creates a parallel resistance.

The most common and efficient type of electrode use in professional settings are "carbon-rubber electrodes because they deliver the most current at the lowest skin impedance (about 200 ohm's) allowing for a more comfortable stimulation".\textsuperscript{8} Knowing how electrical current moves through the human body during electrical stimulation is crucial because everyone has a different maximum muscle stimulant level.

**Conclusion:**

Electrical stimulation is closely related to physics based on supported evidence of the history of electrical stimulation, the circuit mechanism and composition, different types of currents, different types of electrical stimulation, and the effects of currents through the body. The physics of electrical stimulation are of great importance when the outcome is based on whether the circuits and currents are correctly operated.
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Oxytocin – The Cuddle Hormone
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Presented for: Dr, Mancini
Science Symposium
Organic Chemistry
Abstract:

This paper discusses the hormone Oxytocin and the effects or effectiveness it has on the human body, with an emphasis on social bonding and sexual reproduction. It shows a positive correlation between oxytocin and social relationships. Additionally this paper will look at the use of oxytocin in the treatment of some social disorders such as autism, schizophrenia, social phobia, anorexia nervosa, depression (especially that of postpartum depression) and obsessive compulsive disorder. To date no significant research has been preformed to indicate the treatment of these disorders other than an adjunctive treatment of autism, this showed positive result and should receive further research and/or evaluation for efficacy and effectiveness.

Introduction:

When one thinks of social interactions, building strong healthy relationships, and even the feeling of being in love the thought of chemical reactions taking place within once body doesn’t necessarily come to mind. Oxytocin is a hormone that could very well play a key roll in some of the interactions that take place amongst individuals everyday. Oxytocin was first recognized for its role in childbirth, which is inducing contractions during labor and assisting with lactation. In the years that followed it gained popularity as a “love drug” when research studies were performed on its effects dealing with sexual pleasure and social bonding.

In a medical setting oxytocin is used to induce labor, however arguments have been made for the medical use of this hormone in a plethora of ways to aid in mental disorders. Such conditions as; autism, social phobia, obsessive-compulsive disorder, depression, maternal-infant bonding to name a few and many other aspects dealing with psychological responses in the brain when given certain stimuli.

Chemical Composition, Synthesis, Storage and Release in the Body:

Oxytocin (OT) also known as Alpha-hypophamine, is a neurohypophysial hormone, meaning it’s connecting the hypothalamus and the neurohypophysis. The structure of OT is a peptide containing nine amino acids (a nanapeptide). The sequence is cysteine – tyrosine – isoleucine – glutamine –
asparagine – cysteine – proline – leucine – glycine (CYIQNCOLG). Oxytocin has a chemical formula of C_{43}H_{66}N_{12}O_{12}S_{2} and a molecular weight of 1007.23 g/mol. OT is similar in many ways to another hormone in the body called vasopressin. Vasopressin differs from OT by two amino acids but the two are believed to share some common aspects dealing with social bonding and sexual arousal.

OT is made in the hypothalamus and released into the blood from the pituitary gland. The hormone is also made by neurons in the paraventricular nucleus that project into the brain and to the spinal cord. Oxytocin-expressing cells are located in other areas depending on the species. In the pituitary gland, oxytocin is packaged in large, dense-core of vesicles, and bound to neurophysin I a large peptide fragment of precursor protein molecule from which oxytocin is derived by enzymatic cleavage.

Secretion of oxytocin is regulated by the electrical activity of the oxytocin cells in the hypothalamus. These cells generate action potentials that propagate down axons to the nerve endings in the pituitary, which are released by exocytosis when the nerve terminals are depolarized. OT neurons during this action/potential proceed to make other peptides, including corticotropin-releasing hormone (CRH) and dynorphin, as examples, which act locally. The magnocellular neurons that make oxytocin also make vasopressin, which is molecularly similar, in structure to that of OT.

Oxytocin once secreted from the pituitary gland cannot re-enter the brain because of the blood-brain barrier. Instead, the behavioral effects of oxytocin are thought to reflect release from centrally projecting oxytocin neurons, different from those that project to the pituitary gland. Oxytocin receptors are expressed by neurons in many parts of the brain and spinal cord, including the amygdala, ventromedial hypothalamus, septum and brainstem.

**History:**

In 1895 Oliver and Schäfer were the first to discover the biological effects of the pituitary gland on the body. The research performed showed that extracts of the pituitary when injected into mammals increased blood pressure. In 1906 Sir Henry Dale discovered that by taking extracts from the human posterior pituitary gland induced contractions in the uterus of pregnant cats. Oxytocin comes from the Greek word οὐκοξυξ, ῥοξοξξ, meaning "quick birth." Sir Henry Dale came up with the term after the research performed with the pregnant cats. It was 47 years after the work of Sir Henry Dale that oxytocin was first synthesized. This made OT the first polypeptide hormone ever to be sequenced and synthesized by Vincent du Vigneaud who was awarded the Nobel Prize in 1955 for his achievement and contribution to the science community.
One of the most significant moments in the history of oxytocin was in 1952 when the first crystalline derivative of the oxytocin hormone could be isolated. OT was also obtained from hog posterior pituitary glands, which had approximately the same distribution curve as that from beef glands. Of interest to note is that OT obtained from the hog pituitary gland had the same potency and amino acid composition as that obtained from beef. The synthetic product was effective in stimulating labor in full term women, and in the ejection of milk. When the synthetic form was introduced into the body it could not be distinguished from the naturally occurring oxytocin in this action. Approximately 1 µg of either the natural OT or the synthetic form given intravenously to a woman about to give birth induced milk ejection in 20-30 seconds.³

The hype over this hormone began in the 1990’s when research discovered that breastfeeding women are calmer in the face of exercise and psychosocial stress than bottle-feeding mothers.⁴ More recent research has shown this hormone might play other roles in the body when it was realized that oxytocin levels are high under stressful conditions, such as social isolation and unhappy relationships. Animal studies first linked the hormone to bonding between mothers and newborns, as well as in mating adults, giving oxytocin the nickname “cuddle” or “love” hormone.⁵ Further more OT has gained a lot of attention in its role of promoting trust. One company Vero Labs in Boca Raton, Florida has even put oxytocin into a perfume-like spray marketing it as “Liquid Trust”.⁵

Social Bonding and the Vole:

Social bonding is a hard subject to categorize or quantify. How can one say they are more apt to social cues then another, or that the reason someone feels a stronger connection to another individual is because they have more oxytocin. Variables like these are hard to prove, but research suggests that oxytocin might play a crucial roll in the social development and bonding of individuals.

(Figure 2.1 – Prairie vole⁴)
Monogamy is not common among the animal kingdom. Only about 3% of all mammal species participate in monogamous relationships. According to Darwinian theory of survival of the fittest, one of the components to determining one's fitness is the amount of offspring an individual has to carry on their genes. In a monogamous relationship the amount of offspring one can produce is limited by various factors such as; term of labor, amount of offspring possible per delivery, and sometimes the ability to provide for offspring's to ensure they develop into adulthood.

One species of the mammal kingdom that falls into the 3% of monogamous animals is that of the prairie vole. The prairie vole is a sociable rodent, found in the woodlands of Europe and Asia.³ Mating between prairie voles takes almost 24 hours and a tremendous amount of effort, but after which the prairie vole bonds for life. Once they bond for life they spend time with each other, grooming each other for hours and at the end they nest together and avoid meeting other potential mates.³ However a close relative of the prairie vole called the montane vole has a different type of behavior.

Montane voles have no interest in finding a partner for life. Their sexual behavior consists of “one-night stands”. The two different species of voles are more than 99% genetically alike. The genetic difference between the two voles is due to a handful of genes that affect their endocrine function. The endocrine system plays a primary role in regulating mood, growth, development, tissue function, metabolism, sexual function and reproductive processes.⁷ The foundations of the endocrine system are the hormones and glands. Hormones transfer information and instructions from one set of cells to another. (Figure 2.2 depicted above – montane vole⁸)

When prairie voles mate, two posterior pituitary hormones, oxytocin and vasopressin are released. If the releases of these hormones are blocked, prairie voles' sexual behavior changes similar to the montane voles behavior. In contrast if the prairie voles are given an injection of the hormones, but prevented from having sexual reproduction, they still form an inclination for their chosen partner. When the montane vole was given an injection of the same hormones, no change in behavior was produced.
Under further inspection the monogamous prairie vole has receptors for oxytocin and vasopressin in the brain regions associated with reward and reinforcement, where as the montane vole does not. This could possibly prove a link between oxytocin and social bonding but it is unclear as to weather or not humans fall into the faithful 3% category of the mammal kingdom.

**Sexual Reproduction and Behavior:**

Oxytocin is most widely known for the roll it plays in female reproduction with uterine contractions and milk ejection and even used clinically to induce labor. However, OT is also known for having effects on male reproduction dealing with the endocrine and paracrine roles. At the point of male ejaculation, a burst of oxytocin is released from the neurohypophysis into the systemic circulation and stimulates contractions of the reproductive tract aiding sperm release. Indisputable evidence shows that OT is produced within the mammalian testis, epididymis, prostate. Oxytocin receptors located through the reproductive tract facilities a local action for this peptide.

Within the male reproduction system penile erection is one of the most important sexual responses. The ability to achieve an erection is an essential component in reproductive success. Different neural and/or endocrine mechanisms are known in the successful regulation of penile erection. However, oxytocin happens to be one of them and one of the most potent agents known to induce an erection.

(Figure 2.3 – overview of the pararin/autocrine pathways)
“Yanagimoto et al. (1996) have demonstrated that electrical stimulation of the dorsal penile nerve and tactile stimulation of the glans penis elicits a specific activation of 40–50% of oxytocicnergic neurons in the PVN of the hypothalamus. Their study suggests that somatosensory information from the penis is transmitted to the PVN through the dorsal penile nerve. This afferent stimulud results in activation of oxytocicnergic neurons in the PVN leading to the release of hypothalamic OT at ejaculation establishing an OT-based reflex are in the male similar to the Fergusson reflex or the milk let-down reflex seen in the female.9 It could be considered that the systemic pulse of OT at ejaculation is goes hand in hand with the effect of OT on sexual behavior.

It has been found that there is a direct correlation with plasma oxytocin levels and the intensity of orgasms in both men and women. In males the rise in systemic OT at the point of climax could be suppressed by the use of naloxone (a prescription medication used in the treatment of heroin overdose10) this is probably caused by the naloxone acting on the opioid receptors in the posterior pituitary.9 Suppression of the systemic oxytocin pulse has not shown to inhibit ejaculation functions indication that it is not controlled by OT. However eight normal men took place in a double blind study examining the effects of naloxone on plasma oxytocin levels during sexual activity in men. Mean plasma oxytocin levels rose to 362% of baseline values at orgasm with the placebo (saline) but showed no increase with naloxone.11 Subjects in this study indicated a decrease in pleasure and arousal at the point of orgasm suggesting that the release of OT at the point of orgasm played a role in the over all sexual gratification.

Oxytocin in the Treatment of Social Disorders:

Oxytocin has been considered for the treatment of some disorders dealing with social interactions and relationships. Converging evidence from animal studies shows that oxytocin facilitates; social approach or willingness to make contact with new individuals of the same species, social memory or the ability to remember members of the same species encountered before, and bond formation resulting in longer lasting attachments. With this research it is suggested that OT could aid in the treatment of social disorders such as autism, schizophrenia, anorexia nervosa, obsessive compulsive disorder, depression (especially in the area of postpartum depression) and even social anxiety disorder by decreasing the over all amygdala activation and the stress response associated with social threat.13 However, the theory behind these disorders justify why oxytocin might be a potential treatment, no significant or extensive research studies have been preformed behind them with the exception of autism.

Autism is defined as a “neurodevelopment disorder associated with impaired social interaction, impaired communication, and repetitive or stereotyped behavior and interests.”13 The effects of OT appear that it would be helpful in bridging the gaps in
social deficits associated with autism. These would include increasing eye contact, improved bonding to important people, and an increase in empathy. It has been shown that there’s a reduced level of plasma OT in children with autism, and further more a variation in the oxytocin receptor gene (OXTR) relating both the diagnosis and the phenotype of autism.

One study took 16 males with Autism Spectrum Disorder (ASD) ages 12-19 and administered oxytocin intranasal. The subjects were shown photographs of stranger’s eyes and asked to identify what the stranger was thinking or feeling. The subjects who took oxytocin performed better at this test and the conclusion suggested that emotional understanding could become better when associated with autism with the use of OT.

In another study, oxytocin was given to ASD adult via nasal spray. This time studying increased gaze to the eye region. Oxytocin appeared to normalize the way social functioning was processed by regulating neural activity, attention and gaze in response to human faces. Oxytocin was also show to improve social learning in autism by the “Ball tossing” computer game; adults with ASD didn’t discriminate between a friendly stranger (one who tossed the ball back) from a (non-ball passing stranger) non-friendly. Yet once administer Oxytocin via nasal spray they were able to discriminate between the strangers. In two ways self-reported attitudes reporting liking and trust the friendly stranger and in terms of ball-tossing behavior, by tossing the ball more to the friendly stranger.¹³

**The Dark Side of Oxytocin:**

Although a substantial amount of research has been done to show the benefits of oxytocin and how it can positively influence social interactions and relationships there is another side to this wonder drug. There is some debate over the effects of oxytocin on individuals that received a large does of oxytocin when they were younger compared to thoughts that received very little growing up. Its suggested that if an individual received a smaller dose of oxytocin growing up that it could have the adverse affect and actually push them further away from social interactions. Also since oxytocin increases trust and social bonding there could be a potential for abuse. People are more apt to donate to charities, or trust complete strangers when given a direct dose of oxytocin, which could lead to potentially another “date rape” drug on the markets.

