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History of Bloodletting

Paige Cramer

Medicinal bloodletting or venesection is the removal of blood from the body by opening a vein so as to reduce the volume of blood within the body. There were two main bloodletting techniques used during antiquity: venesection, the cutting open of a vein; and cupping. With the advent of more modern times, the methods used in antiquity, though not entirely supplanted by leeching, became less widely practiced. During the Middle Ages 500-1500 AD, barber surgeons were known to use bloodletting as a cleansing and purifying process in bathhouses, sometimes using leeches; the red and white stripes of the barber pole began as bloody and clean rags from bloodletting with a sliver-like bleeding cup on the top. Beginning in the late 1700s, the leech became more popular because it caused less pain to the patient and was more reliable in regulating the amount of blood removed. However, due to the advent of physiology, pathology, and microbiology in the late 19th century, the leech fell out of favor. In 1960, however, M. Derganc and F. Zdravic, two Slovenian surgeons, revived the leech's use, and it was brought back to the medical field for reconstructive surgeries and microsurgeries. Leeches were and still are used in reattachment surgeries of fingers, toes, legs, ears, noses, and scalps—even in breast reductions. Through the ages, bloodletting has evolved from bleeding people to almost to death, as in George Washington's case in 1799, to the mania of leeching in the 19th century to the controlled use of leeches in microsurgery today. The leech is no longer ubiquitous, but has wormed its way back into the medical field. Although it is doubtful that the demand for leeches will ever again place them on the endangered species list, they've assumed a valuable role in the treatment of human disorders.

PHLEBOTOMY, OR BLOODLETTING, IS THE longest-running tradition in medicine. It originated in the ancient civilizations of Egypt and Greece, persisted through the Medieval, Renaissance, and Enlightenment periods, flourished in Arabic and Indian medicine, and lasted through the 19th century. Through the centuries, bloodletting has evolved from venesection and cupping to the use of leeches. Likewise, the uses and methods of medical bloodletting—the removal of blood from the body by means of opening a vein, cupping, or leeching so as to reduce the volume of blood held within the body in accordance with ideologies corresponding to treatments of diseases—has evolved.

Bloodletting was based on an ancient system of physiology called "humoral medicine." Originating in the Hippocratic Corpus in *On the Nature of Things*, humoral medicine was based on the premise that the elements of the body reflected those of the natural world; those natural elements included air, water, earth, and fire. The Greeks believed that the interplay of those elements affected all the forces of the universe. Greek physicians maintained that health depended on maintaining a balance of the humors: black bile, yellow bile, phlegm, and blood. In order to restore health, doctors would drain "excess" humors by purging the digestive tract or draining blood.[1] In *Epidemics Book II*, bloodletting is the cure for flatulence, sphacelus (necrosis, or the localized death of living cells), sudden loss of speech without fever, fractures of the skull, hydrops with cough (an inner-ear problem), and fever.

Venesection and cupping lost favor as time went on and a new method of bloodletting arose—the leech, which was determined to be less painful to the patient. Leeches are part of the phylum *Annelida*, and there are about 300 species of leeches in the class *Hirudinea*. Leeches are freshwater invertebrate parasites found in swamps, ponds, and streams in Central and Northern Europe and America.[2] The leech has

two suckers: a caudal one, which allows for attachment to a substrate from which they are feeding as well as movement, and a cephalic one, by which they bite the host and suck blood.[3] The cephalic sucker houses the chitinous jaws. There are three jaws, each have 70 pairs of horny cutting teeth.[4]

The species of leech used most often in medicine is the *Hirudo medicinalis*, for it inflicts the deepest bite and has the longest time of post-bite bleeding. The medicinal leech can ingest an amount of blood close to that of eight times that of its own weight, 790 percent,[5] seven to fifteen milliliters, and may not need to feed for up to one year after its meal.[6]

In their heyday, leeching could be an expensive treatment. Leeches were carefully selected and graded, then starved for a day. The wound or spot to be leeched was rubbed raw. The patient placed their feet in a tub of hot water to facilitate blood flow, and the leech was attached. Occasionally a leech would bury itself completely inside the patient's body. In these cases, a salt-water enema would be employed to rid the leech from the body.[7] Sometimes it was difficult to persuade the leech to attach itself to the patient. Rubbing the skin until it was red; moistening the skin with sugared water, milk, or blood; rubbing the skin with a piece of meat; and even piercing the skin of the patient until a droplet of blood was in front of the leech were not uncommon methods of persuading the leech to attach.[8]

The leech gained popularity not only because it could be employed in difficult-to-reach places such as the tonsils, hemorrhoids, and the cervix,[9] but also because it didn't cause the patient as much pain as did previous methods of bloodletting. The near or total painlessness of the leech's bite is due to the contents of the leech's saliva, which contains a number of different chemical compounds useful in medicine even today. There is an anesthetic, which makes the bite of the leech painless to its host, who might not even know he or she has been bitten; an antihistamine-like vasodilator, which increases the blood flow to the feeding area by increasing the diameter of blood vessels; and a chemical enzyme called hyaluronidase, which facilitates the degradation of the connective tissues around the bite site, allowing the vasodilatory substance wider access to the area.[10] Along with these three compounds, there is also an anticoagulant, hirudin, which has seen much medical coverage. It was discovered and named in 1884 by J.B. Haycraft. The anticoagulant covalently binds thrombin and prevents the conversion of fibrogen to fibrin. It is the most potent natural inhibitor of clotting known.[11]

The anticoagulant properties of hirudin may be a more effective than those of heparin, a widely used natural anticoagulant discovered in 1916. In a recent study by British physicians, a drug synthesized from hirudin was tested internationally on 17,000 patients in 46 countries, all of whom had previously suffered a heart attack. During the first month after a cardiac arrest, many patients will often suffer a second, fatal heart attack. The British physicians found that patients given the hirudin-synthesized drug were a third less likely to experience a heart attack than patients on traditional treatments, such as heparin.[12]

No one knows exactly when leeches began to occupy an important role in medicine. Varying sources date the leech to 2,500 years ago, when it was used for bloodletting in ancient Egypt.[13] The use of leeches can be seen in the wall paintings found in a sepulchre of pharaohs of 1567-1308 BC.[14] Leeching is also mentioned in a medical encyclopedia from India written in Sanskrit completed between 500 BC and 200 AD.[15]

Leeching reached the height of its popularity in the middle 19th century, when it was espoused by the French physician François Broussais (1722-1838). Broussais was the head French physician of the Val De Grâce Hospital in Paris and a surgeon in Napoleon's Grande Armée.[16] Broussais believed that all diseases were due to inflammation caused by an irritation in the gastrointestinal tract by "sympathy," a concept involving both the neural and circulatory systems. The inflammation in the gastroin-

testinal tract would bring about irritations in other organ systems, bringing on a downward spiral. In order to reduce the building irritation, remedies consisting of changing the diet and bleeding were applied, frequently using leeches for the latter purpose.[16] Broussais promoted the idea that bleeding did not just remove a local excess of blood but created a constitutional weakness. This was his "weakening antiphlogistic regimen."[17] Convinced of his own treatise, Broussais treated his own gastrointestinal indigestion with fifteen applications of fifty to sixty leeches in the course of eighteen days, for a total blood lossof twenty ounces.[19]

Leeching was prescribed for every known disease and ailment, including laryngitis, nephritis (acute kidney pain), mental illness, and even obesity. Broussais treated such diseases as typhoid fever, syphilis, variologa, tuberculosis and even mental illnesses by applying leeches to the abdomen.[20] He would apply ten to fifteen leeches at one time to any one patient, exploiting hundreds of leeches daily in his practice.

The superfluous use of leeches by this illustrious doctor encouraged other French physicians to do the same. It was often the case that physicians would commonly prescribe the treatment of leeches prior to seeing the patient.[21] According to French import records, over a billion leeches were imported into France during the 19th century.[22] Broussais was in fact the biggest consumer in France, ordering two to three million leeches in 1824, and his requisitions rose to 42 million in 1833. A record of 57 million leeches were used in 1854.[23] Between the years of 1829 and 1836, five to six million leeches were used annually in the hospitals of Paris, drawing 673,200 kilograms of blood from patients of Parisian hospitals.[24]

About the same time, leeches were applied to patients in countries outside of France as well. Russia consumed about 30 million leeches annually. There, physicians M.J. Mudrov and I.E. Diadkovsky were equally enthusiastic about leeches. The United States imported 30 million leeches annually from Germany between 1824 and 1833. Given these large numbers, however, German authorities were wary of whether they could supply their own domestic needs. Obtaining European "Swedish" leeches became more difficult for Americans, and in 1835 they were forced to offer a $500 reward to anyone who could breed the Swedish leeches in the United States.[25]

In the treatment of fevers, Robert Jackson, an early 19th-century American physician from Georgia, wrote, "Bleeding is the most important whenever there appear marks of local congestion, inflammation, or that sluggish or torpid action which marks incapacity in the circulation vessels." He continues to discuss the use of leeches as treatment for myocarditis, peritonitis, pleuritis, hepatitis, gastritis, tonsillitis, nephritis, pneumonia, whooping cough, acute laminitis, dysentery, hemorrhoids, acne, and pimples.[26]

The popularity of leeches around the middle of the 19th century even spawned a craze of wearing clothes decorated with a leech motif. Women wore imitation leech decorations and brooches on their dresses.[27]

