HEALTH AND STRESS

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IMAGERY, FAITH, PLACEBOS AND MIND/BODY MEDICINE

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Imagination is derived from the Latin verb *imagineri* (to form an image in one's mind), from *imago* (a likeness or imitation of something). In the 1600's, image included a secondary meaning of "ghost" or "echo". These were also likenesses, but of a much more mysterious nature. Although image and imagination no longer retain these connotations, it is clear that their counterparts had this supernatural and ethereal quality in ancient times. Judaism, Christianity, Islam and all religions involve the notion of a higher power that controlled the universe but could only be imagined. This supreme deity determined a person's health, success and other attributes or could be appealed to in some appropriate way to act on one's behalf. Whether it was by prayer or offering up a sacrifice, such petitions also involved a very personal and private form of imagery. Old Testament Jews forbade the worship of idols because they were externalizations of inner images that violated this intimate and unique relationship. **Imagination was also deemed to be very important in antiquity since it might relay some sort of message from a higher power that provided advice or predicted the future.** The Bible is replete with strange apparitions, visions and dreams that appeared for no apparent reason and although often very vivid, had no significance unless they could be interpreted. Certain people seemed to have special skills or experience in this.

One example is the Pharaoh's dream of 7 fat cows being devoured by 7 lean cows and 7 full ears of corn being consumed by 7 thin ears. Joseph correctly construed this to mean that 7 years of plentiful crops would be followed by 7 years of famine. He advised Pharaoh to start storing as much food as possible during the period of abundance. Egypt was largely spared from the 7 years of famine due to the lack of rain that later devastated the entire region and Joseph became Pharaoh's Prime Minister.

ALSO INCLUDED IN THIS ISSUE

There are numerous similar examples of the importance of symbolism and imagery in other religions and cultures. Participants who partake of the bread and wine in the Christian Communion service also visualize the Last Supper Passover Seder that Christ shared with his disciples. Roman Catholics believe that the bread

and wine truly become the Body and Blood of Christ and that they are purified and transformed in this very old Eucharist sacrament.

Imagination is most often used today to describe some sort of creative artistic talent, flight of fancy or wishful thinking. Up until a few hundred years ago, imagination had a quite different meaning that more specifically referred to how diseases could be caused by mental influences. The imagination was viewed as a force or conduit that transferred messages from the mind to different parts of the body through the spirits or "passions" and that it could also relay signals in the opposite direction. If a person saw someone with the plague, the imagination could create the same symptoms in the viewer. And if a pregnant woman saw a deformed beggar, the "maternal imagination" could cause a similar disfigurement in the fetus. This power of the imagination was a significant departure from medieval beliefs that had always attributed these and other afflictions and diseases as a punishment from God.

Over the last 150 years, this notion of the imagination's ability to cause disease was gradually replaced by concepts based on advances in biology that were deemed to be more scientific. During the 1800's, dozens of articles appeared in *The Lancet* and other prestigious medical publications with titles such as "maternal imagination" and "maternal impression" to explain birth defects. A few prominent physicians also tried to emphasize the potential importance of imagination as a diagnostic and therapeutic aid. They were drowned out by others who held that only dangerous quacks such as practitioners of mesmerism, homeopathy, naturopathy and other unproven therapies would stoop to exploit a patient's imagination. As one noted, "It was not a power to be associated with qualified gentlemen practitioners". Many fetal abnormalities were later explained as genetic defects and the influence of the imagination was viewed as nothing more than superstition based on unfounded folklore. Imagination was considered primarily to be an ingredient that was essential for the creation of great works of music, literature and art. The important role of mind/body relationships resurfaced during the last century and became increasingly popular with the public as well as physicians because of supportive scientific studies. However, the latter no longer referred to "imagination" but rather "suggestion", "persuasion", "psychosomatic, and "placebo" effects. But since none of these terms helped to explain possible mechanisms of action they were really little more than new bottles containing very old wine.