**Concluding Remarks and Personal Statement:**

The hormone oxytocin has shown a great deal of potential in understanding different social interactions, relationships, the role it plays in sexual reproduction and even in the treatment of some social disorders. However all of the aspects of this hormone are not yet fully understood. Research suggests a positive correlation between this hormone and many aspects of human existence. Oxytocin does have the potential to be abused since in can increase trust in people unknowingly and should be regulated.
I chose to write this paper on oxytocin because the possibilities of this hormone are endless. The fascination of chemical reactions occurring in the mind and body when just meeting new people or being in a social setting without even knowing it's happening is amazing. The reason I want to go to pharmacy school is because of inner working of how medications and hormones like oxytocin can make a big difference in one's life.
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The Prospect of Carbon Nanotube Technology
Jimmie Buhrmaster
4/18/2012
PHY 112
Dr. Durandet
Abstract

Recently it has been discovered that carbon can bond with itself in a way to form cylindrical "tubes" nanometers in diameter, which are millions of times longer than they are wide. These are known as carbon nanotubes and their structure allows them to be incredibly durable. They also have recently been discovered to have amazing thermal, electrical, kinetic, and optical properties. There are many implications for the possible uses of these amazing structures in technology from lighter, more durable sports equipment to space elevators, synthetic bone tissue, and a possible solution to the gas crisis.

Structure

Carbon atoms bond very well with one another because they have four valence electrons, each of which creates an excellent site on all four sides for forming covalent bonds with other atoms.

\[ \text{\textbullet} C \text{\textbullet} \]
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\[ \text{\textbullet} C \text{\textbullet} \]
\[ \text{\textbullet} C \text{\textbullet} \]

This allows carbon atoms to bond with each other to form long, extensive networks of bonds. The physics of the lattice structure that is formed when carbons bond together creates different kinds of compounds called allotropes. Another well-known compound carbon allotrope is graphite. In the case of carbon nanotubes the carbon network is the same as graphite, but it is rolled into a cylindrical structure.

The bonds that form in these cylinders are \( sp^2 \) hybridized, which means that the tube will be composed of six-membered rings that are attached to one another with each carbon sharing a bond with three neighboring carbons. The hybridization is the number and types of electron orbitals of the carbon atoms that will be filled. In this case the carbons will share electrons in the p-orbital, which will cause an electron cloud to be formed. This electron cloud has an attractive force, which will pull the bonds in tighter making them stronger and harder to break.

The cylinders can be capped off at the end by what is known as a "Bucky ball hemisphere" where the carbons bond together to form a spherical shape, half of which
caps off the end of the nanotubes. The name comes from another well-known carbon structure, buckminsterfullerene or the “Bucky ball”, which was discovered by in 1985 by Robert Curl, Harold Kroto and Richard Smalley, but is named after futurist and inventor Buckminster Fuller. The Bucky ball also has similar properties to those of the carbon nanotubes.

The structure of the carbon nanotubes can differ in various ways depending on the way the rings orient themselves with one another. Bond angles come from the physical, intermolecular forces that exist between protons and electrons, which repel one another. The conditions under which the tubes are synthesized largely affects the bond angles that the bonds will take and thus affect the structure of the tube itself. There are three kinds of lattices that can form into the tube shape, known as armchair, zigzag, and chiral. Each different kind of lattice structure that the nanotube can take yields different kinds of electrical, optical, thermal and kinetic properties.

The diameter of a carbon nanotube varies based on the type of lattice structure of the tube and the chirality of the tube. The average diameter of a single-walled carbon nanotube is about 1.2nm. The smallest carbon nanotube ever to be measured is an armchair tube 3Å(0.3nm) in diameter.

Carbon nanotubes have also been found to form around one another to create multi-walled tubes. Multi-walled nanotubes have been found to be even more durable than single-walled nanotubes, and contain even more intriguing properties. This happens because the individual properties of the single-walled nanotubes that make up a multi-walled nanotube each lend themselves to the overall character of the multi-walled nanotube. Therefore, the possibility to mix and match the characteristics of single-walled carbon nanotube properties to perform a desired function is there.
Researchers at IBM have actually found a way to wrap ropes of carbon nanotubes around and bond with themselves to form rings\(^3\). The rings typically have a radius of 0.7 microns. The properties of the ring are generally the same also. Because the rings cannot have multiple walls and cannot be made very large the application of the rings may only be in adsorption or to be used for their durability.

Properties

The first characteristic that stands out about why carbon nanotubes are so special is in the fact that they are so small. Their diameter is measured in nanometers (1 x 10\(^{-9}\)m or 1 billionth of a meter), which is just barely bigger than the atoms themselves. Also the length that these tubes can have is millions of times longer than their width. Nothing like this is known in the physics world and it could have significant implications for all kinds of technology.

Not only are the nanotubes extremely small, but they also have incredible properties that they lend to whatever they are being used for.

First of all nanotubes are extremely durable. When carbon bonds to itself it creates a lattice structure. One of the better-known carbon allotropes is diamond, the most durable known compound on Earth. In some cases carbon nanotubes are more durable than diamonds\(^4\) making them the most durable substance known in the world. Theses nanotubes are so strong because of the sp\(^2\) bonding that takes place between the carbons as discussed before.

Nanotubes also have amazing electrical properties. In single-walled carbon nanotubes the different types of lattice structures create different kinds of electrical properties. Most carbon nanotubes are semiconductors, but tubes that have the armchair arrangement in their lattice structure exhibit metallic conductance properties. It has been found that the conductance of metallic carbon nanotubes can theoretically exceed that of copper by 1000 times. Multi-walled nanotubes are known to be superconductors, which
means that electric current can travel through them with zero resistivity. Research has shown that certain multi-layered nanotubes create the best electrical conductors known today. There is one downside about the electrical properties of carbon nanotubes in that they are thought to be one-dimensional only, meaning that electrical signals can only be sent in one direction. It has been suggested, however, that multi-walled carbon nanotubes could be a solution to allowing electrical signals to travel in both directions because of their ability to have multiple properties.

Carbon nanotubes have been found to exhibit interesting optical properties that also make them unique and useful. Specifically they have been found to have absorptions that allow them to be spectrascopically analyzed to determine structure. This is important because of the necessity of researchers to obtain and combine specific types of nanotubes to perform the specific type of function they desire. The advantage of this is that the emission and detection of certain wavelengths is very selective and able to be fine-tuned to create high-powered electromagnetic detectors. This has potential use to optical engineers in creating better LED’s and photo detectors. Another amazing property of the absorption of carbon nanotubes is the fact that it is possible, when vertically aligned, for carbon nanotubes to completely absorb all electromagnetic waves from ultraviolet to infrared. This has incredible implications for making objects undetectable by electromagnetic waves.

It is also interesting to note that multi-walled carbon nanotubes have a very special kinetic property, which lends itself to some pretty exciting scientific possibilities. The property is that inside multi-walled carbon nanotubes there are repulsive forces between the two tubes, and because of this the tube on the inside can actually slide back and forth within the other with almost no friction whatsoever. This also means that the inner tube can rotate with the same ease. This incredible trait has already been used to make the world’s smallest rotational motor, which was 500nm wide. This is the first example of true nanotechnology that the world has ever seen.

Carbon nanotubes have yet another incredible property in their thermal conductivity. They have been found to be very good thermal conductors along the tube, but have also been found to be very good thermal insulators laterally.

Uses In Technology

It has been discovered that carbon nanotubes were being used as early as the 17th century in Damascus steel, which was legendary for its strength, however it was not until the end of the 20th century that the true discovery of their existence occurred. In 1991 Japanese scientist Sumio Iijima discovered carbon nanotubes by accident when he was performing Chemical Vapor Deposition, to create more traditional carbon fibers, and he put the wrong catalyst into the machine. Since then scientists have not been disappointed to find all kinds of exciting possibilities for their use in technology.

First and foremost carbon nanotubes have amazing implications to the nano technology we are already using in electronics such as computers and computing devices, because of their size and amazing electrical properties. They are now known to be some of the best semiconductors known in the world, and in particular carbon nanotubes are being considered for their use as transistors. There is an enormous demand to make
electronics smaller and more efficient and carbon nanotubes have amazing potential to do just that.

Carbon nanotubes are also highly considered for their uses in sporting equipment because of their durability and light weight. Carbon nanotubes differ from other types of carbon fiber that have been used for the past few decades. Carbon nanotubes are being found to be even more durable and even more lightweight. The bicycle industry is one of the main industries already applying this technology in order to make lighter, more durable bike frames. Scientists also look to apply this technology to baseball bats, tennis rackets, golf clubs and even car parts.

It has been discovered that carbon nanotubes can be spun together to form threads that are 17 times stronger than Kevlar. This provides a great potential to create stronger bullet proof and stab proof clothing.

There are some exciting and “space age”-like possibilities of carbon nanotube technology, one of which includes attempts to use carbon nanotubes to design a space elevator, which would transport material from Earth’s surface directly to outer space without the use of rockets. The idea is that carbon nanotube threads could be attached together enough to form a tether extending out into space, along which an elevator car could be powered. At 22,000 miles away would be a station that could remain in geostationary orbit, and extending another 40,000 miles would be a counterweight that would keep the cable taught. Of course there is a lot of progress that needs to be made as the production of such a long length of nanotube fiber would be slow and costly, but the hope is that NASA would have a cheaper alternative to space transportation. And with the closing of the space program more funding is being directed to this research than ever before.
Another science fiction-like application that could become a reality is the use of carbon nanotubes as catalysts to grow bone tissue. Carbon is the main element that makes up bones and bioengineers are discovering that carbon nanotubes act as a biosensor and report bone growth adjacent to them. This could be beneficial for people who suffer from bone deficiency.

There is even research that is showing that carbon nanotubes may be used to make synthetic muscles! One thing about carbon nanotube threads that have been produced is that they have a surprising amount of elasticity. When combined with their amazing strength this makes for a brilliant support structure. Also scientists have recently discovered that when these fibers are connected to electrodes at either end and given an electrical impulse, that the fiber responds in a way that is like flexing a muscle. There is still a long way that research will have to go before we can implant synthetic muscles into humans, but the prospect is intriguing.

Another amazing possibility that has emerged from carbon nanotube research is that nanotubes have anti-bacterial qualities. This is because of their small size they are able to destroy bacteria on a microscopic level.

There is also some exciting scientific research into an idea that carbon nanotube technology could be used to build structures that can store hydrogen. This is exciting because it would mean that we could possibly use hydrogen efficiently as a source of fuel in our cars, which burns cleaner than burning fossil fuels. One of the main problems with using hydrogen for fuel in our cars is that there is no efficient way to store and then inject liquid hydrogen into our engines to burn for energy. The reason for this is that hydrogen is a gas at normal temperatures and needs to be cooled and pressurized in order to be stored as a liquid and there is no viable container that could accommodate this in the cars we have today. Recently however some scientists in Germany think they have found a way to achieve this by using a container that contains carbon nanotubes. The research uses computer modeling to show that when carbon nanotubes are arranged in certain matrices that the hydrogen will adsorb to the surfaces of the nanotubes and that they would be able to store more hydrogen than any other carbon based materials have been able to before in a way that is cheap, lightweight, and non-toxic. The research still has a ways to go before it can make this form of hydrogen storage a reality because of the difficulty in arranging the submicroscopic structures into the intricate matrices created in the computer modeling, but a number of teams continue to work on this promising goal.
References


Anesthetics

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Organic Chemistry 236

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Abstract

This paper looks into the topic of anesthetics and the anesthesia produced by these drugs. Dating all the way back to the Sumerians in 3400 B.C., anesthetics have been an important part of medicine, both in ancient and modern times. As time passed and new technologies, ideas, and compounds were discovered, new ways to achieve medically induced anesthesia became prevalent throughout the medical community. This has ultimately led to the development of safety precautions for administering anesthesia as well. As science progresses, so do anesthetics and the ever-developing scientific field of anesthesia.

Introduction

Anesthetics are a type of drug that causes anesthesia, or the condition of having sensation(s) blocked or temporarily taken away. From Greek translation, anesthesia literally means “without sensation”. Anesthetics are mainly administered by an anesthesiologist, or in Europe “anaesthetists”, to a patient who is undergoing surgery or some other medical operation. There are many different drugs that are classified as anesthetics, with some of the more popular compounds being or having been cocaine, nitrous oxide, and xenon but not all are used in today’s medicine to promote anesthesia. Of the many different anesthetic drugs that are available, there are only three types, or categories, of anesthetic drugs used in medicine: local, regional, and general anesthetics. General anesthetics are the original and most commonly used in the medical community.

Plant Anesthetics

The first traces of general anesthesia date back to 3400 BC, with the Sumerians cultivating and harvesting opium poppy. Around 2225 BC, the Sumerian territory became part of the Babylonian empire, which eventually expanded towards Persia and Egypt. The Egyptians were known to have created surgical instruments as well as deriving sedatives from fruit. Preparations of opium in surgery were mentioned in Egyptian medical papyri, which were texts that recorded medical procedures and practices.

In ancient China, a doctor by the name of Hua Tuo (145-220 AD) performed surgeries using general anesthesia with excellent results. Tuo used only common combinations of herbs or acupuncture to relieve pain with patients, but his real fame came with his use of general anesthesia. Tuo would mix different herbs with wine that would be given to patients to induce unconsciousness before surgery but the recipes and documents of his anesthetics were burned shortly before his death. The main ingredients are believed to have been hashish, opium, jasmine root, rhododendron flower and various other herbs. Sadly, anesthetics and surgery died in ancient China with the death of Hua Tuo due to the teachings of Confucius, who taught that the body is sacred and surgery is a form of mutilation.
Beginning of Inhalation Anesthetics

The middle ages marked the beginning of inhaled anesthetics with the use of a narcotic-soaked sponge. Arabic and Persian physicians were among the first to utilize inhaled anesthetics by placing the sponge under the nose of a patient during operations. Diethyl ether was also first discovered during this time, but it wasn’t until the 19th century that inhaled anesthetics began to resemble today’s general anesthesia. This was mainly due to the discoveries of Joseph Priestley, who discovered nitrous oxide, nitric oxide, ammonia, hydrogen chloride and oxygen. These discoveries had a great deal of interest in the European scientific community. This interest eventually led to advancing treatment for diseases that were previously thought untreatable, such as asthma and tuberculosis. By the 19th century, anesthetics were very common within the medical community and were constantly being examined and updated with new chemicals.

Henry Hill Hickman (1800-1830) was one of the first to experiment with carbon dioxide as a general inhaled anesthetic. He used to experiment with its uses on animals by forcing them to inhale large amounts of carbon dioxide, then determining the effects by amputating a limb and observing if or how the animal reacted. Hickman was unappreciated at the time but today is recognized as one of the fathers of anesthesia. Another great anesthetic to be discovered during Hickman’s time was morphine. Friedrich Wilhelm first isolated morphine from opium in 1804, which today is a very commonly used anesthetic, but was not widely used for another fifty years after its discovery.