As the leech was exploited to the fullest extent, it began to disappear from its natural habitats. The French began to offer rewards to those who could develop new stocks in marshes, streams, and ponds. To feed cultivated leeches, elderly horses were driven into the waters where leeches lived, and frequently died due to loss of blood from feeding the leeches. It was common to see horse carcasses in the countryside.[28] Despite efforts at conservation and cultivation, for a short time the medicinal leech was considered an endangered species.[29]

The reuse of leeches was discontinued when this practice was rumored to transmit some diseases.[30] Several infectious diseases were thought to be transferred from person to person through their applications—syphilis, puerperal fever and erisypelas being a few.[31] Previously, leeches were used multiple times on different patients. However, due to ever-increasing concerns about the potential for infections, each leech was used once on a single patient to minimize infection

from the regurgitation of the leech gut contents.[32]

With the advent of modern pathology, physiology, and microbiology in the late 19th century, bloodletting with leeches fell out of favor.[33] The leeching mania faded slowly away after Broussais's death.[34] After the craze, in the late 19th century, one could purchase 100 Swedish leeches for $5.[35] (Nowadays, one leech costs between $4.75 to $6.50 a piece.[36]) During this period, few references were made in literature with respect to the removal of blood by leeches. It was noted that in one English hospital almost 100,000 leeches were used in 1832; fifty years later, however, less than 2,000 were used.[37] The last famous person to be treated with leeches for bloodletting was 73-year-old Joseph Stalin. On March 16, 1953, Stalin's doctors thought an old remedy would work—leeches to suck the dying man's veins. Stalin died within hours after the application of the leeches.[38] There are a few scattered references to leeching in 20th-century medical texts. Physicians became increasingly disenchanted with leeching, although they were still used occasionally into the 1940s.

The leech was brought back into the medical domain in the middle of the 20th century; its use was called *hirudotherapy*. Its return can be attributed to two Slovenian surgeons, M. Derganc and F. Zdravic from Ljubljana, who published a paper in the *British Journal of Plastic Surgery* in 1960 describing a leech-assisted tissue flap surgery, in which a flap of skin is freed or rotated from an adjacent body area to cover a defect or injury. These surgeons credited their own use of leeches to a Parisian surgeon, Philippe-Frédéric, who reported in 1836 that he had used leeches to restore circulation following the reconstruction of a nose.[39]

With the advent of microsurgery, including plastic and reconstructive surgeries, these doctors found a use for the leech in modern medicine, primarily in the reattachment of fingers, toes, legs, arms, ears, and noses, and even in breast reconstructions.

In operations, one of the biggest problems that arise is venous congestion; the excess blood from injured or reattached tissue needs to be removed. If the blood is not cleared quickly, the blood begins to clot, the arteries that bring fresh, oxygenated blood will become clogged, and the tissues that were reattached will decay and die. Venous congestion may lead to edema, capillary and arterial slowing, arterial thrombosis, flap ischemia, and eventual necrosis.[40] The main reason why leeches are employed in microsurgeries is to reduce this venous congestion.

When attaching the graft or organ, the arteries and veins need to be reattached as well. Arteries are the most important in reattachment because they supply oxygen-rich blood to the newly reattached graft. But there is usually an inadequate number or size of veins available to accommodate the arterial inflow into the graft. The leech removes excess venous blood until the vessels have had a chance to repair themselves. If the leech were not present, arterial blood flow would decrease because the venous blood would become congested and thus cause necrosis of the tissue and ultimate failure of the attached organ or graft. Instead, the leech acts as a substitute vein, reduces swelling in the tissues, and promotes the healing of the new vessels, allowing circulation to be restored.[41]

After the operation has been performed, the use of the leeches is withheld as long as possible. This is due to the anesthetic in the patient's body. A leech in contact with anesthetic will not feed, a phenomenon that has been called the "lazy leech syndrome." Furthermore, wearing gloves is imperative when applying the medicinal leeches to patients; it would be detrimental for the medical personnel, as well as the patient, if the leech were to attach itself to the incorrect host.[42]

Although the main use of leeches was for bloodletting techniques to relieve excess accumulations of blood in the main parts of the body, leeches have been also used in modern day to relieve excess blood around a bruised eye. Indeed, the phrase "black eye" probably came from the application of leeches surrounding a

bruised eye.[43] Leeches have also been known to reduce pain in osteoarthritics. Studies by researchers from the Essen-Mitte Clinic in Germany have shown that when leeches were applied to the knees of patients with osteoarthritis, the pain as well as the inflammation was alleviated.[44]

In one surgical case, thoroughly described pictorially as well as linguistically, the top two-thirds of a 45-year-old male's ear was amputated. The ear was reattached by means of microsurgery. No veins were available during the reattachment process, and thus there was venous congestion about the attachment point. Initially, no leeches were attached within the first 24 hours, but during the subsequent 24-hour period, three leeches were attached every eight hours. At 72 hours, three leeches were applied every eight hours for 15- to 30-minute intervals. The pictures shown at 24 hours, 48 hours, 72 hours, six days, and two months show the progression of the venous congested attached organ to the pink completely healed organ. Over the process of the two months, many leeches were used, and the reattachment surgery was ultimately successful.[45]

Jonathan Osborne, in 1833, wrote about the traveling leech, a problem that continues to occupy doctors. In "The Case of the Disappearing Leech," a case study of a patient who had just undergone a breast reconstruction, he wrote that a leech applied to the breast after the reconstruction migrated into the incision site and was unwilling to become disengaged from the deep tissue. In another case, a leech that was feeding on a forehead flap nasal reconstruction migrated its posterior end across the patient's upper eyelid to attach at the lateral canthal skin. When the patient awoke, the leech body was bridged across his field of vision.[46] In Osborne's day, tying a piece of string through the leech's body prevented it from venturing to places unknown and restricted. Today, utilizing the leech's aversion to salt, doctors employ a saline-dampened piece of gauze with a hole cut in the center, placing it on the site before the leech attaches itself.[47]

Not only does a leech have a propensity to travel while it is attached to the host, there are a few other negatives of using the medicinal leech in microsurgery. Hosting an annelid that is eating your excess blood strikes many people as grotesque.[48] However, according to Biopharm, a leech farm in Swansea, Wales, most patients are happy to be treated with leeches as long as the procedure is clearly and precisely explained prior to the application of the annelids.[49] In fact, Leeches USA recently shipped 240 medicinal leeches to four Philadelphia hospitals. The organization yearly imports leeches from a European source and ships about 30,000 leeches to various medical centers.[50] When pain, disfigurement, or dysfunction is the alternative, patients are tolerant of the medicinal leeches.

Despite the visual absurdity of having leeches attach to a person's skin, some patients are locally allergic to the leech's salivary secreted products.[51] Also, the leech sometimes fails to detach itself from the hosts' skin after a prolonged period of time, probably due to an arterial insufficiency. The leech should not be forcibly removed from the host, as the teeth of the leech may be dislodged from the leech and remain in the bite site, causing infection.

The leech, if still attached for a long period of time, should be treated with a topical solution of cocaine. This solution paralyzes the leech, and then the leech is removed from the patient. One should not place the leech in a solution of alcohol or hypertonic saline solution, for the leech may regurgitate the blood and possibly infect the bite site with its own bacteria. Once the leech has been removed, the patient's continued bleeding, caused by the hirudin of the leech's saliva, allows for more decongestion. However, if the bleeding continues and pressure and a coagulant don't stop the bleeding, the loss of blood to the patient can become detrimental, and a blood transfusion might be necessary.[52]

Possibly the most worrisome complication from using leeches, other than superficial scarring, is *Aeromonas hydrophila*. The bacteria are a

normal inhabitant in the foregut of the medicinal leech. The leech does not contain digestive enzymes to break down red blood cells from the blood, so it relies on bacterial enzyme secretions to digest blood.[53] *A. hydrophila* can infect the bite wound or surrounding skin during feeding. If the leech is squeezed, it regurgitates its gut contents, further increasing the likelihood of infection.[54]

Such an infection presents itself as a local abscess. The infection is not reactive to penicillin but to chloramphenicol and aminoglycosides. The two antibiotics are started on the patient prior to the leech's application to prevent the infection. There is, though, a 20 percent incidence rate of contracting the infection.[55]

During the 19th century, the leech became a prized possession. Not only were leeches hard to find in the wild, but it was difficult for rural doctors to keep them alive for very long. There were attempts to create "artificial leeches" to replace the natural leech. The artificial leeches of the 19th century were usually adaptable to a small area of the anatomy. The puncture wound generally attempted to imitate a leech bite.

The earliest substitute was Sarlandière's "bdellometer" from the Greek *bdello*, "leech." This French manufacturer introduced his device in 1819. The bdellometer consisted of a glass bell with two protruding tubes, one for scarification and one aspirator. It was determined to be no more successful than the cupping devices of the time period.

The second French invention was called the "terabdella" (large leech), created by Damoiseau. The device was introduced some time before 1862. It was similar to that of the bdellometer, more of a cupping device than an artificial leech.