Witch Doctors, Shamans, "The King's Touch" And Faith Healing

Ancient literature also abounds with accounts of the ability of imagination or imagery to produce spectacular cures. While these have similarly been largely dismissed as old wives' tales or coincidence there is growing evidence if not proof that guided visual imagery can produce rather remarkable results in disorders ranging from anxiety, depression, phobias, sexual difficulties and insomnia to obesity, fibroid tumors and a variety of cancers. Many of these reports have been published in respected peer reviewed journals. I am personally familiar with one case in which the regression and eventual disappearance of a well-documented malignant brain tumor in a child could be attributed to nothing else but a guided imagery program. Such successes seem to be more readily achieved in children, which is not surprising, since they are more apt to have very active imaginations and respond to suggestions. **Warts in children are known to disappear following fake X-ray treatment or by nailing a piece of an apple to a tree and explaining that as it withers away and falls off, so will the wart.** Numerous reports attest to the efficacy of hypnosis in adults and in several studies, only those warts that had been specifically targeted spontaneously disappeared. Acupuncture can also be effective. How can such observations be explained? Since warts are due to a viral infection, it has been proposed that hypnosis, imagination, persuasion or suggestion somehow stimulate the immune system to attack and destroy the virus. While this seems plausible, there is no proof that this occurs nor would this mechanism of action explain accounts of other types of cures from hypnosis, faith healers, "The Kings Touch" or the "laying on of hands" in the Bible.

Primitive people had a sense of unity with the universe that emphasized the interrelationship and interdependence of all living things. This is best exemplified by the ancient Chinese concept of *chi*, a vital force, spirit or energy believed to surround and flow through all things, living and non-living. The unimpeded circulation of *chi* and a balance of its negative and positive *yin* and *yang* forms in the body are held to be essential to good health in traditional Chinese medicine. Acupuncture heals because it can remove obstructions to the orderly flow of this imaginary life force. This intimate personal connection between the individual and other people as well as everything in the universe progressively faded away. Most tribes and culture had healers who presumably could communicate with a higher power or tap into and transmit some of this esoteric energy or life force to bridge this gap between the patient and Nature.

These witch doctors, medicine men, Druids or shamans (from the Russian *saman* or ascetic) were usually antisocial, reclusive, austere individuals who commanded great respect or were even held in awe. They were a combination of priest, healer and magician whose healing was accomplished through suggestion, persuasion and the use of imagery or special herbs and potions. However, any cures were related more to their elevated status in the community that inspired a strong faith in their subjects rather than any special powers. There can be little doubt that such practices were effective since otherwise they would not have persisted for so many centuries. In primitive societies, sacred and secular aspects of life were integrated and such healers were also involved in diverse affairs ranging from advice on raising crops and waging war to performing marriages and providing spiritual guidance in any area that was needed. As a priest as well as doctor, such shamans were concerned with both spirit and body, especially since the two were considered to be inseparably intertwined and integrated.

Modern medicine tends to treat body and spirit as separate entities. Diseases are often viewed as being caused by something external that should be destroyed or removed by using drugs, radiation or surgery. Shamans viewed the primary problem as not the pathologic change in the body but the decrease in personal power that had permitted the intrusion of disease. Hence, the first step was to build up the patient's power rather then dealing with any disturbing symptoms. The Navajo Indians used elaborate visualization to achieve this in a rite that included the participation of others to encourage the patient to imagine himself or herself as healthy. **The primary focus was not to improve physical well being but rather on restoring spiritual health.** There was less concern about prolonging life as opposed to improving the quality of life by restoring harmony and nurturing the spirit. Kahunas in Hawaii and the Polynesian Islands employed an elaborate four-step process that involved awareness of thoughts, establishing goals, changing and redirecting the flow of energy and harnessing the patient's imagination to promote healing.