Another father of anesthetics is Dr. Horace Wells (1815-1848) of Hartford, Connecticut. Wells was a dentist who used nitrous oxide as a general anesthetic, successfully performing extractions with its use. Wells was having such great success with his use of nitrous oxide that he and a business partner of his set up a demonstration of a dental extraction with the use of nitrous oxide. Unfortunately, the demonstration was terrible and ended early since the patient screamed out in pain as the dental extraction took place. Wells accidentally administered too little of the nitrous oxide which resulted in the patient feeling the operation and the pain caused by it.

Wells took this extremely hard as he was discredited in the scientific community, which led to his unknowing addiction to chloroform, as the addictive effects of sniffing the drug were unknown at the time. He eventually became so deranged and delirious that one day he threw sulfuric acid all over 2 women and was placed in prison. As the drug cleared from his body, he realized the horror of what he had done. He requested an escort to his home to pick up his shaving razor and committed suicide by cutting an artery after inhaling chloroform to block out the pain. Wells was later recognized for his work done with nitrous oxide in the scientific community and has several monuments and statues in his honor. The final two chemicals of the 19th century to be used and accepted as an inhaled anesthetic were diethyl ether and chloroform.

Modern Inhalation Anesthetics

Today’s anesthetics vary by the way they are administered and what area they are meant to affect, be it a local region or the entire body. General anesthetics are the more
popular type used because they simply affect the entire body and render the patient fully unconscious. General anesthetics were traditionally administered through inhalation but modern medicine usually uses both inhalation and intravenous (IV), or only intravenous methods. General inhalation anesthetics can be gases or volatile liquids that evaporate as they are inhaled through a mask along with oxygen. The amount of anesthetic administered can be rapidly changed by changing the anesthetic-to-oxygen ratio. Inhalation anesthetics enter the body through the lungs and are carried by the blood to body tissues. With today’s technology, inhalation anesthetics are less commonly used alone in practice. They are usually combined with intravenous anesthetics and opioids for pain relief. The most common inhalation anesthetics along with basic information and structures are listed in the table below.

<table>
<thead>
<tr>
<th>Halothane / Fluothane</th>
<th>Little pain relief</th>
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<tbody>
<tr>
<td></td>
<td>Toxic to the liver in adults</td>
</tr>
<tr>
<td></td>
<td>Pleasant smell which works well with children</td>
</tr>
<tr>
<td></td>
<td>Being phased out for other options</td>
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<tr>
<td>Enflurane</td>
<td>Less potent</td>
</tr>
<tr>
<td></td>
<td>Produces rapid onset and faster recovery than most others</td>
</tr>
<tr>
<td></td>
<td>Can’t be used in patients with kidney failure</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>Not toxic to the liver</td>
</tr>
<tr>
<td></td>
<td>Can induce irregular heart rhythms</td>
</tr>
<tr>
<td></td>
<td>Being phased out for other options</td>
</tr>
<tr>
<td></td>
<td>Usually used with nitrous oxide</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Fastest induction and recovery time</td>
</tr>
<tr>
<td></td>
<td>Regarded as the safest inhalation with:</td>
</tr>
<tr>
<td></td>
<td>o No slowing of respiration</td>
</tr>
<tr>
<td></td>
<td>o No slowing of blood flow to the brain</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>Works quickly</td>
</tr>
<tr>
<td></td>
<td>Can cause renal (kidney) damage</td>
</tr>
<tr>
<td></td>
<td>Replacing halothane and isoflurane</td>
</tr>
<tr>
<td></td>
<td>Lack of irritation to airway makes it preferred agent for mask induction</td>
</tr>
<tr>
<td>Desflurane</td>
<td>Second generation of isoflurane</td>
</tr>
<tr>
<td></td>
<td>Irritating to airway</td>
</tr>
<tr>
<td></td>
<td>Most rapid onset and recovery due to low solubility in blood</td>
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</table>

The element xenon is a relatively new general inhalation anesthetic in the medical field, and is not commonly used due to its high cost. Recent advancements, however, are giving rise to new ways to recover and recycle xenon making it economically viable.
Xenon is 44% more potent than nitrous oxide, is not a greenhouse gas like nitrous oxide, and does not otherwise damage the environment, making it a great anesthetic for future use. It also posses fewer health concerns than nitrous oxide.6

Intravenous Anesthetics

Intravenous anesthetics are a type of anesthetic that can only be used through an IV that is connected directly to the patient’s bloodstream. This makes the onset of the drug much quicker than an inhalation anesthetic but it does have a major flaw when used alone as a general anesthetic; As stated before, the amount of an inhalation anesthetic that a patient receives can be rapidly changed for any reason simply by altering the anesthetic to oxygen ratio. Intravenous anesthetics do not have this luxury. In order to alter the degree of anesthesia produced, the anesthetic must be reversed by the administration of another drug. This could be potentially dangerous if a patient has an unforeseen reaction to an anesthetic and the amount of anesthetic administered needed to be greatly reduced in a short amount of time. Fortunately, this does not happen often due to the anesthesiologist’s ability to monitor and administer the correct amount of anesthetics before problems can arise. With that aside, intravenous anesthetics have a variety of different uses that make them extremely useful in different occasions whereas general inhalation anesthetics have one purpose.

Regional anesthesia is the practice of intravenously administering anesthetics to temporarily interrupt transmission of nerve impulses such as temperature, touch, and especially pain, as well as motor function in a large area to be treated.6 Regional anesthetics are used to affect only a large part of the body, such as a limb or the lower portion of the body. It can be administered in a single injection, or continuously through a catheter over a prolonged period of time. Unlike general anesthesia, regional anesthesia does not produce unconsciousness. This means less side effects and recovery time for the patient after the medical procedure is over. If needed, the surgeon could even converse with the patient during the procedure, but this is rarely needed. In childbirths, regional anesthetics called epidurals are used to cause the loss of sensation and to relieve pain by blocking the transmission of signals through nerves in or around the spinal cord. A downside to using regional anesthetics is that it may involve large, which brings up the problem of toxicity. This can lead to seizures and cardiac arrest, which is a significant concern as regional anesthetic techniques have a failure rate as high as 10%, which is a significant percentage in the medical field.7 Therefore, general anesthesia may become necessary even when a procedure was initially planned to be conducted using regional anesthesia. For these reasons, regional anesthesia is always conducted in an environment that is fully equipped and staffed to provide general anesthesia should it be needed.7

Another type of anesthesia that can be administered through intravenous anesthetics is called local anesthesia. Local anesthesia is produced the same way as regional anesthesia, just on a smaller scale. Instead of affecting an entire limb like regional anesthesia, local anesthesia only affects smaller areas such as a tooth or an area of skin. Like regional anesthesia, however, it does not produce unconsciousness. There are two ways to administer local anesthetics: by injection, which is often painful, or topically to the skin or other body surface. Topical anesthetics can be in the form of a
spray, or a solution, of cream that is applied to the skin. Topical anesthetics are the smallest scale of anesthesia that is used to relieve pain (and also itching) caused by a number of conditions. A few common medical conditions that use topical anesthetics are: sunburn and other minor burns, insect bites or stings, poison ivy, poison oak, and minor cuts and scratches. The table below lists local anesthetics as well as basic information about each and their chemical structure.

<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>Information</th>
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| Benzocaine (Ester) | • Topical pain reliever, commonly used in cough drops  
• Well-known cause of methemoglobinemia  
• Allergic reactions possible because of ester structure  
• Most common ‘bulking agent’ for illegal cocaine use in the UK |
| Cocaine (Ester) | • Used in nasal and eye surgery  
• Largely replaced by synthetic derivatives due to:  
  o Intense vasoconstrictor activity  
  o Cardiovascular toxicity |
| Chloroprocaine (Ester) | • Given by injection  
• Used in surgical procedures and labor and delivery  
• Constricts blood vessels resulting in reduced blood loss |
| Procaine / Novocaine (Ester) | • Primarily used to reduce pain of penicillin injections  
• Oldest man-made local anesthetic still in use  
• Vasodilator; often co-administered with epinephrine for this reason |
| Lidocaine / Xylocaine / Lignocaine (Amide) | • Topically used to relieve itching, burning, and pain caused by skin inflammation  
• Injected for minor surgeries as either a dental anesthetic or local anesthetic  
• Also found as a ‘bulking agent’ for illegal cocaine use |

All synthetic local anesthetics used today are derived from cocaine, which explains why the structures above are closely related to each other. They differ from cocaine mainly in that they possess no abuse potential and have less health concerns.
Precautions

Before performing operations that requires anesthetics to be administered, a patient must provide their complete medical history, including a history of allergies in family members. Anesthesia providers, usually anesthesiologists, consider many factors before identifying the correct dosage required for each patient. This may include a patient’s age, weight, allergies, medical history, and general health. The American Society of Anesthesiologists has five classes of patients based on risk levels to help in the decision of which and how much anesthetics to use, which are listed below:

I: Healthy patient  
II: Patient with mild systemic disease without function limitations  
III: Patient with severe systemic disease with definite functional limitations  
IV: Patient with severe disease that is life threatening  
V: Dying patient not expected to survive for 24 hours with or without an operation

There are also four stages of general anesthesia that range from anesthesia induction to emergence. They are the following:

Stage 1: Beginning with the induction of anesthesia and ends with the patient’s loss of consciousness. The patient can still feel pain at this point.

Stage 2: The REM stage includes uninhibited and sometimes dangerous responses to stimuli, including vomiting and uncontrolled movement. Administering a barbiturate, which depresses the central nervous system, before the anesthetic agent is commonly used to shorten this stage.

Stage 3: The surgical stage is when the patient’s papillary gaze is central and the pupils are constricted; this is the target depth of surgical anesthesia. During this stage, the skeletal muscles relax, the patient’s breathing becomes regular, and eye movement stops.

Stage 4: The over dosage stage is when hypotension or circulatory failure occurs. Death may result if the patient cannot be revived quickly.

Leading up to a surgery, most patients are asked not to eat 12-24 hours before being administered anesthetics due to the risk of vomiting. Vomiting greatly increases the risk of complications during anesthesia and should be avoided whenever possible. Emergency surgery is obviously an exception to this rule of not eating, and other precautions are then taken to minimize the risk of vomiting.

Depending on the patient’s level of anxiety and the procedure to be performed, patients are often premedicated. Most medications given before general anesthesia are anxiolytics, which reduce anxiety, or analgesics, which are painkillers. Patients in severe pain before surgery are given morphine or fentanyl, which are both very potent analgesics.
In the Body

Each anesthetic affects the body differently in the individual symptoms they produce, but they achieve their specific anesthesia in the same fashion. Local and regional anesthetics, for example, induce anesthesia by blocking nerve transmission to pain centers in the central nervous system. This is done by binding to and inhibiting the function of an ion channel in the cell membrane of nerve cells known as the sodium channel. This inhibiting stops the movement of nerve impulses near the site of injection, but no changes occur in other areas.

In contrast, general anesthetics induce a different sort of anesthetic state, one of general insensibility to pain. The patient loses consciousness yet their vital functions, such as breathing and maintenance of blood pressure, continue to function. Less is known about the mechanism undertaken by general anesthetics compared to local and regional. What is known is that general anesthetics cause a reduction in nerve transmission at synapses, the sites at which neurotransmitters are released and exert their initial action in the body. Precisely how this reduction is achieved is not yet fully understood.

Profession

There are three main professions that directly involve the use of anesthetics, which are anesthesiologists, anesthesiologist assistants, and anesthesia technicians. Each of which partake in an important role in the safe administration of anesthetics to a patient.

The anesthesiologist is the lead role in the administering of anesthetics to a patient. They are physicians (M.D. or D.O.) who have chosen to specialize in anesthesiology. Their duties include maintaining the patient in a state of controlled unconsciousness, providing pain relief and monitoring the patient’s critical life functions as they are affected throughout surgical or other medical procedures. Anesthesiologist also have critical roles outside of the operating room such as preoperative assessment of the patient and identifying the best anesthesia plan for each individual patient based on many personal factors. They are also responsible for the well being of the patient as the person is recovering from the effects of anesthesia. Additionally anesthesiologists help stabilize critically ill or injured patients in intensive care units.

Anesthesiologist Assistants (AAs) are skilled health professionals who work under the direction of anesthesiologists to implement anesthesia care plans. They work exclusively within the anesthesia care team and cannot practice outside the field of anesthesia or apart from the supervision of an anesthesiologist. Anesthesiologist assistants as well as registered nurse anesthetists are certified as non-physician anesthetists.

The Anesthesia Technicians (AT) role is to support the work done by the anesthesiologist by managing the equipment used and providing proper maintenance. Their exact roles vary based on the individual level of expertise of each AT. The duties can include cleaning, sterilizing, assembling, calibrating, troubleshooting, and recording of inspections and maintenance. They may also operate a variety of mechanical, pneumatic and electrical equipment used to monitor, evaluate and manage the patient undergoing anesthesia.
Conclusion

The medical field of anesthesia has come a great way from its origins of opium poppy. From relieving pain to medically induced anesthesia, anesthetics have developed into a vital part of the growing medical practices used today. As the amount of surgeries performed grows each year, the need for anesthetics will continually grow, as will the need for anesthesiologist to administer them. This will ultimately lead to new anesthetics that perform better and can be safely administered with less side effect and recovery time.
Bibliography


The Physiological and Nutritional Affects of the Paleo Diet

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April 20, 2012
Abstract

The paleo diet is one that recommends lean meats, vegetables, minimal fruits and nuts, and a balance of omega-3 to omega-6 fats in a ratio of 1:2 or less. The major macronutrients are broken down into the categories of carbohydrates, fats/lipids, and proteins and the physiological process that occurs when following the paleo diet. The keys to making the paleo diet successful are eliminating grains, diary, legumes, refined sugars, and processed foods while adhering to the recommended foods.