The most successful of the mechanical leeches of the 19th century was Heurteloup's Leech, created by Frenchman, Charles Louis Heurteloup. It consisted of two parts, a scarifier and a suction pump. It could hold about an ounce of blood. It was sold in the late 19th century for as much as $15. It was created for eye ailments and was applied to the temples.[56]

Over the past decade there have been advances in phasing out the natural leech and replacing it with mechanical devices. The thought is that there are too many negatives of the natural leech that are not outweighed by the positives. In a 2003 study by Hartig, Connor, Heisey, and Conforti, the medicinal leech and the mechanical leech were compared to give data about the volume of blood removed, surface tension, and oxygenation levels. The volume of blood removed from both the leech and the device was comparable, as was the surface tension of the skin. However, there were differences in the skin color and the levels of total decongestion and oxygenation of the surface and subcutaneous tissue oxygenation. The medicinal leech did prove to be productive at relieving congestion, but the number of leeches required over an extended period of time to do so do not outweigh the advantages of the mechanical leeches of the late 20th and early 21st centuries. In this study, on average, 215 leeches were used per patient over a 6.6-day period to save eight free tissue attachments.[57] The number of units of blood needed to retain the patient's hemocrit level was, on average, 13 units. The mechanical device has the ability to auto-transfuse the blood it collects, so no blood transfusions are necessary, and it was able to decongest a larger, deeper area, increasing tissue oxygenation levels. The mechanical leeches remove blood even more passively than the medicinal leech, releasing a heparin spray that mimics the hirudin of the leech.[58]

Despite the advantages of using a machine to remove excess blood, there are limitations to the mechanical leech. It is unable to treat small confined tissues such as replanted ears or digits due to the size of the machine, and the mechanical leech can only be used from four to six hours on a single device wound. The natural leech, thus, can not be replaced completely.

The symbiotic relationship, which has survived for over 2,000 years, is unlikely to disappear overnight, and indeed the closing decades of the 20th century and the early years of the

21st century have already seen a revival of interest in this amazing creature.[59] Through the ages, bloodletting has evolved from bleeding people almost to or to death, as with George Washington in 1799, to the mania of leeching in the 19th century by François Broussais, to the controlled use of leeches in microsurgery in the 21st century. The leech has not again become ubiquitous, but has wormed its way back into the medical field. Although it is doubtful that the demand for leeches will ever again place them on the endangered species list, they have again assumed a role in the treatment of human disorders.

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Detecting SIDS:

The Faulty Transition from Fetal to Adult Hemoglobin as a Diagnostic Indicator for Sudden Infant Death Syndrome

Lisa Bazzle

As the leading cause of death of infants one month to one year of age, the exact etiology of Sudden Infant Death Syndrome (SIDS) remains uncertain. The initial emphasis on environmental factors such as infant sleeping position and second-hand smoke as the primary causes of SIDS has been replaced by a new focus on the low levels of adult hemoglobin in infants as a biological precursor to this fatal occurrence. Adult hemoglobin is a tetramer protein molecule in red blood cells whose specific structural conformation enables it to carry oxygen from the lungs and release it to the rest of the body. With an altered structure, fetal hemoglobin has an increased affinity for oxygen, facilitating the maternal transfer of oxygen in utero, but decreasing its ability to relinquish oxygen to tissues after birth. Therefore, delayed transition between fetal and adult hemoglobin can hinder the perfusion of oxygen in infants, leading to possible respiratory depression or an increased reliance on passive immunity, conditions that have been shown to increase infant susceptibility to SIDS. Research continues to study the differences in protein structure between each of these molecules as it relates to gene expression, but in the meantime, analysis of fetal hemoglobin levels remains a promising tool in the diagnosis of SIDS.

SUDDEN INFANT DEATH SYNDROME (SIDS) IS responsible for nearly two deaths for every 1,000 births in the United States, with the highest incidence of mortality occurring between two and four months of age.[1] While environmental factors such as cigarette smoke, sleeping position, and overheating have all appeared to play a role in the etiology of SIDS, recent research has focused on the delayed production of adult hemoglobin during the final weeks of gestation as a biological precursor to SIDS.

Because newborns with elevated levels of fetal hemoglobin continue to have a higher risk of SIDS, the physiological mechanisms differentiating adult and fetal hemoglobin play a role in the etiology of sudden death.[2] To understand this relationship, the function of hemoglobin must first be explored, as well as the differences in structure and oxygen affinity between adult and fetal hemoglobin. Through these analyses, the correlation between the faulty transition of fetal to adult hemoglobin and the increased susceptibility to SIDS will be corroborated.

The complexity of each living thing is belied by the simplicity that rests at the core of all life. The same two requirements are shared by all living things: a constant supply of oxygen and the efficient removal of carbon dioxide (CO_2). Both demands are fulfilled by the same molecule—hemoglobin. Hemoglobin is a protein molecule found in red blood cells that is responsible for delivering oxygen from the lungs to the tissues and for removing CO_2 from the tissues.[3] The structure of adult hemoglobin, two alpha and two beta chains of amino acids folded in a unique conformation to allow an iron atom (heme) to be positioned at the center of each of the four chains, allows this gas delivery to occur.

All gas exchange relies on the variable affinity of these heme groups to oxygen molecules. In the lungs, where oxygen concentration is high, the iron in hemoglobin has a high affinity for oxygen, and oxygen molecules bind to each of the four heme groups with increasing ease.[4] The oxygen-saturated hemoglobin is circulated via red blood cells to oxygen-poor tissues and muscles where the affinity for oxygen is low, resulting in the dissociation of oxygen from the heme groups into the tissues. At the same time, CO_2 that has accumulated in the tissues has reacted

with water to form bicarbonate ions and protons in the blood plasma. The unsaturated hemoglobin now has a strong affinity for protons. As two protons bind to each hemoglobin molecule, equilibrium continues to shift in the direction of CO_2 decomposition, helping to remove CO_2 from the bloodstream. In this way, hemoglobin transports CO_2 back to the lungs, where it can be ejected.[4] In this way the pH of the body, which is determined by proton concentration, is kept in check by the ability of hemoglobin to bind to excess protons.[3]

Unlike adult hemoglobin, fetal hemoglobin is composed of two alpha chains and two gamma chains, which create a different conformation. As a result, fetal hemoglobin has a higher affinity for oxygen than adult hemoglobin. In utero, this higher affinity facilitates the transfer of oxygen from mother to infant. However, this benefit is lost once the infant is born, as fetal hemoglobin is less likely to relinquish its oxygen molecules to oxygen-deprived tissues. To avoid this, a normal infant begins the transition from fetal to adult hemoglobin during the last weeks of gestation, so that by six months of age only traces of fetal hemoglobin are still present in the blood. Without this transition to adult hemoglobin, oxygen perfusion to vital tissues is severely compromised. This has recently been suggested as a causative factor of SIDS.[2]

Among the 3.2 million live births in California between 1990 and 1997, infants with elevated fetal hemoglobin levels had a higher predisposition to sudden death.[2] One possible explanation for this phenomenon is that the decrease in oxygen perfusion contributes to a state of chronic hypoxia. This hypoxia has pronounced depressive effects on the respiratory system during slow-wave sleep, which is a normal respiratory depression that occupies a majority of total sleep time in infants from two to four months of age.[5] Due to this hypoxia, ventilation decreases, leading to further respiratory depression. Ultimately, this creates a downward spiral ending in cessation of respiration, which leads to death.

An alternate theory suggests that infants who have difficulty transitioning from fetal to adult hemoglobin also show difficulty in switching from passive to active immunity, and that this latter predisposition is associated with the increased risk of death due to SIDS or respiratory infection. However the mechanism, the correlation between elevated fetal hemoglobin and vulnerability to SIDS is quite high.

The abnormality may have positive effects. The effect of elevated fetal hemoglobin levels in neonates living in oxygen-poor environments—where the partial pressure of pressures is greatly reduced, such as at high altitudes—also needs to be considered, as elevated fetal hemoglobin levels in these locations may actually be advantageous, as they may compensate for the lower external oxygen concentrations.

Further research continues in an attempt to increase the value of using adult hemoglobin levels as a tool for identifying infants with the greatest risk of SIDS.[2] To identify the cause for this abnormality it is necessary to pinpoint the specific gene responsible for the transition from fetal to adult hemoglobin.

Overall, the difference in oxygen affinity in adult and fetal hemoglobin plays a profound role in an infant's vulnerability to SIDS. Though the exact etiology of this syndrome remains elusive, the elevation of fetal hemoglobin levels has proven to be a useful diagnostic indicator for SIDS.[1]

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ADHD: A Biologically or Environmentally Based Disorder?

Meaghan Mackesy

It is estimated that 3 to 5 percent of the school-age population in the present-day United States has been diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and that approximately 60 percent of those so identified will continue to have symptoms throughout their adult life. It is important to understand the underlying causes and potential treatments of this disorder since it has a significant effect on one's ability to participate in society; those diagnosed with ADHD often have difficulty in completing college, maintaining employment, being an effective spouse or parent, and following societal norms. This paper examines the question of whether ADHD is a biologically or environmentally based disorder and the social implications of supporting only one of the two arguments. Support of one approach over the other depends on popular culture, societal values, and the vested interests of those making the assessment at any given point in time. It is concluded that there can be both biological and environmental factors involved in the development of ADHD. By focusing on only one argument, valuable insight into other causes and alternative treatments may be ignored. Consequently, all aspects of the underlying origins and effective management of the disorder should be considered.