The bottom line is that any such healing came from within rather than from divine intervention or the special power that only a shaman or some other healer possessed. The body is its own best pharmacy and each of us has a vast innate potential for self-healing if we can learn how to gain access to this. A few are occasionally able to achieve this through prayer, deep meditation, or a firm faith in a practice, individual, medication or anything they strongly believe will be successful. Indeed, if you think about it, the history of medicine up until the last century is essentially a demonstration of the power of placebos and faith in someone, whether it was a physician or a healer who acted in this capacity. Throughout the ages there have been doctors in diverse cultures who were renowned for their ability to consistently achieve cures when others had failed, including Hippocrates, Galen, Maimonides, Paracelsus, Sydenham and Mesmer. Yet, we now know that with few exceptions, what they prescribed or advised

was worthless and have failed to stand the test of time. The reason patients got better was because of their trust and faith that these doctors would cure them as well as the physician's own faith in what was being prescribed and the ability to persuade and inspire confidence. Ancient Greek physicians were well aware of this and as Galen noted, "*He cures most successfully in whom the people have the most confidence*."

The Four Humors, Hysteria, Temperament And The Anatomy Of Melancholy

Hippocrates is often referred to as "The Father of Medicine" because he was the first to accurately describe many diseases. Much of his advice about how to care for patients in the Hippocratic Oath traditionally taken by all physicians is still followed, including: first, do no harm, treat all patients fairly, always seek to preserve life, avoid attempting to do things that others can do better, preserve patient confidentially, always conduct yourself morally and never have sex with a patient. Little was known in his era about what caused disease or promoted health and medicine was shrouded with superstition. During the fifth century B.C., Hippocrates proposed that there were four humors or fluids that pervaded the body: yellow bile, black bile, phlegm and blood. Each of these humors was believed to correspond with different dispositions, seasons, organs, temperatures and degree of dryness. Aristotle and others subsequently developed their own concepts based on this but it was the second century physician Galen who expanded on all of these and whose humoral theory of disease and teachings were to dominate Western medicine for well over 1500 years.

Galen believed that good health depended upon a balance between the four humors and that all diseases stemmed from some disturbance in this equilibrium (*dyscrasia*). An excess of any humor produced characteristic dispositions, e.g. yellow bile (easily angered, bad tempered), black bile (despondent, sleepless), phlegm (calm, unemotional) and blood (courageous, hopeful, amorous). If persistent, these could lead to various disorders. He had observed that cancer of the reproductive organs occurred more frequently in women who were melancholy, which was due to an excess of black bile (Gr. *mélas chole*). As noted in a prior Newsletter, a variety of surveys and studies have confirmed that depressed women are more likely to develop cancer of the breast, cervix and uterus. We still describe individuals as being bilious, melancholy, phlegmatic or sanguine and many continue to believe that such traits predispose to different diseases. There are also remnants of the humoral theory in contemporary medicine. We use terms like humoral immunity or humoral regulation to refer to antibodies and hormones that circulate throughout the body and blood dyscrasia to describe blood diseases or abnormalities.

Galen believed that humors, vital spirits, imagination, and nerves were all closely linked and that thoughts and feelings were constantly circulating through the body exerting their effects by direct physical contact with particular anatomical structures. He thought that hysteria, from the Greek *hystera* or uterus, was an exclusively female disease caused by sexual deprivation, particularly in passionate women, in which the womb wandered throughout the body seeking sexual gratification. During its journey the uterus would bump into various structures causing different symptoms. Aromatherapy was popular at the time and treatment consisted of placing putrid scents under the nose and pleasing ones near the vagina in an attempt to coax the uterus back to its proper position. Galen's teachings ruled medicine in medieval times, during which hysteria was increasingly diagnosed in virgins, nuns, widows, as well as married women. The prescription then changed to intercourse if married, marriage if single, or massage by a midwife as a last recourse. In the Victorian era, a physician claimed that one in four women suffered from hysteria because the stresses associated with modern life caused civilized women to be more susceptible to nervous disorders and faulty female organs.