Introduction

There seems to be a vast debate about where humans came from. Not in the sense of short-term lineage such as what part of the country, but long-term origins. Depending on the person being asked, each will have different opinions on creation and evolution. One thing is certain; it is hard to argue with the facts of science. Approximately 98% of our DNA is common with that of chimpanzees, and we share nearly all of our genes with our cousin species. The human genome has changed less than 0.02 percent in 40,000 years. Due to the significant similarities of humans today and their ancestors, it would be logical to eat like those of the past. The diet of Paleolithic ancestors consisted of simple nutrients due to the land of which was occupied. The diet consisted of macronutrients of protein, carbohydrates, and lipids. There is a suspicious similarity between the nutrients that were eaten by the people of the past and that of which humans thrive for today.

The paleo diet is exactly that. It has the philosophy, and research, to determine that humans today should eat like the relatives of the past. The diet points out that the same balance of macronutrients hunter-gathers ate thousands of years ago will still apply to today’s standards. This diet suggests that there be a balance of the macronutrients. It is important that proteins come from lean meat which supplies more than 55 percent of calories. Lean meats are any meats considered to be over 60 percent protein. Carbohydrates must come from fruits and vegetables only. It is important to stay away from refined sugars, grains, legumes, and dairy due to the damage they cause on the digestive system. Lipids must also be that of healthy fats. Polyunsaturated and monounsaturated fats are those that provided the greatest benefits for one’s health. To better understand the required nutritional content the body requires, this paper will take a look at the paleo diet and its physiological and structural components that make it as successful as it is.

Macronutrients

Macronutrients are essentially the basic building blocks of the paleo diet. These can be broke down into three categories; carbohydrates, proteins, and lipids (fats). Each category plays an intricate role in the overall health of the body. The United States Food Pyramid has been created as a nutritional guideline for Americans to follow in order to attain optimum health. The original pyramid was created in 1992 and can be seen to the right. It is obvious that the United States Department of Agriculture recommended a diet high in carbohydrates, followed by fruits and vegetables with dairy and meat portions to follow. This diet is one that can have devastating biochemical ramifications for an individual seeking a healthy lifestyle, which will be explained
later. According to the recommended food pyramid of 1992, the two micronutrients that were included were recommended as two of the three least required. In June 2011, the food pyramid was replaced with a plate. Nowhere does the food pyramid, or the food plate, define the building blocks of nutrition. To better understand the required nutritional content the body requires, this paper will reflect how the hunter-gathers ate which has been laid out by the paleo diet.

**Carbohydrates**

Carbohydrates are one of the three main macronutrients. Carbohydrates are the most important source of energy for your body. Your digestive system changes carbohydrates into glucose (blood sugar). Your body uses this sugar for energy for your cells, tissues and organs. It stores any extra sugar in your liver and muscles for when it is needed. Carbohydrates are one of three types of sugars. The three types of sugars consist of monosaccharides, disaccharides, and polysaccharides. According to the paleo diet, carbohydrates should come from fruits and vegetables during every meal and account for 22 to 40 percent of the daily calories. If an individual gets their carbohydrates from fruits and vegetables, then the body is able to slowly digest and absorb the sugars which then eliminates a blood sugar spike which causes the mid-day drowsiness.

Today, many Americans get their source of carbohydrates from food other than fruits and vegetables such as breads, pastas, and grains. These are missing some of the essential minerals and vitamins as well as cause drastic spikes in the blood sugar thus having devastating
effects on one’s insulin levels. Insulin is release from the beta cells of the pancreas primarily in response to increasing blood levels of glucose and amino acids. Glucose is the main energy source for the brain and red blood cells. Sudden spikes of falls in insulin, then effects blood sugar which in turn can affect the brain and cause dizziness and hunger to unconsciousness and death. This constant spike and fall in blood glucose levels and insulin causes extreme stress on the body and can lead to conditions such as Syndrome X. Syndrome X consists of type 2 diabetes, high blood pressure, heart disease, and dyslipidemia which is low HDL cholesterol, elevated triglycerides, and small dense LDL cholesterol. Yet many health care practitioners believe that carbohydrates consisting of grains, breads, and pastas should be consumed on a regular basis. If one’s body no longer needs carbohydrates, they are then converted to fat in the form of a short-chain saturated fat called palmitic acid (PA). This is then attached to fatty acids and a glycerol molecule (TAGs), proteins, cholesterol, and then forms a very low-density lipoprotein (VLDL).

This brings up the topic of cholesterol. The paleo diet is said to balance out the levels of high-density lipoproteins (LDL: bad cholesterol) with high-density lipoproteins (HDL: good cholesterol). VLDL and LDL carry TAGs and cholesterol from the liver and supply the rest of the body to be used for fuel and the components of building cells. HDL does the opposite of the VLDL and LDL. After further research, it has been shown that the size of LDL is most important. The large “fluffy” kind of LDL is the uncompromising cholesterol that have little to no negative effect on the body. The LDL that has the most impact on the body is the small dense sizes that get stuck to the walls of the arteries. The small, dense, reactive LDLs are born from the VLDL that is the product of high-carbohydrate intake. As it can be seen, the diet of majority of western civilization is one that causes great destruction to the body due to the enormous amounts of refined carbohydrates such as cereals, breads, muffins, doughnuts, pastas, cakes, etc. This devastation can all occur without fats and proteins being considered.

Lipids

Fats in the human body play numerous roles. It is a fuel for and a vital part of the building blocks for many of our cell membranes and hormones. Fat makes up some of our body as well, such as the brain and some of the nerves. Fat also makes up our hormones throughout the body also. Paleo diet evaluates fats on their ability to help, or hurt, the body. The fats that are
beneficial are recommended in a certain ratio to optimize health. Fats can be labeled into three main categories based off their structure and physiological actions. The three classifications of fats are: saturated, monounsaturated, and polyunsaturated. Within the name are clues to the chemical structure of the fat. Saturated fats designate that all the carbon bonds contain only single bonds of hydrogen throughout the molecule. On the opposite end of the spectrum are unsaturated fats which contain one or more carbons double bonded to hydrogen. Also embedded in the name is the length of the fat chain. If the fat is a mono-fat, then it contains one carbon double bonded to hydrogen. If the fat is a poly-fat, then we know that there is more than one carbon double bonded to hydrogen. This is important due to the ability to be broken down in the body at the weak points were the double bonds exist. Further explanation will help clarify how fats affect the body and why the paleo diet recommends certain ratios.

Saturated fats, as previously mentioned, are fats containing carbons that all have single bonded hydrogen. These have typically been the fats that were thought to cause high cholesterol. As previously mentioned in the carbohydrate section, it is not fats that are the main culprit in raising cholesterol, but the amount and type of carbohydrates the body is ingesting. If one has high carbohydrate intake, then adds high amounts of saturated fats, it is then that the saturated fats live up to their name and will raise cholesterol like most were led to believe. This is why the paleo diet recommends that the carbohydrates come from fruits and vegetables, so that saturated fats and carbohydrates can have a homeostatic relationship.

\[
\begin{align*}
\text{\text{O}} & \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{C-C-C-C-C-C-C-C-C} & \quad \text{H} \\
\text{O\text{H}} & \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{Saturated Fat}^9
\end{align*}
\]

Monounsaturated fats are beneficial fats have been linked to many health benefits such as improved insulin sensitivity, improved glucagon response, and decreased cholesterol levels in humans.\(^9\) Monounsaturated fats reduce the overall risk of heart disease by lowering the level of total cholesterol, but not the HDL cholesterol, in the blood and also help prevent LDL from oxidizing and contributing to the artery-clogging process.\(^4\)

\[
\begin{align*}
\text{O} & \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{C-C-C-C-C-C-C} & \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{O\text{H}} & \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{Monounsaturated Fat}^9
\end{align*}
\]
Polyunsaturated fats are the most important group of fats available for human consumption, with one minor exception. These fats are so important that they are considered the essential fats. The body has no way of building these fats and must get them from a balanced diet. These fats can be broken down into two categories: omega-3 (n-3) and omega-6 (n-6). The paleo diet recommends a ratio of 1:1 or 1:2, n-3 to n-6. This is because the n-3s are considered anti-inflammatory, whereas the n-6s are typically pro-inflammatory. The hunter-gatherers had a very balanced fat consumption of 1:1. Today’s typical diet has a ratio of 1:10 to 1:20, or greater, due mainly to the introduction of refined carbohydrates and vegetable oils. These are extremely high in n-6s which, as previously mentioned, are pro-inflammatory. There have been numerous studies relation inflammation as an underlying factor for a plethora of diseases such as cancer, Parkinson’s, Alzheimer’s, and fertility. Many people have heard of the benefits of taking fish oils containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are considered n-3s. EPA is a potent anti-inflammatory, decreases platelet aggregation (thins the blood), and blocks angiogenesis (growth of new blood vessels) which is one of the growth mechanisms for the spread of cancer. DHA is the other essential fat that also helps in anti-inflammatory and potent antitumor actions. The body has the unique ability to convert EPA to DHA and DHA to EPA. It is most efficient if one gets the required polyunsaturated fats from diet.

\[ \text{Eicosapentaenoic Acid (EPA)} \]

\[ \text{Docosahexaenoic Acid (DHA)} \]

**Proteins**

Proteins are the most abundant organic molecules in animals, playing important roles in all aspects of cell structure and function. Each protein is made of up amino acid subunits that are joined by amide linkages called peptide bonds. The nitrogen (amino) group is essential for synthesizing specialized proteins in your body. There are twenty one amino acids and eight of which are essential for optimal health, but are only achieved from proper diet. These essential amino acids are isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. Proteins have an amazing range of structural and catalytic properties as a result of their varying amino acid composition. The variance comes from the structural composition of the amino acid. As previously mentioned, each amino acid has an amine group, but also has a carboxylic acid group. What makes each amino acid unique from each other, and also serves for identification, is the side chain that is attached to the chiral carbon (α-carbon) in all amino acids except glycine. In reality, amino acids can react at the amine group, the carboxylic acid group,
or the side chain depending on the presence of any other functional groups. Because of this versatility, proteins serve an astonishing variety of functions in living organisms. Some of these functions include replicating and repairing DNA; transporting oxygen to the cells; regulates glucose metabolism; and causes contraction of muscles. It is because of these unique capabilities that the body is so reliant upon this amazing structure. The paleo diet understands the importance proteins play on the functionality of the human body.

According to the paleo diet, your physiology runs best on a high-protein intake. Protein from animal sources provides the basic building blocks for your muscles, plus many of your hormones and neurotransmitters and also nutrient dense with b-vitamins, zinc, and iron. Hormonally, animal protein release glucagon, which not only helps to regulate energy levels, but also help to maintain insulin sensitivity. This is why the paleo diet recommends eating lean meat, veggies, and good fats, as low glycemic load veggies release relatively little insulin.

**Key Factors in the Paleo Diet**

When deciding to attempt to follow the paleo diet, there are some very key factors that must be met. The paleo diet consists of lean meat, vegetables, and limited fruits and nuts. This diet eliminates grains, dairy, legumes, refined sugars, and processed foods. Grains contain a protein called gluten. Gluten is found in everyday items that contain flour, wheat, rye, oats, millet, sorghum and barley. Other grains such as corn and rice have similar proteins, but cause less issues. The plants are variants from wild grasses that have been managed and bred for over 2,000-5,000 years. Grains contain a certain protein called lectins, which stick to specific molecules that allow the body to identify them. The paleo diet explains that wheat germ agglutinin (WGA), is one of the most destructive lectins, but also one of the most studied. WGAs are found in all grains and are problematic for numerous reasons.

First, lectins are not broken down in the normal digestive process. This leaves large proteins intact in the lining of the gut. Typically most food digested is broken down into the smallest particles possible for absorption through the lining of the small intestines. This process does not occur when grains are ingested as food. Grains, as well as dairy and some other foods, also contain protease inhibitors, which further block the digestion of dangerous lectins. Second, lectins attach to receptors in the intestinal lumen and are transported intact through the intestinal lining. Third, these large, intact protein molecules are easily mistaken by the body as foreign invaders like bacteria, viruses, or parasites. The immune system is extremely reactive near the
intestines since everything that is absorbed through digestion happens in the small intestines. Not only does WGA enter intact, it damages the intestinal lining allowing other proteins to enter. The immune system mounts an attack against these foreign intruders and makes antibodies to help fight them off. The antibodies are specific to the shape of the proteins entering through the damaged gut. The devastation occurs because these proteins often mimic the beginning shapes of other proteins that are vital in optimal health. WGA and other lectins have a dramatic effect on an enzyme called transglutaminase (TG). TG is an enzyme that modifies every protein in the human body. Since lectins cause problems with TG, and TG causes problems with all the proteins in the human body, one can now start to see what the paleo diet is so beneficial. This is also why the diet suggests removing legumes and diary from one’s consumption. These foods also have proteins that can cause very similar physiological affects to the proteins in grains.

Conclusion

The paleo diet has provided a significant difference in the overall health for my family. My wife has struggled with lifelong complications from due to unknown dietary reasons. Until approximately 4 years ago, she had no idea that she was gluten intolerant/celiac. One day she broke out in an allergic reaction after eating bread sticks. The reaction was so severe, it borderlined anaphylactic. She was rushed to Urgent care where she received treatment. After eliminating everything with gluten that we knew of, she was still having issues with bloating and gut irritation. After deciding to try the 30-day trial of the diet, she started seeing major improvements and I started looking and feeling better throughout the day. My wife has since lost the bloating feeling and lost 10lbs without any exercise. I have seen a decrease in abdominal fat and bloating with a more constant stream of energy throughout the day. This occurs because your body shifts from using all the excess carbohydrates as fuel to using fat, a process known as ketosis. I used to struggle with blood glucose spikes/falls after each meal and fight to stay awake due to the vast amount of refined carbohydrates that were “recommended” as being the most important factor in the daily diet. Many people still think this way and continue to eat refined carbohydrates throughout the day. I can personally say that my wife and I have had huge success following the paleo diet along with numerous other friends. I recently recommended a book about the diet to a physician assistant friend and after reading it she to saw the benefit the diet brings. It is because of the direct success of the diet that I will continue this as a part of my lifestyle and recommend it to anyone struggling with health issues, or to those who just choose to become healthier.
Bibliography


Biomechanical Differences in the Hip and Knee may Increase Susceptibility to Knee Pain and Injury.