ALTHOUGH EVERYONE IS OCCASIONALLY DISTRACTED and restless, some people are continually inattentive. At one time they might have been described as brain-damaged. Over the last forty to fifty years, however, psychologists and sociologists have identified these behaviors as symptoms of a disorder known as Attention Deficit Disorder (ADD). Common symptoms of ADD include inattention, daydreaming, slowness to respond, withdrawal, and passivity. Although many people believe that the terms ADD and Attention Deficit Hyperactivity Disorder (ADHD) are synonymous, they were designated as separate disorders in 1987. ADHD is characterized by hyperactivity, inattention, impulsivity, aggression, over-reaction, and low self-esteem.[1] Although hyperactivity seems to be the primary difference between the two disorders, another less easily defined characteristic of those diagnosed with ADHD is that they "simply do as they please"[1] without regard to consequences or the opinions of others.

Since the clinical symptoms of ADHD were first described and recognized in the early part of the twentieth century, scientists and educators have argued whether this disorder is caused by biological or environmental factors. This paper will examine the background of ADHD, its diagnosis and treatment, parties that have competing interests in ADHD, the argument for biological causes of the disorder, the argument for environmental causes of the disorder, and the social implications of supporting only one of these two arguments.

Background

ADHD, the disorder formerly known as hyperactivity, was first described by Sir George Frederick Still and Alfred F. Tredgold in the early 1900s.[2] They suggested that this behavior was caused by either a biological defect or a brain injury. The belief that hyperactivity was associated with brain damage persisted through the middle of the twentieth century. For example, after an encephalitis epidemic spread throughout Europe and the United States in 1917 and 1918, many professionals found that children who had survived the disease became hyperactive and developed learning disabilities.[2]

By the end of the 1950s, "the concept of brain damage as a single causative factor in the causation of [hyperactivity] was challenged."[2] At

that time, clinicians put forward other ideas concerning the cause of hyperactive behavior including environmental factors such as poor parenting. By the 1980s, as a result of continued research in the area, "hyperactivity came to be seen as a condition with a strong hereditary component, chronic in nature and causing significant handicap in the areas of academic achievement and socialization."[2]

As can be seen by the swings in thinking about ADHD over the last century, support for either a biological or an environmental cause of ADHD shifted over time. This can be attributed to the lack of supporting evidence for one argument over the other. And even though ADHD is perhaps the most and best studied of all psychological disorders of children, this continues to be the case; an understanding of its causes and nature is still incomplete.[3]

In the present-day United States, it is estimated that 3 to 5 percent of the school-age population is diagnosed with ADHD.[1] Through early adolescence, it is diagnosed four times more often in males than in females. But by college age, men and women are diagnosed with equal frequency. Most children do not outgrow the disorder; approximately 60 percent of those identified as having ADHD during their childhood continue to have symptoms as long as they live.[4]

Diagnosis and Treatment

At this point in time, there is no simple diagnostic tool to determine whether or not one has ADHD. It cannot be determined from either a blood test or a simple IQ test. The most common methods of diagnosis are by observation of the classic ADHD behaviors in a child by a parent or the reporting of unusual or disruptive behavior by a teacher.[2] Either may lead to the evaluation of the child by a qualified medical professional.

The problem with a diagnosis based on observation is that it is not objective because it depends on who is doing the observing. For example, different people look on the activity levels of children in different ways. This can account for the reason that children in the upper and middle classes are more often diagnosed with ADHD than those in the lower socioeconomic classes.[2] The upper and middle classes tend to be more concerned about the education of their children and react strongly to comments by teachers about disruptive classroom behaviors. Parents who are in the lower socioeconomic class are apt to look upon hyperactive or inattentive behaviors as phases of growing up and are less likely to seek medical opinions or intervention. To them, over-activity and daydreaming are neither unusual nor cause for alarm. Even if they are concerned, they may not have health insurance or they may not be able to take time off from work to have a child's behavior evaluated.

In an effort to find a truly objective physical diagnosis for ADHD, scientists began to use modern technology, including brain scans, which can be used to compare the brains of those diagnosed with ADHD to those of "normal" individuals. This was first done after reviewing results of primate research conducted in the late nineteenth century. The data indicated that "frontal lobe ablation in monkeys produced excessive restlessness and poor concentration."[2] Since these symptoms mimic those of individuals with ADHD, CT scans and MRIs were used to examine specific regions of the brain, especially the frontal lobes. In one brain-scanning experiment undertaken at Massachusetts General Hospital in 1999, a chemical imbalance was found in the brains of six adults diagnosed with ADHD as compared to thirty normal volunteers. These results were greeted with relief from some doctors studying ADHD, as they welcomed a test for a condition whose diagnosis had been based on "observation and psychological testing, so there [had been] an element of ambiguity about it."[5]

Although this particular study shows promise, it was performed on a small group. Therefore, it should be replicated in order to

determine the precision of the results. Additionally, some individuals have criticized the use of modern diagnostic tools such as brain scans because of potential adverse side effects, including allergic reactions to dyes used during the tests. Furthermore, exposure to low-dose radiation required by CT scans could increase chances of future leukemia or brain tumors. However, it can be argued that hospital radiologists have been working with these technologies for years and have generally determined safe radiation levels; furthermore, severe allergic reactions are extremely rare and usually can be reversed in the hospital or clinic where the tests are administered.[2]

At this time, the primary course of treatment for children diagnosed with ADHD is medication. Ironically, even though hyperactivity is one of the symptoms of ADHD, the drugs of choice are the stimulants Ritalin and Dexedrine.[1] Stimulant medications act on transmission signals in the brain that control attention impulses and regulate behavior. By activating neurotransmitters, the stimulant medications have been shown to reduce hyperactivity, decrease impulsivity, and improve the ability of children to focus.[6] This also leads to improvement in classroom performance.[7]

Medication for ADHD patients is often supplemented with training for parents and other caregivers in behavioral management, and with psychotherapy to deal with the patient's low self-esteem. Some studies indicate that teachers who reinforce positive behaviors and academic successes of individual hyperactive children successfully affect change in the classroom behavior of these children.[2] The implication of these studies is that the children benefit from individual attention and instruction. The reality is that special education programs for academically challenged children are often cut back or eliminated when school budgets are under-funded. Additionally, not all children with ADHD receive the same educational opportunities. For example, children who live in wealthy suburban cities and towns have access to more special education programs and individual attention than those who live in poor urban school districts because the wealthy cities and towns spend more money on the school system.[2]

Adults with the disorder are encouraged to establish support systems or join support groups in order to learn how to make friends and to reduce the impact their symptoms have. Adults are also encouraged to use planning and organizational tools as a means of imposing external controls on their lives.[1]

Competing Interests

Is ADHD caused by biological or environmental factors? And which is more important? It is particularly difficult to answer these subjective questions because a number of different interests, in addition to those diagnosed with the disorder, are invested in the answer. Among these groups are parents, the education industry, the government, the drug industry, and the medical industry.

Since ADHD is a childhood disorder, parents are actively involved. Many parents lobby educators and the government in their attempts to deal with the effects of the disorder, particularly as they are manifested in an educational setting. Teachers are involved because they have to balance the special needs of those who have ADHD with those of the rest of the class. The "private" education or tutoring business has a financial interest in ADHD; entities such as Sylvan Learning Center, Kaplan, and Princeton Review advertise the advantages of individual instruction for children. Government agencies are involved in establishing criteria and defining the parameters of diseases and disorders as well as funding research for them. Additionally, since the government pays for treatments through various federally and state-funded insurance programs, it has a financial incentive to try to control and limit costs.

The two biggest interest groups involved in ADHD are the drug and medical industries. Drug companies are in business to make a profit. They profit from this disorder as long as they

can convince medical professionals and the general public that their products can help alleviate the symptoms of ADHD. If one of their products no longer generates a profit, they try to develop a new product to take its place or create a need for their product in another group of people. This can be illustrated by actions taken by the drug manufacturer Eli Lilly. When the manufacturer realized that the number of ADHD children was not going to increase substantially, they turned their attention to adults with the disorder. Since adults with ADHD do not respond as well to stimulant medications as children do, Lilly developed and received FDA approval to market the first non-stimulant drug, Straterra, to treat the disorder. According to a story on CBS' "Sixty Minutes," physicians wrote one million prescriptions for Straterra during its first six months on the market.[8] Lilly created an informational website for the drug which includes a simplistic self-evaluation that visitors to the site can take to determine whether they might have ADHD, though the company does suggest seeking the advice of a doctor to confirm the diagnosis.[9] Additionally, Lilly's website for Straterra emphasizes the genetic causes of the disorder, thereby dismissing possible environmental causes for it. The claim that there is a genetic cause suggests that medication will work to alleviate the symptoms of ADHD. If the cause is environmental, it might be possible to eliminate these triggers and, therefore, the need for a drug. It can be argued, then, that the drug company is emphasizing genetic causes to increase drug sales.

The medical industry also has a vested interest in the disorder. As long as a biological or physical cause for the disorder can be suggested, medical professionals can be actively involved in its diagnosis and ongoing treatment. Medical professionals are able to influence this perception of ADHD by publicizing their beliefs by writing books, giving lectures, and appearing on television and radio. An example of this is the flood of popular literature over the past decade postulating a genetic basis for ADHD. For example, in *The Edison Gene*, Thom Hartmann suggests that the symptoms of ADHD (creativity, impulsiveness, and distractibility) are components of a highly adaptive and useful skill used by our hunter-and-gatherer ancestors rather than signs of a disorder.[10] This is a leap in evolutionary psychology for which there seems to be no basis. Another researcher, Russell Barkley, Ph.D., told a group of mental health care providers that ADHD is a genetic disorder and a life-long disability.[11] It is possible that one of the reasons he was invited to speak was the popular success of his book, *Taking Charge of ADHD*. Additionally, Edward Hallowell, M.D., has authored books dealing with ADHD. In his works, *Driven to Distraction* and *Answers to Distraction*, Hallowell states that the United States has a higher rate of diagnosed ADHD than European countries. He attributes this fact to the type of people who colonized and settled the United States and to a collective gene pool with a greater concentration of ADHD genes.[12] However, there is no data to support this speculation. A more reasonable explanation may be that there is a difference in the way in which Americans and Europeans approach individual behaviors that have societal implications.