Bradley Day

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Dr. Casey Durandet
Abstract

The knee, one of the largest and most complex joints in the body will be analyzed from a biomechanics perspective. The basic anatomy and kinematics will be examined, as well as several scenarios that pose potential risk to knee injury. Several specific knee injuries, the forces that cause injury, and how to prevent knee injuries will also be examined from a biomechanical perspective.

Basic Anatomy and Biomechanics

The human knee is one of the largest and most complex joints in the body. It is situated between the two largest bones, the femur and the tibia, and is therefore exposed to large forces. In order to withstand these forces and prevent injury there are many biological tissues and mechanisms that help to increase knee stability, however, only the bony structure and the knee ligaments will be examined. The knee itself is composed of two separate joints that act to move knee in the three different planes of movement. The tibiofemoral joint is the joint formed by the tibia and the femur and is moveable in all three planes, but most of its movement takes place in the sagittal plane. The second joint, the patellofemoral joint, is formed by the femur and the patella meeting. The patellofemoral joint serves two important functions; firstly, the patella protects the knee against any forces directed posteriorly by spreading these forces over a larger area, therefore decreasing stress on the femur. The second function of the patella is to increase the moment arm of the quadriceps muscle and in turn increase the leverage the quadriceps muscle has about the knee joint. However, the bony structure surrounding the knee is only one part of the knee joint and there are several other surrounding components that aide in increasing stability of the joint.

Aside from the bony structure of the knee, the knee ligaments are an integral part of the knee joint. There are several ligaments in the knee and each helps provide added stability while restricting abnormal knee motion due to externally applied loads. The most well-known ligaments, the Anterior Cruciate Ligament (ACL) and Posterior Cruciate Ligament (PCL) both prevent hyper-extension of the knee as well as anterior and posterior translation, respectively. The other two ligaments in the knee, the Medial Collateral Ligament (MCL) and Lateral Collateral Ligament (LCL) prevent excessive internal, external, and "side to side" movements of the knee. Due to the composition of ligaments in general, these structures are able to withstand loads and stretching and be able to return to their original state, assuming these factors don't exceed their maximum threshold. When speaking of ligaments and their ability to withstand loading, it is important to recognize the relationship between stress and strain and how each affects a ligament. Stress is defined as "the load per unit cross-sectional area of a ligament," and is given by the formula $\sigma = \frac{F}{A}$. In the formula, $\sigma$ is stress, $F$ is the load applied by external forces, and $A$ is the cross sectional area. Strain is defined as the “deformation per unit length of
a ligament,” and is given by the formula \(\epsilon = (l - l_0)/l_0^2\). In the formula, \(\epsilon\) is the strain, \(l\) is the length after an external load is applied, and \(l_0\) is the initial length. Figure 1 depicts a stress-strain curve for a ligament that is undergoing tensile testing. This figure can be broken down into several parts: the beginning of the graph shows the “toe region” where the ligament first experiences a deformation, next is an area that is linearly proportional to the strain (also referred to as Young’s modulus), and finally the peak of the graph is where “ultimate stress” and “ultimate strain” converge and anything beyond that area is considered ligament failure, or rupture. There are other factors that influence the ability of a ligament to withstand forces such as age, history of use, and genetic factors.

Normal and Abnormal Knee Mechanics

When examining knee mechanics it is important to not only look at the knee, but the hip as well. One study reported that there is “some degree of epidemiological, neuromuscular, or biomechanical evidence to support the concept that proximal factors [the hip] may influence knee loading and, therefore, contribute to injury.” During normal gait, in the loading response phase shortly after heel strike, the hip flexes roughly 20° and adducts and internally rotates between 10° and 15°. However, excessive adduction and internal rotation may shift the central point of the knee medially resulting in “dynamic knee valgus” and is a contributing factor to many knee injuries such as ACL injury. On the opposite spectrum, when weakness in the hip abductor muscles occurs, the body may shift the center of mass away from the stance limb in what is called the “Trendelenburg sign.” An implication of this movement is the ground reactant force vector will pass away from the center of the body creating knee varus, the opposite of valgus, straining the LCL and iliotibial band (IT band). Figure 2 demonstrates several loading patterns and a typical ground reaction force vector while jumping onto one foot. Figure 2A demonstrates loading while the pelvis is neutral and the ground reaction force vector passes

![Figure 2](image-url)

**Figure 2.** 2A – Neutral pelvis creating a slight knee varus. 2B – Contralateral pelvic drop and excessive knee varus. 2C – Excessive hip adduction and knee valgus.

![Figure 1](image-url)

**Figure 1.** Stress-strain curve for a ligament.
medially of the knee, creating a slight varus in the knee. Figure 2B further demonstrates the “Trendelenburg sign” showing an excessive contralateral drop and knee varus will result. Figure 2C shows excessive hip adduction and the ground reaction force vector passing laterally to the knee, in this scenario excessive knee valgus will result.

Knee varus and valgus are not the only motions that may increase risk for injury. Hip and trunk position will also dictate knee mechanics in the sagittal plane. One study examined the forces present on both the hip and knee while jumping from a platform onto the ground. They found in their study that an increased forward trunk lean will move the ground reaction force anteriorly, therefore increasing the forces on the hip while decreasing the forces on the knee. In the study, a more erect trunk landing will decrease the forces on the hip while substantially increasing forces on the knee. Figure 3 dictates these findings; the jumper in figure A will experience greater forces on her hips, whereas the jumper in figure B will experience greater forces on her knees, the arrow indicates the direction of the ground reaction force vector.

![Figure 3. 3A - The jumper will experience a greater force on her hips. 3B - The jumper will experience a greater force on her knees.](image)

**ACL Injury**

Injuries to the Anterior Cruciate Ligament are by far the most common injury and an estimated 250,000 ACL injuries are sustained in the United States annually. 70% of ACL injuries are termed “non contact” and the most common mechanisms of injury are landing from a jump or while performing a maneuver called “planting and cutting” when an athlete rotates on a
fixed foot. After an ACL injury is sustained, the injured person is at an even high increased risk for further complications such as degenerative arthritis.

The basic mechanism of ACL injury, called tibial torsion, occurs when the tibia rotates with respect to the femur. One example of this occurrence happens in the sport of alpine skiing. It has been shown that although lower extremity injuries have decreased over the years in alpine skiing, the number of ACL injuries has actually increased. This is mainly due in part to an improved design in skiing boots and bindings that prevent tibia and ankle fractures (coined boot-top fractures), however this design does not prevent knee ligament injuries. With this design, alpine skiers are at risk of ACL injury when falling backwards with a “hyper flexed” knee and the skier’s weight falling inside the leg, effectively internally rotating the tibia while in a flexed state. Outside of alpine skiing, another potential injury risk occurs with the combination of an anterior tibial force and internal tibial torque while the knee is near full extension, and it has been stated that this combination of movements produces the greatest risk for ACL injury.

However, the bones and ligaments in the knee are only static stabilizers, meaning they do not actively move; the surrounding musculature, or dynamic stabilizers, also plays an important role in knee stabilization. In order for an ACL injury to be sustained due to tibial twisting, the outside force must be greater than the muscular force generated to protect the knee. The two muscle groups most involved are the quadriceps and the hamstrings and each muscle group impacts the knee and ACL in a particular way. The quadriceps muscles are knee extensors and therefore increase the force on the ACL by providing an anterior translation during knee extension. The hamstrings have the opposite role, they act as knee flexors and therefore decrease the force on the ACL. Due to these mechanics, it has been shown that a massive quadriceps contraction may cause ACL injury in alpine skiers in order to prevent falling backwards. One study proved this theory by providing an “aggressive quadriceps load of 4500N,” which is similar to a normal, physiological quadriceps contraction, while the knee is locked in 20° flexion. The researchers found that the tibia translated anteriorly an average of 19mm and as a result, the ACL ruptured in 100% of all trials. As a result of these trials, scientists learned the importance of co-contraction of the hamstrings during the quadriceps contraction in order to preserve and protect the ACL. In a sport setting, muscle fatigue has been found to lead to increased knee valgus which increases strain on the ACL, further increasing susceptibility to injury.
PCL Injury

Posterior Cruciate Ligament injuries are much less common than ACL injuries, but PCL injuries are often much more complex. There are two typical mechanisms for a PCL injury. The first mechanism is receiving a posteriorly directed force while the knee is in flexion or hyperflexion, as in the case of a bent knee impacting a dashboard during an automobile accident. Another mechanism of injury occurs during hyper extension; an example of this type of injury is a football player being tackled low in the front and tackled from the back; this will cause the foot to remain planted on the ground and the knee to become hyper extended. However, several studies have confirmed which knee flexion angles are most susceptible to injury and it was found that at 90° of flexion the PCL is receiving the most force, and near full extension the PCL is receiving the least amount of force. Furthermore, they found that 100N of a posterior tibial load combined with external tibial torque decreased the force on the PCL where as forces with internal tibial torque increased the force on the PCL. PCL injuries are often fairly complex in that the PCL is typically not the only ligament injured. Along with PCL injuries, it is common to find a Medial Collateral Ligament injury as well making them a complicated injury to rehabilitate.

Knee Pain

Knee pain, more specifically patellofemoral joint pain (PFP), is the most commonly seen lower extremity condition seen in orthopedic clinic and is "cited as the most common overuse injury in persons who are physically active". Interestingly, PFP is reported 2.2 more times greater in women than in men. There are several known causes for PFP, two of which being patellar mistracking and an increased lateral pull on the patella from the hip, from an increased Q angle. Patellar mistracking is mostly the cause from abnormal knee mechanics, causing the patella to not properly track along the distal femur. Studies have shown, however, that internal rotation of the femur underneath a stable patella may in fact be the largest contributor to patellar mistracking. Treatment for patellar mistracking is fairly conservative; taping, training of the vastus medialis muscle, and knee braces are the most common methods for treatment.

Another known cause for PFP is an increased Q angle. The Q angle is an imaginary line drawn from the anterior superior iliac spine to the midpoint of the patella, and another line is drawn from the tibial tubercle to the midpoint in the patella, and the angle is then measured. The normal range for a Q
angle is measured to be approximately 14° for males and 17° for females. An increased Q angle predisposes the patella to increased lateral forces via the quadriceps muscle tendon, which runs along the femur and Q angle. One study has shown that a “10° increase in Q angle resulted in a 45% increase in peak contact pressure on the lateral aspect of the patellofemoral joint”

However, inconsistent biomechanical results in studies present a lack of agreement on the extent of which the knee is susceptible purely from a Q angle aspect. It has been said that additional research is needed to determine relationship between PFP and “proximal factors” at the hip.

**Knee Injury Prevention**

While knee injuries are common in an orthopedic clinic, knee injury prevention is relatively simple. There are several things to consider while looking at knee prevention. First of all, stretching before engaging in any activity will help “warm up” muscles, also engaging in proper technique either while at the gym, carrying a heavy box, or jumping will help reduce chance for injury. If engaging in a sport, avoid taking quick turns, as the foot may not turn as quickly as the thigh. Also, weight bearing exercise has been shown to increase bone and muscle strength, which will help reduce chance for injury while engaging in activities.

**Conclusion**

The knee is one of the largest, most complex joints in the human body. Due to its location between the body’s longest level arms, the femur and the tibia, it is subject to very large and sometimes harmful forces. Thankfully, there are many structures around the knee that help increase knee stability and reduce the susceptibility of injury. However, knee injuries are still common and the most common being an ACL injury. Occurring mostly due to flexing and rotating forces, ACL injuries are most common in athletes and particularly skiers. Aside from injuries to the ligaments, there is a genetic factor to knee pain, and the genetic factor being the Q angle. There are ways to reduce the likelihood for injury however, exercising frequently and stretching before a bout of activity will help increase both muscle strength and reduce risk for knee injury.
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DMT: The Businessman’s Special

Tyler Duncan
April 16, 2012
Abstract

N,N-dimethyltryptamine is classified as a strong, psychoactive drug that induces visual, audio, psychological, and emotional effects. From historic shamanistic brews to recreational use to clinical studies, DMT has found its way into many uses. With suspicion that DMT is produced in the pineal gland, it has mystical properties that are associated with the Buddhists' enlightenment. While DMT is used often for personal gain, it is also used to determine how the mind works in psychotic patients. DMT can be tracked down from the simplest of plants to the synthesis of tryptamine, and when altered slightly or combined with certain inhibitors, it becomes more accessible and powerful.

History

The first known usage of DMT dates back thousands of years to South American shamanism. These medicine men would gather special plants that contained the psychoactive drug, such as *Psychotria viridis*. In this certain plant, scientists have discovered that one of the most active ingredients was DMT. The plants would be ground up and boiled for several hours to produce a widely common drink known as ayahuasca.¹ Ayahuasca was drunk by male shamans so that they would be able to travel to spirit worlds to gather specific information. Shamans also drank ayahuasca to be able to perform certain tasks and ceremonial rituals. Non-shamans who were part of a tribe would also drink ayahuasca so that they would be able to perform in the ceremonial rituals. Ayahuasca was used socially rather than recreationally in indigenous cultures.²

The first record of DMT use was provided by Ramón Paul. Paul was a Spanish friar who accompanied Christopher Columbus while he was on his second trip to the New World. Paul wrote down that the natives had sniffed kohobba in order to communicate directly with the spirit world. Kohobba, parica, and yopo were the names of mixtures ingested by the natives that contained psychoactive ingredients. In 1931, the first person credited to synthesize DMT was Richard Manske, a Canadian chemist. Manske was also the first person to synthesize harmaline, a psychoactive alkaloid, in 1927.¹ Because of this discovery, DMT was also found in the cells and tissue of the human body and brain. DMT became popular in the mid 1900s, which led to many scientific trials. These trials included the effects of DMT with schizophrenia and near-death experiences. In 1970, the United States Congress put the Controlled Substances Act into play, which brought a period of inactivity to the research and testing of DMT. However, very few studies are now being conducted to study the subjective effects of DMT.²

Dried leaves of the *Psychotria viridis* plant contain 99% DMT.
Synthesis

DMT is a hallucinogen that consists of the tryptamine core and two methyl groups substituted for the two hydrogen atoms attached to the terminal nitrogen. DMT stands for dimethyltryptamine, with the IUPAC nomenclature N,N-dimethyltryptamine. The N,N- is a position indicator stating that the two methyl groups are attached on the amine group.  

![Tryptamine and DMT structures](image)

DMT can be synthesized from tryptamine and methyl iodide. Tryptamine and isopropyl alcohol are mixed together and methyl iodide is added. Immediately, a cream-colored precipitate forms. After stirring for twelve hours at room temperature, the solids were removed and isolated through vacuum filtration. The solid is washed twice with isopropyl alcohol and warm isopropyl alcohol and then allowed to air dry. The solid collected is N,N,N-trimethyltryptammonium iodide. In order to obtain a high percent yield of DMT, the iodide salt undergoes demethylation. N,N,N-trimethyltryptammonium iodide is added to tetrahydrofuran (THF) and a solution of lithium triethylborohydride in THF is added. The mixture is refluxed for nine hours and allowed to cool. Dilute hydrochloric acid is added to acidify the mixture and the THF was removed under a vacuum. The remaining residue is added to dilute sodium hydroxide and is extracted with diethyl ether. The extracts are combined and the solvent is removed under vacuum to yield N,N-dimethyltryptamine.

Another way to synthesize DMT is the demethylation of the chloride salt. N,N,N-trimethyltryptammonium iodide is made into a hot, aqueous solution and is mixed with silver chloride. The mixture was boiled for fifteen minutes and the silver halides were removed through filtration. Water was removed from the filtrate as fast as possible. To the residue, a small measurement of methanol is added, followed by acetone. The mixture crystallizes to form N,N,N-trimethyltryptammonium chloride. The mixture is decomposed under a hard vacuum and the residue is distilled. The distillate collected is dissolved in a small measurement of methanol and then is acidified with a solution of dilute nitric acid. Any insoluble material was removed by filtration and the aqueous phase was washed with chloroform. It is then turned basic with the addition of sodium hydroxide and extracted with more chloroform. The solvent is then removed under vacuum and to the residue, a solution of hot picric acid is added. The hot solution slowly cools to form the picrate of DMT. The picrate was made into an aqueous suspension and then turned basic by adding excess aqueous sodium hydroxide. The picrate is then extracted with diethyl ether and the solvent is removed under vacuum. The residue crystallized and was
pressed against a porous plate to desaturate the sample. The sample is washed with petroleum ether to yield N,N-dimethyltryptamine.  

Side Reactions

[Chemical structure image]

DMT's sister tryptamine is 5-methoxy-N,N-dimethyltryptamine, or 5-MeO-DMT. Its effects are very similar to that of DMT except it is substantially more potent. 5-MeO-DMT can be synthesized from 5-methoxyindole, anhydrous diethyl ether, and oxalyl chloride. 5-methoxyindole and anhydrous diethyl ether are mixed and cooled and oxalyl chloride is slowly added. The solution was stirred for 10 minutes and the red solids that formed were removed by filtration. The solids were then washed with diethyl ether and returned to the reaction beaker as a suspension in anhydrous diethyl ether. To remove the red coloring, dimethylamine in anhydrous diethyl ether was added. The solution was stirred again for 30 minutes and the solids were removed by filtration and washed with diethyl ether. The solids were further suspended in water and then alternatively washed with water and diethyl ether. When recrystallized from tetrahydrofuran/diethyl ether, fine white crystals were produced. These white crystals were mixed with hot benzene and then added to a suspension of lithium aluminum hydride in anhydrous diethyl ether. The mixture was held at reflux for an hour and a half and then cooled with an external ice bath. To decompose the reaction complex and excess hydride, water was cautiously added. The inorganic solids were removed by filtration, the filter cake was washed with diethyl ether, and the filtrate collected and the washing were both combined and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum filtration and the remaining residue was distilled fractionally, then crystallized upon cooling, producing 5-methoxy-N,N-dimethyltryptamine.

How To Make DMT

If one feels adventurous and has the patience, DMT can be made by using the plant Mimosa hostilis. To start off, the plant must first be grinded into a fine powder. For there to be significant percent yield, the ground material must be very fine. Freezing the plant and then blending it in a blender works well. Next, a jar is filled two-thirds with distilled water and a small amount of muriatic acid. If muriatic acid is not favorable, distilled white vinegar will work as well. It is important to note that the pH level of the water...
should be 2 after adding the acid. The ground up root-bark should be placed into another container of equal size. The next step is to convert the alkaloids into salts. The acidified water from the first jar is poured into the second jar with the ground up root-bark. To speed up the process, the contents of the jar can be shaken or heated, but not to a boil. After the contents have been mixed together, the jar should be left alone for 24 hours. After the mixture has reacted, the contents of the jar are poured into a funnel lined with cotton-filter, which opens into another jar. The purpose of the cotton-filter is to separate the root-bark from the mixture. The root-bark is placed back into the second container. This process is called extraction and it should be carried out two more times, from acidifying the water up until filtering out the root-bark. Instead of waiting 24 hours for the mixture to react, it is necessary to wait about one week and then filter out the root-bark. Each extraction should be placed in the third jar for a total of three extractions. The next step is to filter the extracts with a paper coffee filter. The coffee filter is placed at the bottom of a funnel, just like the cotton-filter, and the extracts are filtered through into a new container. After this, the next step is to remove all of the fats and oils so an organic, non-polar solvent is added to the solution, such as ether or chloroform. After defatting the solution, it is time to transform the salt into a free base form. A jar is filled with three ounces of distilled water and lye is mixed in slowly. The pH of the jar should now be 12. Now the root-bark extracts are added into the jar with slow stirring until the pH ranges from 9 to 11. The contents of the jar should be shaken, avoiding any pressure buildup inside of the jar. The solution should change in color and have a gel-like consistency. After sitting for roughly 12 hours, an emulsion should form and separate into two layers. The solvent layer, which in most cases has a slight tint, should be removed and placed into another jar. Once all of the solvent has been extracted, it should be placed in a glass baking pan and left alone to evaporate. The left over material is dimethyltryptamine.  

It is very crucial to mention that DMT is classified as a Class A drug according to the 1971 Misuse of Drugs Act. Being a Class A drug means that it is illegal to make, supply, or possess in any kind of form. The maximum penalty for possessing DMT is seven years in jail. In layman’s terms, it is not worth the risk of getting caught!

![DMT crystals without impurities.](image)
MAOIs

DMT, when ingested orally, is usually not effective. The DMT is broken down by monoamine oxidase, MAO, which catalyzes the oxidation and inactivation of monoamine neurotransmitters. MAO is a very important enzyme and it helps to break down the chemical compounds of drugs and poisons. When MAO-inhibitors are introduced, they interfere with the MAO enzyme and actually cause the breakdown of DMT to stop. Therefore, when DMT is combined with a MAO-inhibitor, it makes the drug effective when orally ingested. Some examples of MAO-inhibitors are Syrian rue, Passionflower, and Yohimbe.

MAO-inhibitors fall into two categories: irreversible and reversible. Irreversible MAO-inhibitors, such as phenelzine, bind directly onto the enzyme and can cause MAO inhibition for up to one to two weeks after ingestion. Irreversible MAO-inhibitors are also used to clinically treat depression. Reversible MAO-inhibitors, such as moclobemide and harmine, also bond directly onto the enzyme, but are effective for a much shorter time from 1 to 24 hours. Reversible MAO-inhibitors are also used as antidepressants. Most people, who recreational drug users, use mainly harmine and harmaline, which is the reduced, hydrogenated form of harmine.5

Cons Of DMT

When taking DMT with an MAO-inhibitor there are many dangerous side effects if one is not careful. Most MAO-inhibitors increase the power of the cardiovascular effects of tyramine and monoamine, which are found in common foods. For example, if a person eats aged cheese, yeast, citrus fruits, or chocolate after taking an MAO-inhibitor, they put themselves at a high risk for a blood pressure that is dangerously high. When combined with MAO-inhibitors, the effects of amphetamines, alcohol, general anaesthetics, and sedatives are prolonged and intensified. All of these negative results occur mainly with irreversible MAO-inhibitors rather than reversible MAO-inhibitors.5

If DMT is smoked, the person holding the pipe, or burning apparatus, often burns themselves due to a loss of control after the drug has taken effect. After the plateau of the psychoactive drug, the comedown is often described as an abrupt return to reality, meaning that the user experiences disorientation after the drug wears off. For those who use DMT frequently, they tend to suffer from psychological and emotional difficulties for up to a couple weeks afterwards. Another negative aspect of DMT is that its smoke is incredibly harsh and can cause throat and lung irritation. Integrating DMT with a person’s daily life is looked down upon because of its negative effects. For example, it can cause anxiety and anxiety attacks, focusing on daily tasks becomes immensely difficult, a person’s thinking is fixated with the experience and not on the task at hand, and it can also cause insomnia. Likewise, 5-MeO-DMT is capable of inducing nausea, sweating, panic attacks, and disturbed vision.9

How It Effects You

With different dosages and the different ways DMT can be taken, there are numerous results. DMT can be taken orally, intramuscularly, subcutaneously, by smoking, and
intravenously. The following information is based on Alexander Shulgin’s experience with the drug DMT. Shulgin is credited for the use of MDMA, especially in psychopharmaceutical use and to treat depression and post-traumatic stress disorder.

When taken orally, the dosage that has effect on a person is greater than 350 mg. At 150 mg there were absolutely no observable effects, psychic or vegetative. At 250 mg there were still no effects and the DMT was inactive. At 350 mg there was no psychological or physiological effect. When 100 mg of DMT was taken via the buccal mucosa, between the bottom lip and teeth, there was numbness at the site, but no other effects were experienced.

When taken intramuscularly, the dosage that has effect on a person is between 60 and 100 mg. Intramuscularly means that the DMT was injected into the skin at a 90-degree angle. At 20 mg there were transparent visuals of patterns that evolved into more complex visuals that were reminiscent of kaleidoscopic images. At 30 mg the eyes began to dilate and there is an increase in perception disturbances. At 50 mg a person’s view might become blurry and paranoia sets in. At 60 mg a person will begin to hallucinate, the body might become tingly and numb, and a sense of freethinking takes over. At 75 mg there were symptoms of vegetative effects, such as trembling, tingling sensations, and increase of blood pressure and heart rate. A few minutes later, optical illusions and hallucinations begin to appear. People see things from brilliantly colored designs to exotic scenes. A person’s emotional state is now elevated up to euphoria. Also, a person’s attention is solely fixed on his or her hallucinations, preventing them from describing word for word what is happening to them. At 80 mg perceptual distortions were seen when the eyes were open and closed, blood pressure is increased, pupils are fully dilated, and a person feels a strong emotional connection to his or her hallucinations.

When DMT is smoked, the dosage that has effect on a person is between 60 and 100 mg. At 30 mg there was instantly a feeling of light-headedness and pressure of the temporal lobe. Eyesight may take on a hue and then the drug takes full effect. The person has no control and a few minutes after the plateau, the person begins to regain awareness. At 60 mg there was an elaborate and exotic feeling in the head. There is a slight sense of cruelty but happiness that a person would experience. A person would experience a rapid onset that would leave them in “a completely stoned isolation” for a few minutes. One’s perception of time is completely distorted for 30 minutes can feel like it was 2 hours. After the plateau, an afterglow, or pleasant feeling is experienced. At 100 mg there was a rapid increase in heart rate and sweating of the palms. There was a feeling of identity being destroyed. An event called ego death sometimes can set in where a person feels and goes through the imaginary aspect of the ego.

When taken intravenously, the dosage that has effect on a person is between 4 and 30 mg. At 15 mg there was an instantaneous head rush and a disorienting feeling. Visuals were rapid and very colorful and there were random noises, none, however, were the sounds of people talking. A person would not be able to think clearly. At 30 mg the dosage hits the person very hard. The effects are similar to that of when 60 mg of DMT is smoked. The only differing experience is that the euphoria is not as prominent.³
Pineal Gland

In the human brain, the pineal gland contains the building blocks that are necessary to make DMT. The pineal gland possesses the highest levels of serotonin in the entire body. The pineal gland has a special function that allows serotonin to be converted into tryptamine, which is a very critical step when forming DMT. When looking closely, it is a pea-sized gland located in the center of the brain and thought to harness spiritual aspects. French philosopher René Descartes was obsessed with understanding who we are as human beings and began to question if we really know who we are. Descartes believed that the soul is in sync with the entire body, but the pineal gland exercises that function the most. A couple hundred years later, Dr. Aaron Lerner had discovered melatonin, which is produced in the pineal gland from the neurotransmitter serotonin. Melatonin is responsible for making humans relaxed and for putting us to sleep. Lerner had also discovered that the production of melatonin varied depending on the time of day. Melatonin production stopped during the day, and after it became dark, melatonin production picked up. It was unknown how the pineal gland could detect light and dark, but with later research, it was discovered that there is a link between the pineal gland and the retinas of eyes. Oddly enough, the retinas contain melatonin. The pineal gland was given the nickname “the third eye” due to its location regarding the seven chakras, centers of spiritual energy. As hallucinogen became popular, scientists discovered that the hallucinogenic drugs became highly concentrated in the pineal and pituitary gland. The drugs produce an altered state by imitating serotonin at the synapse, where neurons can communicate with each other. Because melatonin and serotonin are both concentrated in the pineal gland, the “third eye” is considered to be a portal to consciousness. The psychedelic DMT has been characterized by a blinding white light, timelessness, rebirth, and contacting a powerful and loving presence, all of which are characteristics of denominations. The link between the pineal gland and its function in the life of the spirit is undeniably interesting. With more research being done, the pineal gland has started to take on a more spiritual role, bearing the spirit molecule.
Trials

In 1956, a trial was performed with 24 female patients, 20 of whom were chronic schizophrenics. DMT was administered to them using 1 milligram per kilogram of body weight. The results showed differences in response to the drug from normal test subjects and psychotic test subjects. With the schizophrenic test subjects, the vegetative symptoms were delayed and the vegetative manifestations were not as intense. In four cases, the vegetative symptoms were not even present. Also with the schizophrenic test subjects, no new hallucinations were produced and there was a lack of after-effects. With the non-schizophrenic test subjects, their reaction was the same as normal test subjects, experiencing the full range of the drug. Based on this information, it is clear that there is a reduced sensitivity to DMT observed in schizophrenics. An explanation proposed for this information is that there is a disturbance of cerebral metabolism going on in the psychic process of schizophrenics. It is believed by some that DMT can be used as an aid in assessing the likely course of the disease.11

Conclusion

In conclusion, DMT is an extremely powerful, psychoactive drug. It can be combined with MAO-inhibitors to be taken orally, smoked, or injected. DMT affects all types of people with different conditions and produces a range of visual and psychological hallucinations and scenarios. It is theorized to be rooted in the pineal gland and is often described as a “third eye” as a result of its mind-bending properties and its relationship with the retina of the eyeball. Further research and trials of DMT can possibly result in a new understanding to mental illnesses and enlightenment.
Bibliography

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Natural Supplements on Polycystic Ovarian Syndrome

Abstract

Polycystic Ovarian Syndrome is the most common condition within the endocrine and reproductive systems in the female body. Hormone levels within a woman with PCOS are unbalanced and cause physiological changes like cystic ovaries, male characteristics from increased androgens, anovulation, and weight issues, and may lead to other diseases like diabetes and heart conditions. Current treatment of PCOS involves synthetic drugs such as birth control, insulin sensitizers, and androgen blockers that have adverse side effects. An alternative option to Western medicine is natural supplements that help to regulate or aid in the health condition of the bodily systems and include adaptogenic substances like Chasteberry, Maca Root, Apple Cider Vinegar, Licorice, Green Tea, and Spearmint, along with many more.