One common factor in these books is the pronouncement that the cause of ADHD is genetic. These authors dismiss the possibility of social or environmental factors as contributors to the disorder, effectively minimizing personal and societal responsibility for ADHD. Again, one must consider the bias of the source of this information; it is possible that the authors feel they will sell more books by promoting the idea that ADHD is an inborn trait and cannot be blamed on food, parents, or society. Speculation that some historical figures, including Thomas Edison (hence the "Edison gene"), may have had the symptoms of ADHD may help sell books and may help those with the disorder feel better about themselves, but it is not necessarily good science. The authors and the drug companies also seem to supply simplistic answers to the problem—a pill for every ill.

Although there is some evidence to support their conclusions, there is no definitive proof of a genetic cause for the disorder. In this instance, one can compare the belief in a genetic cause of ADHD with the assertion that there is a genetic cause of breast cancer. In truth, some genes predispose women towards breast cancer, but not everyone who has the gene will develop the disease. For example, "mutation carriers who have a risk of developing breast cancer that may exceed 50 percent comprise no more than 5 to 10 percent of breast cancer cases."[13] In many instances, women with a breast cancer gene will not develop the disease unless they are also exposed to an environmental insult. Similarly, some genetic researchers have concluded that ADHD "is associated with the presence of the DRD4/7R allele"[14] but again, the presence of the gene is no guarantee of future ADHD. While any information linking genes to diseases receives a great deal of publicity, that information may not be accurate or thorough. Individuals may be harmed if they make medical decisions without full understanding of the condition. For example, most people taking the self-evaluation on Eli Lilly's Straterra drug website will be convinced that he or she has ADHD. Without additional research into the condition, some may come to believe they have it—and seek unnecessary treatment—when in fact they do not.

The Argument for Biological Causes

A significant amount of research has been done in an attempt to determine if there is a biological basis for ADHD. Some studies examine the possibility of an abnormality in the way the brain works, while others have focused on the possibility of a genetic or heritable link to the disorder. Scientists in search of a malfunctioning brain have turned their attention to the neurotransmitter dopamine.[2]

Researchers have long suspected that dopamine levels in the brain are involved in ADHD because the stimulant drugs used to treat children with ADHD calm them down instead of exciting them. Speculation is that stimulant drugs compensate for a dopamine deficiency.[2] Consequently, researchers are now examining genes that affect dopamine communication.[15] One of the problems with studies of individual genes involved in dopamine transmission is that the results have not been uniformly duplicated and therefore adequately confirmed. Additionally, even though researchers have identified several genes—including DAT1, DRD2, and DRD5—with the potential to have a significant impact on dopamine transmission, closer examination reveals that no single gene has a significant impact on increased ADHD incidence. Recent research has revealed that no matter how much so-called ADHD genes affect dopamine transmission, they do not cause the disorder alone; scientists have estimated that they only add a 1 to 3 percent increased chance of developing ADHD.[15] It is likely that a number of genes act in concert to establish a significant genetic increase in ADHD because no single gene appears to be critical in altering outcomes.

"Over the past decade, more than ten studies of twins in far-flung locations have suggested that ADHD has a strong genetic component." [15] Other research indicates that "heritability for ADHD—meaning that if one identical twin has it, the other will too—ranges from 65 to 90 percent."[15] One potential problem with conducting research on the heritability of ADHD using twin studies is that it is impossible to discount the impact of environment. For example, some twins are placed with different members of the same family. This means that their environments are very similar, which makes it impossible to separate the impact of genes and those of the environment on the individual. Additionally, twins have the same prenatal environment. It is possible that similarities in the behavior of twins may be attributed to their prenatal environment and not their genes.

The same problem of differentiating between a genetic and an environmental basis for disorders arises in family studies. The asser-

tion is that if a parent has ADHD, a child is more apt to have the disorder than a child who has no ADHD parents.[12] This may be because either the child inherited ADHD traits from a parent or they developed ADHD because they are exposed to the same environment as their parents. Much research needs to be done in order to separate, isolate, and identify the effects of genes and the environment on ADHD because no studies provide conclusive evidence that there is only a biological basis for the disorder.

The Argument for Environmental Causes

The major nonbiological factor that may cause ADHD symptoms, either alone or in concert with biological factors, is the environment, particularly the parents. Some studies have focused on the mother's physical and emotional health during pregnancy. For example, a prospective study of Scandinavian women provides evidence that "prenatal exposure to stress and smoking is independently associated with later symptoms of ADHD in human children, particularly for boys." [16] Another study examined the effect of maternal anxiety on the development of ADHD in children after birth and concluded that prenatal exposure to maternal anxiety without smoking also results in ADHD symptoms in eight and nine year olds.[17] This particular study indicates that maternal anxiety during the twelfth to twenty-second week of pregnancy is particularly significant. Further research in the area of anxiety seems advisable since both of these studies were conducted in Europe, and cultural biases do have an impact on the type of research proposed and the manner in which it is conducted. For example, Europeans have a cultural bias in favor of environmental and social causes for ADHD.[2] Additionally, these studies suggest that the mother may be to blame for the child's disorder. While this may be discomforting to some—especially mothers of children with ADHD—the role of the mother cannot be completely discounted, since the prenatal environment may play an important role in contributing to the development of ADHD.

Most research into the relationship between the family environment and ADHD is inconclusive. Virtually all the research indicates that relationship problems exist between hyperactive children and other family members. However, much of the debate on the role of the family is reminiscent of the question, "which came first, the chicken or the egg?" One school of thought contends that the presence of a hyperactive child distorts familial relationships, while others contend that a child's hyperactivity comes from a lack of parental response, particularly that of the mother, to child-initiated interactions.[2] Other studies suggest that the family environment has little to do with the development of ADHD.[2] Clearly, more research is needed to make a valid assessment of the role of the family in the development of ADHD.

The physical environment has also been evaluated as a potential causative factor in the development of the disorder. Various studies have implicated food allergies, nutritional deficits, and long term exposure to television as causes of ADHD. For example, in *The Edison Gene*, Hartmann cites medical journals that contain studies linking mineral and fatty acid deficiencies and too much sugar and television to learning problems and hyperactivity.[10] Conclusions of this sort are generally well publicized and received favorably by the public. However, none of the studies linking food and hyperactivity have ever been duplicated, and it is now speculated that excessive television watching is a symptom, rather than a cause, of ADHD.[2]

Social Implications

ADHD has significant societal implications because individual behaviors have societal consequences. For example, individuals with ADHD have difficulty internalizing language, so they have problems with social norms as well as rules and instructions.[1] They also have trouble managing time, and this makes it difficult for them to obtain and retain jobs. Additionally,

these symptoms make it difficult to maintain social relationships and to be an effective spouse or parent. For example, ongoing research conducted by Barkley on a group in Milwaukee indicates that "only 5 percent of those with ADHD graduated from college compared with 35 percent of the others and that ... the ADHD group has worse driving records and are much more likely to have been fired from a job." [18]

In attempting to uncover the causes of the disorder, the decision to focus solely on either biological or environmental causes can have serious consequences, because ignoring some causes may result in more individuals whose symptoms are not relieved and whose lives continue to be negatively impacted by the disorder. If one believes that biological factors are the primary cause of ADHD, one would tend to use medication as the preferred treatment for it. Therefore, in an effort to find more effective medication, continued research would be encouraged. This would be an advantage to society because more research would eventually lead to a better understanding of ADHD and therefore a more effective treatment of it. It also could lead to a means of detecting who is most at risk and a method for curing it. Additionally, a belief that ADHD is biologically based will remove some of the negative social aspects of the disease because people will assume that those with it cannot help their behavior. However, focusing exclusively on the biological aspects of the disorder could lead to the discounting of other potential causative factors. For example, women may continue to smoke and ignore stresses during pregnancy. Also, school systems could be tempted to cut costs by eliminating behavioral support and one-on-one teaching if they believe the environment has nothing to do with the disorder.

Conversely, if one focuses solely on environmental factors, one would stress behavioral modification for those with the disorder and its prevention. These treatments would have some advantages regardless of their efficacy in treating ADHD, as anyone can benefit from healthy lifestyle and diet changes, as well as from better teaching and parenting skills. However, ignoring the possibility of a biological basis may discourage individuals with ADHD from obtaining medication that may be beneficial to them. It may also discourage investment in research that could lead to a better understanding of the disorder. Additionally, teachers may resort to blaming parents for a child's behavior, while parents in turn blame the teacher.