Introduction

Polycystic Ovarian Syndrome, or PCOS, is a disorder that affects as many as 1 in 10 women throughout the world, with up to 1 in 20 sufferers being within child-bearing age. It is an unpreventable, complex metabolic condition that is considered to be hereditary. This syndrome is marked physically by small cystic growths on the surface of the ovary (figure 1), irregular menstrual cycles, infertility, pelvic pain, acne, imbalance of male and female hormones, hirsutism (male pattern hair growth), and depression/anxiety. PCOS also affects insulin levels, weight, sleeping patterns, and the condition of the heart. It is the leading cause of infertility, and also causes complications during and after pregnancy. A woman diagnosed with PCOS is likely to have lower self-esteem from her altered appearance, and has higher risk for heart attack, diabetes, high blood pressure, and endometrial cancer. More than half of all women with PCOS will develop diabetes, and the likelihood of heart attack is 4-7 times greater than women without the syndrome.

Metabolic Causes

Hormones secreted from the pituitary gland in the brain and ovaries in the reproductive system regulate ovulation and overall “feminine” features of the female body. The primary biochemical involved in PCOS is the hypersecretion of luteinizing hormone, or LH. LH, along with Follicle Stimulating Hormone, or
FSH, are gonadotropins, as they stimulate the gonads to engage in reproduction. They are glycoproteins (figure 2, beta) composed of smaller alpha and beta subunits, the alpha units being generally the same and the beta units being the unique binder to different receptors. FSH causes stimulates of the ovarian follicles to mature, along with a pre-ovulation surge of LH in the body that allows the egg to be released. These hormones work in a negative feedback system, with a track between the ovaries, pituitary gland, and hypothalamus (figure 3). The hypothalamus releases LH-releasing hormone (LH-RH, otherwise known as GnRH), which triggers the pituitary to secrete LH and FSH. The ovaries, once the levels of hormones needed is achieved, signals the hypothalamus to reduce the LH-RH. LH, after allowing the mature egg to be released, then aids in the ovaries production of progesterone, estrogen, and testosterone. Usually, the ratio of FSH to LH is roughly equal under normal circumstances. In a woman with PCOS, the ratio of LH to FSH is 3:1⁴. Hypersecretion of LH causes testosterone to be produced in excess. This increases the free and total testosterone levels in the body, producing masculine physiological changes like hirsutism, deepening of the voice, acne, anovulation, and abdominal weight gain.

Insulin resistance is another issue related to PCOS. When a PCOS sufferer is insulin resistant, they have a high chance of developing diabetes mellitus. Insulin is what allows the glucose extracted from digested food to pass through the cell membrane and give energy to the cells. When there is not enough insulin, or the body is insulin resistant, the glucose builds up in the blood plasma. The glucose is converted into fat and deposited mainly in the abdominal region as visceral fat in lieu of being burned. The visceral fat (fat around the organs, as opposed to subcutaneous which is just under the skin) leads to other health complications, including the heart issues related to PCOS, and aids in the unbalanced hormone levels by the hormonal secretion of the adipose tissue. Eventually, the continuous high blood sugar level leads to Type 2 diabetes. The excess amount of insulin directly affects the secretion of hormones by the ovaries and by the adrenal glands (figure 4). The ovaries are stimulated by the excess insulin to produce higher levels of testosterone than estrogen and progesterone, increasing the level of free-androgens in the body.

**Current Treatment**

The most widely used of current treatment of PCOS includes birth control, insulin sensitizers, and androgen blocking therapy. These all have been deemed effective for some,
but not all PCOS sufferers. Most treatments are synthesized drugs, and have adverse side effects; whether by causing other symptoms or in fact making the original syndrome worse if the drug is not administered.

Unarguably the most frequently used treatment is birth control. This is used to introduce more estrogen and progesterone into the body to better feminize it, regulate ovulation, and help with acne. Progesterone and estrogen are the two “female” sex hormones, called steroids (four cycloalkane rings), and are in birth control pills. Multiple symptoms can seem to be better while on birth control, but no effects last if taken off of the pill. Also, the pill is directly putting hormones into the body, eventually, as the body keeps receiving hormones from outside sources, it will slowly stop producing its own. If a woman decides to stop taking the pill, it may leave her with a condition that is worse than the beginning. Besides this, many have recorded adverse effects from birth control, ranging from mood swings, weight gain, palpations, depression, and anxiety. Birth control also cannot be administered to anyone with pre-existing liver conditions, heart conditions, hypertension, diabetes (which is likely with PCOS sufferers), clotting disorders, or genetic predisposition for breast or cervical cancer.

Another therapy for PCOS is administering insulin sensitizers. Insulin sensitizers allow the body to use insulin as a normal body would by allowing the glucose into the cell and therefore lowering blood sugar. The reduction in insulin would also lower the androgen production (refer back to figure 4). Metformin, the commonly used sensitizer, is usually paired alongside birth control to help with PCOS. There are less serious side effects with Metformin unless someone is severely allergic to it. Another possible side effect is lactic acidosis (excess lactic acid in the body), or kidney and liver problems. Aside from side effects, Metformin may not be suitable for PCOS patients, simply because not everyone is insulin resistant just because they have PCOS.

The third treatment used for PCOS is an androgen blocker. Androgen blockers have no effect on the production of androgens in the body, but rather stop the body from utilizing the excess by blocking the receptors on different cells. The main blocker used is Spironolactone. It is mainly used to combat the male characteristics often seen in women with PCOS like hirsutism, acne, voice deepening, abdominal weight placement, and male pattern baldness. There are serious side effects to Spironolactone, as one can overdose, be allergic, or suffer from loss of muscle control, vomiting, enlarged or tender breasts, stomach pain, irregular bleeding, and fainting, among others.

Other treatments include ovarian drilling, hysterectomy, or “wedge resection”. Ovarian drilling only breaks up the current cysts to reduce the chance of enlargement and possible destruction of the ovary. Removal of the ovaries and uterus will not cease production of hormones, as there is also the adrenal gland that secretes hormones. Also a large problem of
PCOS sufferers is infertility, and this obviously helps to stay infertile. Wedge resection is a surgery where the part of the ovary containing cysts is removed in hopes of producing ovulation. Both drilling and resection increases fertility, but the effects are short lived and cause scarring and adhesions on the ovarian organs, while possibly limiting long term function of the ovaries. Surgery may cause permanent damage, along with possible surgical complications that may occur, including death by anesthesia.

Why Alternative Medicine?

Many people choose natural medicine for a variety of reasons. First, it has been practiced for centuries, as conventional medicine did not exist yet. Some feel it better corresponds to their practices and belief systems. Others believe it is safer to treat themselves with herbs than synthetic drugs. There is a war within doctors who prefer Western to Eastern medicine, with the Western medicine being dubbed as one who works for the pharmaceutical companies to only treat symptoms and not causes in order to create more business, while Eastern medicine being called unscientific and unrealistic to use plants to treat disease.

The philosophy of natural medicine is to pinpoint, understand, and treat a cause and not only a symptom. While conventional medicine definitely has a place in surgeries, emergencies, and many diseases, natural medicine works to help heal the body by strengthening the organ systems and providing nutrients to solve deficiencies that cause complications, rather than cover up the effects of the disease. For PCOS, many of the supplements mimic effects that conventional medicines have on the body, or they provide building blocks for the body to proceed with its own natural processes (as opposed to birth control, which loads the body with hormones, supplements can help the organs to regulate themselves in the proper manner, which would create a balance of hormones by itself).

Another pro of natural medicine is its tendency to treat the person, as opposed to the disease. Besides supplements, a lifestyle change is usually included, combining exercise, diet, and supplements, which together can heal the being as whole. Many problems can stem from sedentary lifestyles and unhealthy food choices. A healthier diet would help provide the proper nutrition the body needs to keep homeostasis, fight disease, and heal wounds more efficiently. Exercise helps control weight gain and drastically improves circulation and digestion - vitamins and minerals are better absorbed into the body from food, and the blood does a better job of carrying these necessary substances to the cells that desperately need them.

Supplements for PCOS include Chasteberry, Maca Root, Licorice Root, Apple Cider Vinegar, Green Tea, and Peppermint, among a cornucopia of others. These supplements have different effects on the body, some providing to the health of the pituitary gland, some having an effect on insulin, and some having anti-androgen or androgen blocking properties. Used in conjunction with a diet low in simple carbohydrates and sugars, and a moderate exercise program, PCOS can be treated quite effectively. Weight loss is always suggested to women trying to treat PCOS, as it has a positive effect on both insulin and androgen levels, as well as bettering overall health of the individual.

Adaptogens
Adaptogens are substances that are “innocuous and cause minimal disorders in the physiological functions of an organism...[and] must have a nonspecific action, and...usually has a normalizing action irrespective of the direction of the pathological state”. Chasteberry, Licorice, Green Tea, Peppermint, Apple Cider Vinegar, and Maca Root are all adaptogens that will help to regulate hormone levels no matter is elevated or deficient.

Supplements for Polycystic Ovarian Syndrome

Widely used for PCOS, Chasteberry, also known as Vitex, is the berry of a small shrub-like plant native to Central Asia and the Mediterranean. It has been used for centuries to help ease menstrual issues with women, from PMS to menopause. It is generally thought that Chasteberry acts on the pituitary gland and not the ovaries. It holds steroidal precursors along with flavonoids, alkaloids, and antioxidants (testosterone works off of an oxidative process). It raises progesterone by acting on the hypothalamic-pituitary axis. It also limits release of prolactin which helps with breast tenderness. Side effects of Chasteberry are generally mild, with a possibility of gastrointestinal discomfort, headache, and acne. Chasteberry is ingested orally through capsules, teas, and tinctures.

Another remedy is Maca Root, a plant native to Peru. Maca is very high in glucosinolates, which are an amino acid and glucose derivative. Aromatic isothiocyanates are hydrolyzed from these glucosinolates, and aid in cancer prevention. Maca’s high amino acid concentration along with fatty acids and sterols also affect the hypothalamic-pituitary axis to regulate hormonal ratios. In its native parts of Peru, Maca is eaten raw or used as flour but is generally used abroad in powdered form and consumed as a shake, or swallowed in pill form. Due to high fiber content, intestinal issues are common and it’s common practice to start with very low doses (a fourth of the recommended dose) and gradually build up to the maximum dose. Elevated energy and a better sense of well-being often occur while taking Maca, which may help depression and anxiety in PCOS patients. It is also known to clear acne, and has been reported to help ease hirsutism.

Licorice root has been touted for its many uses and was originally used in medicine in the Middle East, Europe, and Asia. It has mass effects on the body as a whole but definitely in the endocrine glands and the balance of the reproductive system. In an Italian study in 2004, Licorice proved to lower testosterone significantly after only 2 months of being administered. Lower androgen levels can help treat signs of hirsutism, acne, balding, and other characteristics synonymous with having elevated testosterone. A substance in the licorice called glycyrrhizin can also help with weight loss, aiding in PCOS symptoms. Low doses of licorice must be taken for short periods of time as licorice may cause high blood pressure and low potassium if used improperly.
The uses of Raw Apple Cider Vinegar are endless, especially as a medicine. Raw Apple Cider Vinegar is a murky, unfiltered vinegar made from whole crushed apples, and holds a “web” like substance on the bottom. This is referred to as “Mother”, and consists of the beneficial bacteria and enzymes. Commercial Apple Cider Vinegar is clear, filtered, and holds none of the nutrients that Raw Apple Cider Vinegar has. For those needing to lose weight with PCOS, Raw Apple Cider Vinegar is used to help the body detoxify itself to better metabolize fat. Taking Apple Cider Vinegar has been proven to make the body less insulin resistant, allowing for weight loss, in turn helping to regulate menstrual cycles and hormone levels. Apple Cider Vinegar also help lower blood pressure and risk of heart disease, while also preventing and slowing cancer growth. The fermentation process produces the enzymes and the high amounts of potassium, magnesium, and antioxidants in the vinegar work to balance the body. Apple Cider Vinegar is usually administered within a glass of water, sometimes with the addition of raw honey for a more pleasurable taste. The only precaution of Raw Apple Cider Vinegar is its high acidity— it should never be taken before diluting with water, as acid erosion may occur to the teeth and esophageal lining.

For many cultures, tea is a cure for any ailment. It can be used for its antimicrobial properties, calming effects, cancer preventative properties, mood enhancement, cardiovascular health, metabolism stimulation, antioxidants, and other general criteria. Recently, the benefits of Green Tea have been in great interest, bringing promising findings on health because of the caffeine and flavonoids, more specifically the catechins. Research has shown that caffeine consumption elevates SHBG which would help to lower testosterone levels in those with PCOS, while lowering estrogen levels (commonly elevated from PCOS). Catechins are a polyphenol and acts as a strong antioxidant and help with cell and DNA health. The EGCG (the most famous catechin) can help in sustaining a healthy condition of the endocrine system, while also lowering the risk of endometrial cancer, aiding in weight loss and blood glucose levels, and preventing heart disease. Green Tea is best consumed in tea form, or in extracts or capsules. Only those sensitive to caffeine should take precautions in consuming Green Tea.