There are reasons to both support and discourage pharmacological intervention for everyone with ADHD, either as the primary course of treatment or as an adjunct to behavior modification and lifestyle changes. Medication appears to be a viable option because of its apparent success in altering the behavior of children in the United States. However, there is also cause for concern, as 75 percent of American children with the disorder are medicated while virtually none of the European children are.[2] The possibility exists that these medications are overused in the United States, indicating that they may be used to modify the behavior of overactive children who do not have the disorder. This conclusion is reached by the fact that 5 percent of all American children take ADHD medications even though fewer actually have the disorder.[2] For example, some parents will search for a doctor who will prescribe Ritalin to their overactive child even though the child has not been diagnosed with ADHD. Additionally, there have been no studies that examine the effect of putting children on what is essentially speed and keeping them on it for the rest of their lives; it may be worth noting that the FDA banned amphetamines when they were used in diet pills. Perhaps there is no concern because of its low dosage and beneficial results, but it does seem appropriate to closely examine the nature of these substances and their long-term physiological and psychological impact.

Conclusion

ADHD is both a societal and an individual problem. The majority of cases result from a

biological source that can be affected by the environment. However, in a limited number of cases, ADHD can be caused purely by the environment.[2] Because the disorder is highly complicated and not completely understood, it is impossible at this point in time to focus on any one cause. Every individual has different genes, home environments, and school environments, so many causes for this disorder may act in concert with one another. Thus, all facets of the causation and management of ADHD should be investigated until a greater understanding of the disorder has been attained. Otherwise, individuals with ADHD will not be treated effectively and society will continue to bear the consequences.

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Training for Ethical Decision-Making in Neurosurgery

Hari Nandu

This paper discusses the responsibilities of medical professionals in the field of neurosurgery, specifically ethical decisions. Neurosurgery is a very difficult and demanding profession that requires precision of technique and careful planning for success. It also requires an all-encompassing plan for patient care, beginning with diagnosing the patient, recommending imaging studies, planning treatment, operating, determining pathology, and monitoring patient progress. The nervous system is extremely delicate, and intensive six-year residency programs incorporate rigorous study of a vast amount of physiological, surgical, and medical knowledge to obtain proficiency in neurological surgical procedures. At the same time, neurology interns must also learn fundamental ethical practices including proper bedside manner, the equal treatment of all patients, discussion of neurosurgical procedures informatively and professionally with patients, and delivery of bad news to family members in a professional and compassionate manner. The ethical duties of neurosurgeons also include serious issues such as determining brain death, paralysis, and vegetative states, and making decisions regarding treatment plans for inoperable tumors and tumors located in areas that contribute to higher thought in the brain. Because the ethical demands on neurosurgery residents are so high, these residents are specifically trained to deal adeptly with difficult ethical dilemmas involving a variety of medical situations.

THE NERVOUS SYSTEM IS A DELICATE AND complex system that, when damaged, requires the work of highly trained professionals to manipulate and correct it. For this task, neurosurgeons must be prepared with an extensive knowledge of the anatomical, physiological, and pathological characteristics of the central, peripheral, and autonomic nervous systems.

Neurosurgeons are bestowed with the responsibility of important ethical decision-making concerning the lives and neurological status of patients. To carry the weight of this kind of decision-making, surgical and ethical training for neurosurgeons is both rigorous and challenging. This intense training yields doctors capable of making decisions involving the wide spectrum of neurological disorders under difficult circumstances.

Medical Duties of a Neurosurgeon

According to the American Association of Neurological Surgeons, "Neurosurgery is the medical specialty concerned with the prevention, diagnosis, treatment, and rehabilitation of disorders that affect the spinal column, spinal cord, brain, nervous system, and peripheral nerves."[1] Neurosurgeons must take a 360-degree approach to patient care, which begins with observing a patient's symptoms and progresses to analyzing imaging studies such as computed tomography (CT) scans and magnetic resonance imaging (MRI), making a diagnosis, formulating a treatment plan that often includes surgery, learning the pathology, and finally following up on the patient's progress.[2] Neurosurgeons must have knowledge of related medical fields to ensure that their treatment plans don't adversely affect the rest of the patient's medical care.

Significant skill is required for neurosurgical operations, which is acquired during the six to eight years of training necessary to become a neurosurgeon. For example, surgeries such as brain tumor resections involve a great deal of planning and the intra-operative use of modern equipment. This equipment includes surgical

microscopes, which precisely remove a tumor without damaging cranial nerves, and computerized image-based navigation systems that orient the surgeon three-dimensionally to the size and shape of the tumor and assess the extent of resection of the tumor.

History of Medical Ethics

To understand the importance of ethical decisions made by neurosurgeons, we must first understand the impact of ethics on medical science. Medical ethics stems from the need for a society to observe and follow guidelines that reflect the society's moral codes. It is, therefore, as old as medicine itself; medical ethics existed in the ancient cultures of China, India, and Persia. The Hippocratic oath, the foundation of western medicine written in 400 BCE, established ethical principles for physicians. Further elaborations of medical ethics that reflected the societal and institutional changes of the day were made in the 1700s and the 1800s, and are seen in Thomas Percival's writings on the increase in medical technology in the 1800s.

The evolution of medical ethics has only become more complex as modern life-preserving medical technology itself has grown increasingly sophisticated. Until the 1950s, doctors adopted a paternalistic attitude toward their patients. For example, they frequently failed to fully disclose medical information to their patients, considering it to be out of the realm of the patient's understanding. After the social and technological revolutions of the 1960s, however, the patient's rights movement gained significant strength.[3] The result has been a still-evolving system of medical ethics that daily addresses new situations encountered by doctors navigating issues regarding a patient's decision-making capabilities and/or quality of life.

Ethical Duties of a Neurosurgeon

Current events have brought to the public eye the importance of ethical decision-making as it particularly pertains to care of the neurologically impaired patient. Brain death, paralysis, and a vegetative state are conditions that neurosurgeons face on a regular basis, and the ethical implications of dealing with these conditions have led to the creation of laws and statutes to assist in managing the thorny problems of treating patients experiencing these conditions.

The field of neurosurgery, however, has also adopted rigorous standard procedures for managing these conditions. To be determined brain dead, for example, a patient must meet specific criteria, including loss of eye movement; fixed dilated pupils; lack of gag and cough reflexes; lack of voluntary movement; and lack of response to other reflex tests.[4] Furthermore, the patient must be tested for apnea, a state in which the brain is no longer able to support regular breathing, another significant criteria for brain death.[5]

Other ethical decisions must be made independently, beyond strict established guidelines. When operating on patients who have brain tumors in areas of eloquence (areas of the brain that control speech and higher thought), neurosurgeons must balance removing as much of the tumor as possible with minimizing impairment of the patient's thinking and speaking abilities. Neurosurgeons must evaluate with the patient and their family the best treatment plans for tumors in inoperable areas of the brain, such as near the brainstem. They must weigh the consequences of giving radiation and chemotherapy and its attendant loss of quality of life alongside possible benefits of extending life. Because ethical decision-making is a central skill of a neurosurgeon, it is a vital component of the neurosurgicy residency program.

Application Process for Neurosurgery Residency

Neurosurgery residency programs incorporate a large volume of medical and surgical knowledge in an organized, cumulative process spanning six to eight years. The application process is known as the Neurological Surgery Residency Match and is sponsored by the Society of Neurological Surgeons. The neurosurgery match process

begins earlier than match processes for other residency programs in the fourth year of medical school, and starts with the applicant ranking the different residency programs for which he or she wishes to apply.

The application requires a student to have excellent grades, three letters of recommendation from neurosurgeons, some sort of distinguishing factor such as an internship or research, and a completed neurosurgery rotation. A neurosurgery residency applicant typically undergoes interviews with twelve different programs, during which the personality and aptitude of the applicant are evaluated.[6] The programs rank all the applicants, and a computer then matches the applicants with the programs based on a comparison of the student's and the program's rank numbers.

Ethics in Neurosurgery Training

Ethical principles are integrated into the neurosurgery residency program at all levels of training. The Accreditation Council for Graduate Medical Education requires that all residents be evaluated every six months throughout the course of their residency based on six core competencies: fund of medical knowledge, patient care, interpersonal and communication skills, professionalism, systems-based practice, and practice-based learning. Ethical principles fall in the category of professionalism, and thus are a required part of learning in the neurosurgery residency program.[7]

The ethical principles involved in decision-making are expected to be increasingly demonstrated by residents as they progress through the program. In the New York Medical College neurosurgery residency program, for example, post-graduate year-one residents are trained in general surgery, neurology, and critical care. After this year, first-year neurosurgery residents work under the supervision of attending physicians and the chief resident. They are taught to be proficient in ethics in the form of proper bedside manners, appropriate speech, talking to family members about simple diagnoses, and treating culturally diverse patients equally. Second-year residents are trained in emergency room and inpatient consultations, neuroradiology, neuropathology, and cadaver dissections. Responsibility for ethics increases as the second-year residents spend more time speaking to patients and family members.

Third-year residents are on call for surgeries during the week, receive clinical and administrative responsibilities, participate in conferences, learn more advanced neurosurgical procedures, and take the board exams for credit. Their ethical responsibilities grow to encompass some pre-operative decisions such as how invasive a surgery must be or how much tumor to remove under the guidance of an attending physician. The NYMC neurosurgery program limits clinical demands of fourth-year residents so that they are able to perform a year of laboratory research and prepare a manuscript for publication based on their findings.

Finally, fifth-year residents are eligible to become the chief resident and are responsible for patient care, mastering the neurosurgical procedures, performing morning rounds, administrative duties, and coordinating conferences.[8] The fifth-year resident, under the guidance of an attending physician, is also given the responsibility of declaring brain death. The fifth-year resident must also raise end-of-life issues with and deliver bad news to patients and their family members in the face of catastrophic neurological problems. Informed consent, a significant ethical practice, is also of great importance to the fifth-year resident, because he or she must discuss all the details of a potential treatment, its risks, and its side effects with the patient before a decision can be made to follow that particular treatment. To aid students in performing these difficult tasks, during their training they are taught proper poise, character, and body language so they are able to sympathetically convey what is sometimes devastating information.[9] Overall, the fifth-year resident is expected to exhibit all the ethical decision-making skills of a professional neurosurgeon

while under the guidance of an attending physician, thus preparing him or her for future practice.

The 360-degree approach to patient care found in neurosurgery and the need for ethical decision-making skills demand a rigorous residency program. Learning ethical practices during the neurosurgery residency program is facilitated by working under the guidance of experienced neurosurgeons, and this aspect of the neurosurgeon's education is fully incorporated by the final year of residency. This preparation gives neurosurgeons the ability to diagnose disorders, discuss treatment plans with patients, operate, and follow up on patients exhibiting a wide array of neurological disorders. Neurosurgeons, upholding their ethical responsibilities, allow society to benefit from equal, fair, and quality care for those of its members suffering from neurological disorders, regardless of cultural differences or severity of pathology.

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Mental Stress as a Predictor of Atrial Fibrillation

Natasha Hu

Atrial fibrillation (AF), a heart rhythm disorder characterized by irregular, fluttering contractions of the atria, causes about 15 percent of the strokes every year in the United States. Therefore, aggressively treating atrial fibrillation and its underlying causes is a crucial step towards preventing strokes. In recent years, anger and hostility have been suspected to have a direct correlation to the development of atrial fibrillation. One study found that these personality traits to be significant predictors of AF. Animal studies on stress and arrhythmias also agree with these findings.

SINCE 1900, HEART DISEASE HAS REMAINED the number-one cause of death in the United States.[1] The success of heart disease prevention requires that it be put into effect at an early stage, an improbable feat due to the undetectable nature of early heart disease. Therefore, it is important to find the triggers of heart disease to prevent large numbers of deaths.

In the field of psychosomatic medicine, personality characteristics that cause social stress have been long suspected, tested, and finally widely acknowledged to have a definite association with heart complications such as coronary heart disease (CHD), which causes the heart's arteries narrow drastically. Only in the past few years, personality traits such as anger and hostility have been suspected to have a direct correlation with a heart problem called atrial fibrillation.

Atrial fibrillation (AF) is a heart condition characterized by irregular, fluttering contractions of the atria, the upper chambers of the heart. During AF, the atria, which normally contract about sixty to eighty times per minute, contract a whopping 400 to 600 beats per minute. This condition causes the heart to work harder, pumps blood inefficiently, and increases the risk of heart disease and stroke. A stroke can occur when fluttering contractions cause blood to remain in the heart and form clots that travel to the brain. The National Center for Chronic Disease Prevention reports that over the last two decades, AF mortality has more than doubled in the United States; discovering its possible causes has become imperative. Although most cases of AF are a benign arrhythmia or abnormal rhythm of the heart, AF still causes about 70,000 strokes every year.[1] This paper explores the biological consequences of psychological stress and the possibility that it is a predictor of AF.

The possibility that anger and hostility, a form of stress, cause AF is based on the fact that psychological factors can influence health. How exactly can the mind override matter? This has been proven on many accounts, specifically with CHD. Hostility, anger, impatience, and a competitive drive are common components of what is labeled Type A personality; people with Type B personality have an opposite easy-going attitude. A project called the Western Col-laborative Group Study interviewed 3,154 men ranging from 39 to 59 years old and labeled them either as having type A or type B personalities.[2] Those with Type A behavior were twice as likely to develop CHD. Type A men between the ages of 39 to 49 developed heart disease six times more frequently than men with Type B personality. The results of this study are positively striking without any knowledge about the effects of mental stress on the body.

When a person feels stress—or a disagreeable state of arousal—the body's sympathetic nervous system, which is composed of involuntary nerves that prepare glands and muscles for defense, activates. Specifically, the adrenal gland secretes epinephrine (a.k.a. adrenaline) and norepinephrine, which cause the heartbeat to accel-

erate, muscle tension to increase, blood pressure to rise, and blood sugar to rise, as well as a number of other defensive responses. At the same time, the hypothalamus and pituitary gland are both working to secrete another hormone that releases free fatty acids into the bloodstream. Through this process, the body is preparing itself to use more energy to either fight or run away. However, the price to pay for these stressful moments is costly: Frequent occurrences of high blood pressure risk damaging arteries, and fatty acids floating through the bloodstream cause a plaque lining to build up slowly but surely. As one can see, excessive stress can increase the risk of heart diseases such as hypertension (high blood pressure) and CHD.

The first human study on the correlation between anger, hostility, and Type A behavior and the development of AF was undertaken in 2004 to explore AF's risk of causing stroke. Scientists thoroughly analyzed 3,873 male and female subjects with a mean age of 48.5, who were monitored for CHD, AF, and total mortality for ten years. Increased trait-anger—the tendency to perceive situations as anger-provoking and respond with expressions of anger—hostility, and symptoms of anger were found to be significant predictors to the development of AF in men, as was trait-anger in women. The probability of developing AF was 30 percent higher in men who had scored high on the standard test for hostility and anger given to them at the start of the study.[3] Overall, this study also supports the idea that there is a greater risk of AF in men than women.[4]

Although the 2004 study is so far the only one done on humans, its results agree with animal studies. One 1998 experiment studied stress-induced rats and their vulnerability to any type of heart arrhythmias.[5] The researchers advanced the hypothesis that there are direct correlations between the concentration of norepinephrine, heart rate, and arrhythmia responses. This is because the increase of norepinephrine and heart rate are symptoms of stress response. The rats that experienced short intervals of social stress caused by being in another rat's territory showed high norepinephrine levels and occurrences of rhythm disturbances. Of the two types of rats used, wild-type and Wistar rats, the latter strain seemed to have a greater parasympathetic counteractivity to sympathetic nervous system responses.[5] The parasympathetic nervous system is responsible for calming the body in an attempt to conserve energy.

The difference in vulnerability to social stress between the two strains of rats is an important observation. Monitoring those differences in a future experiment could help discover how stress causes AF on a molecular level. Another significant detail that can be learned from the 2004 human anger and hostility study can also be considered for further study: While the connection between mental stress and AF is evident, it is not yet clearly understood. Continued research can lead to treatments for intermediate complications of stress that may cause AF.

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Short and Sweet:

Human Growth Hormone for "Normal" Children

Priti K. Julka

Use of the human growth hormone (hGH) has become surprisingly popular among children of normal height in the United States. Many supporters of hGH believe that taking the hormone can remarkably improve a child's self-confidence and social interactions with others. However, some argue that the long-term physical and psychological effects of taking hGH could be rather harmful. This paper assesses the benefits and risks of giving "normal" children human growth hormone. Strong support is shown against giving "normal" children hGH, due to its potentially dangerous effects. In addition, emphasis is placed on the need of society to rid itself of the idea that shortness is a sickness. Instead of changing short individuals to fit a norm, it is essential that society change its perceptions of what is normal. Ultimately, it is important that individuals aware themselves of the effects of giving hGH to "normal" children, especially as further research is conducted on the hormone.

As a young boy, my friend John was unusually short for his age. At the age of six, he was about f inches shorter than most of the children in his first grade class. However, he never thought much about his short stature before going to school, probably because shortness was commonplace in his family: His mother was short, his aunts were short, and many of his cousins were short. In fact, he was one of the taller members of his family. Thus, it was not until elementary school that he learned what it really meant to be short. He was not only shunned by the students in his class, he was made the object of ridicule. The boys in his class would make comments such as, "You're so small I need a microscope to see you!" and would often chase him on the playground, playing "catch the midget." He never really understood why he was treated so differently by his peers. All he knew was that he wished he could do something about it.

For the past year or so, many kids like John have been able to take human growth hormone (hGH) to help them grow taller. These children do not have a disease or a hormone deficiency that causes them to be short; all they have to blame for their shortness is genetics. Although some would think otherwise, these children are "normal." They are only interested in hGH because of the potential social benefits it could afford them. This paper will explore the benefits and risks of giving children human growth hormone. In addition, the ethical concerns of treating "normal" children with hGH will be discussed.

Biological Background of hGH

Growth hormone, also known as somatotropin, is a protein produced by the pituitary gland. The hypothalamus, a structure in the brain, sends signals to this gland to produce growth hormone, which then travels through the bloodstream to other parts of the body. This hormone is known to instigate the growth of bones and other body tissues. Growth hormone directly stimulates epiphyseal growth plates in bones, which control bone elongation. In addition, growth hormone triggers the release of the protein insulin-like growth factor-I (IGF-I), which prompts the growth of muscle, bone, and other body tissues. This protein, in turn, regulates the release of growth hormone from the pituitary gland.[1]

When hGH is injected into a child's body, it stimulates an increase in the production of human growth hormone and causes the child grow. Multiple studies conducted on the effects

of human growth hormone in hGH-deficient children suggest that hGH can help children grow on average an extra 1.5 to 2.8 inches of height by adulthood. However, hGH does that work as easily as some think. Most children must continue to take six hGH shots a week for about four to five years before a change in their height is apparent.[3] Also, it is important to note that long-term studies have not been conducted on the effect of growth hormone in "normal" children. There is a possibility that non-hGH-deficient children may not even react to increased levels of hormone injected into their bodies.