Not all tea is created from a usual tea leaf. Many herbs and spices can be steeped and consumed as a “tea” for its health benefits or for pleasure. Spearmint can be used in such a way. Studies have shown that the consumption of Spearmint Tea can help to considerably lower the free and total testosterone in the blood while increasing FSH to balance out the LH:FSH ratio in the body. This has value to those suffering from hirsutism caused by elevated androgens. By lowering the androgens capable of attaching to hair follicles, hirsutism can be controlled in those suffering from PCOS. Spearmint can be consumed as tea, taken in extract form, or used as a spice in foods, desserts,
and drinks. Those with kidney or liver problems should not use spearmint as it may complicate issues further.

There are many other herbs and vitamins that can be supplemented with a healthy diet to treat PCOS. A few other supplements are:

**Inositol:** this vitamin B-complex aids in ovarian function and insulin resistance, and may help with weight loss. A 14-week study also showed an increase in progesterone, and not just regulated menstruation but regulated ovulation (helpful for those suffering from infertility)\(^\text{19}\).

**Vitamin D:** A study found that women with higher vitamin D and calcium in their blood serum were less likely to be insulin resistant. The supplementation also helped in ovulation and fertility\(^\text{20}\).

**Magnesium:** Magnesium is another element that assists in insulin resistance and those with PCOS that have also developed Type II diabetes better control the diseases. It also helps those with insulin resistance prevent it from progressing into diabetes\(^\text{21}\).

**Chromium:** may also aid in weight loss as chromium assists in glucose tolerance for those that are insulin resistant\(^\text{22}\).

**Saw Palmetto:** Saw Palmetto reduces the ability of an enzyme in our body called 5-alpha reductase. This enzyme makes a conversion of testosterone to a more androgenic form of testosterone, called DHT. DHT wreaks more havoc on the female body as it is a “stronger” male hormone, and lessening the amount of DHT produced can have beneficial effects on hirsutism and acne\(^\text{23}\).

Although there are many ways to help PCOS, any new supplement and regimen should be discussed with your doctor. Even though these are natural herbs and supplements, this is still medicine, and proper precautions should always be taken before starting a new routine. Always check with your doctor and herbalist about possible side effects, medicine interactions, and preexisting disorders that these supplements might complicate further.

**Personal Statement**

There are hundreds of alternative ways to treat the ailments we suffer from every day, whether it is temporary or permanent, small or large, painful or bearable. Conventional medicine will always have its place in medicine, and is a vital part of the progress of biotechnology, saving millions of people, all the time. Neither natural nor conventional medicine is completely better over the other. My argument is that if nature gave us an issue, it can also give us an answer. A lot of the above can be easily obtained, without a feeling of being a “sick patient” and needing complicated treatment. As someone who was diagnosed with PCOS about 2 years ago, I understand the frustration of having the disorder. I suffered for many years not knowing of my condition, and it took a long time before doctors took my symptoms seriously. I was never given any other option besides birth control, which I do not completely trust putting into my body. I truly believe in natural supplementation (with plenty of research). The body is made to heal itself, but with today’s diet and lack of nutrition, it no longer has the building blocks to heal properly. Knowledge of a condition and what deficiencies may cause it can automatically give you the answer to how to solve the problem, and supplementation allows for this process to go forth. PCOS is something that can wreak complete havoc on a woman, not only physically, but cause severe mental and esteem issues, along with serious bouts of depression, anxiety, and feelings of “not being good enough” as a woman. It is a very serious condition that is taken all
cause severe mental and esteem issues, along with serious bouts of depression, anxiety, and feelings of “not being good enough” as a woman. It is a very serious condition that is taken all too lightly, and I wish that more will be put into bringing PCOS into a brighter light. I have tried very hard to fight being another statistic, and slowly but surely am succeeding. Personally, I have seen great results with Chasteberry, Magnesium, Green Tea, and a daily multivitamin, and am an avid preacher to others suffering from ailments that natural medicine is very beneficial. Anyone who understands science can comprehend how too many chemicals and synthetic substances in the body can do more harm than good, and natural medicine is a great alternative to get what is needed without what is not wanted. Plenty can testify to natural medicine’s effectiveness, including myself. A syndrome will not keep me or anyone else with it from living as we all want to, treating ourselves as a human and not just a symptom. Today, through natural supplementation, I am both happy and healthy, have never taken birth control, and am certain I never will.
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Bacterial Meningitis: A Deadly Disease

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ABSTRACT

Bacterial meningitis (BM) is a major cause of morbidity and mortality in children, although its annual incidence in the United States is declining with the widespread use of vaccinations. Clinical signs and symptoms are unreliable in distinguishing between the various causes of meningitis, including, bacterial, fungal and viral or aseptic meningitis. It is still treated as a medical emergency and prompt use of empiric antibiotics based on epidemiological data, are necessary even before the workup for the diagnosis is fully complete. The focus of this article will be on bacterial meningitis, its changing epidemiology as a result of the use of conjugated vaccines, pathophysiology, signs and symptoms as well as its treatment.

INTRODUCTION

Meningitis is an inflammation of the immediate covering of the brain and spinal cord called the meninges. From without inwards, the meninges comprise of the Dura mater, Arachnoid mater and the Pia mater. Between the Pia and Arachnoid mater lays the cerebrospinal fluid, which bathes the brain. This fluid is very important in the diagnosis of meningitis.

There are several causes of meningitis. These include bacterial, viral or aseptic, fungal and chemical meningitis caused by drugs.

BACTERIAL MENINGITIS

Worldwide, bacterial meningitis is a menace, causing a significant number of deaths especially in sub-Saharan Africa.

EPIDEMIOLOGY

In a surveillance study from 27 states in the United States from 1978 to 1981, annual attack rate of bacterial meningitis was 3.0 per 100,000 populations. The most common pathogens were streptococcus pneumoniae, hemophilus influenzae, neisseria meningitides, accounting for more than 80% of cases.
In 1986, a second laboratory based study in 5 states, including Los Angeles County, in the United States, put the overall incidence of meningitis at 2 to 3 fold higher than the previous study. Again, the 3 most common organisms were hemophilus influenzae, Neisseria meningitides and streptococcus pneumoniae, accounting for 77% of the cases.\(^{[4]}\)

Since these reports were made, the incidence of bacterial meningitis has dramatically decreased in the United States, primarily because of the introduction of vaccines. In 1995, a laboratory based study in all acute care hospitals in 4 states, with a population of over 10million, showed a steep decline in the incidence of meningitis, especially that due to hemophilus influenza type B. The incidence had decreased from 2.9 per 100,000 population\(^{[2,3]}\) in 1986 to 0.2 per 100,000 in 1995. This decrease was primarily attributed to the availability of vaccines.

In another surveillance study between 1998 and 2003, the incidence of meningitis further decreased as a result of the availability of the pneumococcal vaccine in 2000.\(^{[4]}\)

In other parts of the world, bacterial meningitis continues to be a high cause of morbidity and mortality. Sub-Saharan Africa has one of the world’s greatest disease burdens. In the year 2000, 500,000 deaths were caused by hemophilus influenza B and streptococcus pneumonia. Neisseria meningitides is responsible for recurrent epidemics accounting for over 700,000 cases in the last 10 years.\(^{[8]}\)

**Causes of Bacterial Meningitis (BM)**

Bacterial meningitis usually happens when another part of the body is infected and blood carries the bacteria from the infected area to the brain and spinal cord. Bacteria can also infect the brain when there is an ear or sinus infection, or after a skull fracture; this is called contiguous spread, since it tracks along tissue lines to the meninges.

Some forms of bacterial meningitis can be spread from person to person. The bacteria can be spread by close contact with lung and throat secretions for example, from coughing or kissing. The bacteria that cause meningitis are not as contagious as the viruses that cause the common cold or flu. They are not spread by casual contact in public places, such as when you go shopping or visit the library.

**Risk Factor**

Conditions that may lead to bacterial meningitis include respiratory infection, otitis media, mastoiditis, hemoglobinopathy, and HIV infection, immunocompromised status, alcoholism, head injury, diabetes mellitus, and surgery (e.g., neurosurgical procedures, cochlear implants with positioners, and abdominal surgery). People most at risk for bacterial meningitis include neonates and infants; older adults; college students living in close proximity to one another (e.g., in dormitories); residents of and travelers to endemic areas (e.g., sub-Saharan Africa and Saudi Arabia); and recipients of cochlear implants < 18 years of age. In pregnant women, a type of meningitis called listeriosis is often found. It is caused by the bacteria called listeria.
The three most common causes of bacterial meningitis based on epidemiological data are discussed below:

**Hemophilus influenza B (Hib)**
This is an encapsulated organism that can cause meningitis. There has been greater than 90% reduction in the incidence of influenza B in the United States and Western Europe in recent years.

This bacterium is believed to be responsible for serious illness in about 3 million people per year and an estimated 386,000 deaths per year mainly through meningitis. It usually strikes children less than 5 years old. The bacteria spread from person to person via respiratory droplets. Humans are the only known reservoir. Hib does not survive on surfaces of inanimate objects. If the bacteria stay in a child's nose, and throat, the child may not get sick; this is termed colonization.

Hib meningitis is a serious problem in the developing countries with high mortality. About 15-35% of survivors have a permanent disability including mental retardation and deafness. Before immunization, Hib was the leading cause of meningitis in the USA and other developed countries.

Below is a picture of Hib bacterium. It is encapsulated; allowing it to escape most of the body's fighting mechanisms.

![Haemophilus influenzae type b](image)

**Neisseria Meningitidis**
Neisseria meningitidis is a common bacterium and lives in the noses and throats of about one in four people who are carriers (Sheffield Teaching Hospitals NHS Foundation Trust, 2010). It was first discovered by Anton Weichselbaum, an Austrian pathologist and bacteriologist in 1887. It cannot survive outside the body, and close contact is needed in order for it to be passed on, between people.

About 2500 to 3500 cases of Neisseria meningitides infection occur annually in the United States. The case rate is about 1 in 100,000 population. Children under 5 years are at greatest risk. In sub-Saharan Africa, the rate is between 1 in 1000 to 1 in 100.
Most *Neisseria meningitidis* infections are asymptomatic (without symptoms), but there are occasions when the organism enters the bloodstream and causes meningococcal disease. It is not understood why a few people are susceptible to serious illness but others carry the same bacterium without experiencing illness.

*Neisseria meningitidis*

**Streptococcus pneumonia**

*Streptococcus pneumonia* is also commonly found in the nose and throat of 5-10% of healthy adults, and 20-40% of healthy children. It commonly causes meningitis in babies and those aged over 45 years (Wisconsin Department of Health Services, 2011). Meningitis caused by streptococcus pneumonia is not thought to be contagious (Centers for Disease Control and Prevention, 2007). This type of meningitis is usually caused by the spread of infection through the bloodstream.

Below is a picture of streptococcus pneumoniae. It is a diplococccie. It is encapsulated. This makes it easy for it to escape the body's defense mechanisms.

*Streptococcus pneumonia*
Symptoms

Clinical presentation of bacterial meningitis may include severe headache, high fever, stiff neck, photophobia, nausea, vomiting, drowsiness, papilledema (i.e., edema and inflammation of the optic nerve caused by increased intracranial pressure [ICP]), confusion (especially in older adults), anorexia, lethargy, petechial rash, myalgia (body aches), rigors, profuse sweats, weakness, rapid breathing, dilated nonreactive pupils, seizures, and coma. Neonatal signs include poor feeding, listlessness, irritability, shrill crying, lethargy, apathy, fever, hypothermia, jaundice, bulging fontanelle, hypotonia, hypoglycemia, seizures, and shock.
Some of the antibiotics for the treatment of bacterial meningitis are cefotaxime, ceftriaxone and vancomycin.

**Cefotaxime**

It has broad range activity against Gram positive and Gram negative bacteria. In most cases, it is considered to be equivalent to ceftriaxone in terms of safety and efficacy.
Cefotaxime is a type of antibiotic called a cephalosporin. These antibiotics are related to penicillin. It is used to treat infections caused by bacteria. It works by interfering with the ability of bacteria to form cell walls. The cell walls of bacteria are vital for their survival. They keep unwanted substances from entering their cells and stop the contents of their cells from leaking out. Cefotaxime weakens the bonds that hold the bacterial cell wall together. This allows holes to appear in the cell walls and kills the bacteria.

Cefotaxime is a broad-spectrum antibiotic that kills a wide variety of bacteria that cause a wide variety of commonly-occurring infections, including the ones that cause meningitis. It is given by injection into a vein or muscle, or via a drip into a vein (intravenous infusion).

**Vancomycin**

Vancomycin belongs to a group of antibiotics called glycopeptides. Bacteria have an external cell wall that is reinforced by molecules called peptidoglycans. The cell wall is vital for protection against the normal environment of the body in which the bacteria live. It works by blocking the formation of these peptidoglycans. By doing this, the walls of the bacteria become fragile and it results in the death of the bacteria.
Conclusion

Bacterial meningitis remains a dangerous threat. Children can be protected by ensuring that they are completely up to date with their routine vaccinations. Along with an awareness of symptoms of meningitis, especially the early red flag symptoms, the impact of this deadly disease on children and young adults can be greatly reduced. The current drugs used for the treatment of bacteria meningitis which are cefotaxime, ceftriaxone and vancomycin. Seems to be very efficient in combating the deadly disease.

I first heard of bacterial meningitis when a friend’s brother died from it in August 2011, shortly after complaining of a severe headache. The autopsy revealed he had bacterial meningitis. The shocking death of the boy arose my curiosity. Bacterial meningitis is not just like any bacteria infection. It is a deadly disease that affects the meninges surrounding the brain and spinal cord. Bacterial meningitis can strike without warning and can kill in hours. It can bring a healthy child to the brink of death within 24 hours.
I personally think that at the slightest manifestation of symptoms, attention should be given to the possibility of meningitis. Thus one needs a low index of suspicion to be able to seek immediate medical attention.
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