History of hGH

The human growth hormone was first extracted from the pituitary gland in 1958 by a well-known endocrinologist named Maurice Raben.[7] Raben's use of purified hGH in hormone-deficient children was effective and revolutionized a movement in which doctors all around the world began extracting hGH from the pituitary gland of cadavers. Although the process of obtaining hGH was successful, it was soon discovered that natural hGH caused neurological disorders in many patients.[4] This finding led to the use of hGH strictly for individuals with growth hormone deficiency.

In 1985, researchers were able to produce hGH synthetically, due to advances in gene technology.[4] Synthetic hGH was soon approved by the Food and Drug Administration (FDA) and given to children who were deficient in growth hormone. According to clinical trials done by hGH manufacturer Eli Lilly, hormone-deficient children taking the synthetic drug grew on average 1 to 1.5 inches more than the placebo group. Sixty-two percent of the children tested grew more than two inches over their predicted adult height, and 31 percent gained more than four inches. Despite the children's height increase, the research was questioned due to the high dropout rate of children in the study. Many believe that the subjects who endured the study were the ones who demonstrated the most extreme growth and were not representative of the population.[3]

By 2003, the FDA approved the use of Humatrope, a synthetically prepared hGH nearly identical to the hGH secreted by the pituitary gland, for the treatment of non-hormone-deficient children who were expected to grow no taller than five feet, three inches, in the case of boys and four feet, eleven inches, in the case of girls, putting them in the in the bottom 1.2 percentile.[3] The use of hGH in these "normal" children, who are identified as having idiopathic short stature (ISS), is still highly debated today.[4]

Possible Advantages of Taking hGH

The use of human growth hormone is known to provide social advantages to individuals who are short. First of all, studies show that increased height is correlated with employment rates and the likelihood of finding a spouse.[8] Thus, by taking the hGH, shorter individuals increase their chances of finding a job and getting married. In addition, we live in a society in which sports players are envied. Due to the fact that increased height is often advantageous when playing sports, many children feel the need to take growth hormone to allow them to be more competitive in athletics.[9] These factors—and the verbal abuse short children commonly face—all add to the lowered self-esteem and increased aggression found in these individuals. It is likely that taking hGH would help them gain self-confidence and avoid aggression, characteristics that are especially important for younger children who are just learning to deal with social issues in the outside world.

Possible Disadvantages of Taking hGH

There are numerous risks associated with the use of human growth hormone that many people are unaware of. First of all, despite the extensive research done on hGH, many of the long-term effects of taking hGH are still unknown. For instance, some researchers speculate that taking of hGH can cause cancer, due to the fact that it stimulates the liver to produce

IGF-1, which is associated with breast cancer. In addition, some researchers believe that intake of hGH can cause resistance to the hormone insulin, which can lead to increased levels of blood sugar and the possible onset of diabetes.[7] It is probable that with time, researchers will confirm the link between these diseases and taking hGH.

According to geriatrician Dr. Rajbans Singh, "You shouldn't take hGH if you don't need it, as too much of the hormone is not good. ... Growth-hormone therapy should be for therapeutic use only because it has side effects in excess."[2] Some common side effects that are associated with taking hGH include an increase in blood pressure, problems with fluid retention, joint pain, and swelling of soft tissues in the body. Antibodies to the body's own growth hormone can also develop with the intake of hGH. This outcome would be particularly distressing to "normal" children who were not actually deficient in growth hormone. These children would now develop a growth problem by taking hGH. In other words, taking the hGH would counter their ability to grow.[7]

The psychological and physical risks children face from the repeated injections required for the treatment. According to Jenny Everett, whose nine-year-old brother, Alex, takes hGH, the procedure of injecting hGH into your body is one of the most stressful experiences a child can go through. Every day her brother has to swipe an alcohol-soaked gauze pad over his thigh, insert a three-inch needle into his leg, turn a knob on the pen five times and watch as his dose is inserted into his leg. Not only do the injections cause her brother a lot of pain, it has made him look at himself in a negative light. Children like Alex often acquire a negative image when they believe that they are going through such a painful process because something is wrong with them. Such a view of themselves can cause these children to have destructive social problems in the future.[3]

The large expense associated with buying hGH is another disadvantage of using hGH in children. On average, hGH costs about $35,000 for each inch a child grows.[6] Many children who are hormone deficient can get their insurance company to cover their treatment; however, it is unlikely that any insurance company would pay for the treatment of a child with idiopathic short stature. Families of such children are left with the stress and burden of paying such expenses themselves.

Social Effects of Treating "Normal" Children with hGH

Today, the use of human growth hormone in "normal" children raises many ethical issues. First of all, by allowing non-hormone-deficient children to take hGH and by characterizing them with idiopathic short stature, society is accepting the mindset that shortness is a sickness. Instead of establishing shortness as a normal condition many individuals share, it is distinguished as a problematic medical concern that needs to be cured.

There are two ways to approach the social problem of shortness. One can say that it is important for short individuals to change themselves so that they fit the norm, or that society change its perceptions of what is normal. As Dr. Ross Feldberg, assistant professor of biology at Tufts University, states, "Medicalizing this 'problem' transfers the responsibility for the discrimination away from those doing the discrimination and to the victims."[4]

Another ethical concern involved with the use of hGH in non-hormone-deficient children is its effect on what is classified as "average" height. If "normal" children use hGH to increase their height, the average height will then become higher. Eventually, children who are not using hGH will become the new "abnormal." Thus, instead of weakening the bias against short children, the widespread use of hGH could end up intensifying the bias against short individuals.

In addition, many are concerned that allowing "normal" individuals to take hGH will cause an increase in the gap between high and low

socioeconomic classes. Due to the fact that hGH is extremely expensive, the wealthy will be able to afford the hormone, whereas others will not. Thus, the wealthy, once again, will have an unfair advantage over the poor. They will benefit socially because of their taller stature, while the poor will be left to deal with their unavoidable shortness.

The Biomedical Industry's Role in the Use of hGH

To fully understand the FDA's approval of hGH for non-hormone-deficient children, it is important to analyze the biomedical industry's gain with such a decision. According to Dr. Feldberg, there are about 400,000 non-hormone deficient children who will be eligible for the hGH treatment. He suggests that because the treatment will cost about $20,000 per child, a maximum of about 40,000 children will decide to take the treatment. Thus, the industry could potentially bring in about $800 million a year with the treatment of "normal" children alone. In the words of Dr. Feldberg, "Is it any surprise that the treatment was approved?"[4]

Another important question to ask is if the biomedical industry will regulate the use of hGH, given the potential profit they could gain. Although many manufacturers of hGH have stated that they will abide by regulations and only allow pediatric endocrinologists and certain pre-approved pharmacies to prescribe hGH, it is unlikely that the hormone will be so regulated. For example, soon after the drug Viagra was first approved by the FDA, it became the fastest-selling drug on the internet, frequently sold without a prescription. This phenomenon is already happening with hGH. Type "human growth hormone" into any search engine and you will find site after site selling the hormone on the internet. However, it is important to note that the websites selling the hormone offer only small amounts, which are unlikely to do harm or good. Nonetheless, it seems as if the regulation of hGH is already out of control.

Will Use of hGH in Children Really Make a Difference?

When debating whether to take human growth hormone, it is important to know whether being a few inches taller is really worth spending thousands of dollars and enduring years of both psychological and physical pain. In the end, will taking hGH really make a difference? Many believe that changing a child's height by even a few inches can greatly benefit them socially, which is more important than money or temporary pain. These children could potentially have fewer problems with their peers in school and would be able to focus more on their classwork. In addition, it is possible that they would be more self-confident and less aggressive due to the decrease in pressure these children feel to fit in.

On the other hand, according to David Sandberg, an associate professor of psychiatry and pediatrics at the University of Buffalo, taking hGH does not change children's lives in the end. Sandberg suggests that even though short children are often teased and treated as if they were younger than they actually are, it is unlikely that increasing their height by a few inches will make much of a difference in their lives because "our lives are so much more complicated than one single factor." He states that anyone who believes that growing a few inches will change a child's life around is a victim of simplistic thinking.[3]

Although many agree that the social benefits that come from taking hGH are remarkable, the potential risks "normal" children using hGH face are serious. Even more importantly, it is necessary that our society rid itself of the idea that shortness is a sickness. People should learn to be happy with who they are and not feel that they have to fit a social norm. In the words of Miriam Schulman, director of external communications for the Markkula Center for Applied Ethics:

> We should approach enhancement as we would any other technology that reduces biodiversity. There's inherent good in pre-

> serving differences among people, just as there is in preserving differences among species. When we set up a particular constellation of characteristics as normative and try to medicate everyone into conformity with them, who knows what we will lose—in the strength of character people develop as they cope with their differences, in the perspectives they bring to our common problems, in the advantages they may offer, which we, with our puny knowledge of human biological complexity, can not yet begin to fathom.[5]

Looking back at my friend John, it is incredible to see how his childhood experiences turned him into the proud, self-assured man he is today. When talking to John about his life as a short child, he defined his shortness as a characteristic that helped him overcome adversity. He states that because individuals often overlooked him because of his height, he had to learn to use his intelligence to keep people's attention. His shortness not only helped him understand that everyone is different in their own way, but it also taught him that being different is not a bad thing. He realized that no matter what people say, in the end, it is really what is in the inside that counts.

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