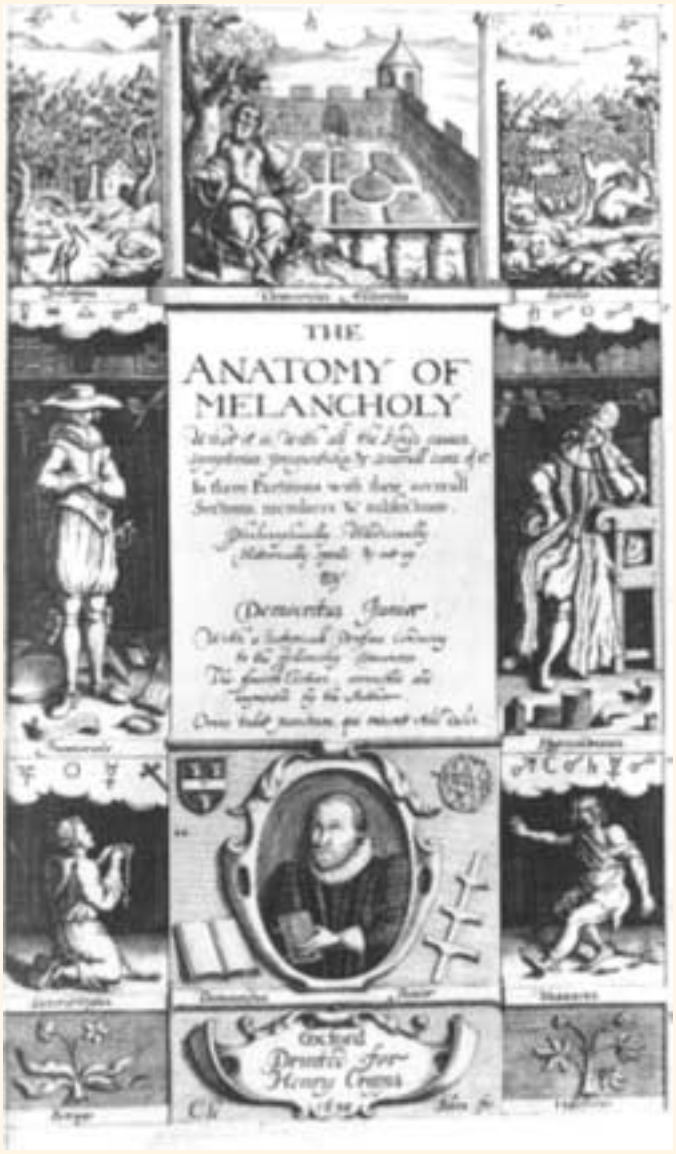
These patients were quite profitable since they were not seriously ill, required frequent treatments and clockwork driven massage devices had become available that did not require a midwife. These also reduced the time to get results from hours to minutes. An electromechanical vibrator was used at an asylum in France in 1873 and by 1900, the advent of home electricity made the vibrator available to consumers a decade before electric irons and vacuum cleaners.

A 1918 Sears, Roebuck and Co. catalog had a page of home electrical appliances with several vibrators that included a portable one with attachments for $5.95 described as "Very useful and satisfactory for home service."

Although hysteria is no longer a recognized medical diagnosis, vibrators of all types and shapes are readily available and apparently even more popular.

Galen also identified four temperaments in which one of the qualities, warm, cold, moist or dry predominated and another four in which a combination of two, warm and moist, warm and dry, cold and dry, and cold and moist prevailed. This last quartet, (named for the humors with which they were associated - sanguine, choleric, melancholic and phlegmatic) eventually became better known than the others and is still used to describe different dispositions. While "temperament" now refers only to personality characteristics, Galen used it to include bodily dispositions that determined a person's susceptibility to particular diseases as well as behavioral traits. He thought that humors were formed in the body rather than ingested but that various foods could stimulate the production of different humors. Warm foods tended to produce yellow bile while cold foods tended to produce phlegm. Blood letting, emetics and purges were utilized to expel harmful humoral excesses and continued to be part of mainstream of American medicine well after the Civil War. Other treatments used herbs and foods associated with a particular humor to counter its symptoms; people who had a fever and were sweating were considered hot and wet and were therefore given substances associated with coldness and dryness.

It was essential to keep the four humors in balance to preserve mental and physical health and prevent what Galen called the "passions or perturbations of the soul." The twelfth century physician Moses Maimonides similarly wrote, "It is known ... that passions of the psyche produce changes in the body that are great, evident and manifest to all. On this account ... the movements of the psyche ... should be kept in balance ... and no other regimen should be given precedence." This belief in the influence of strong emotions on physical health and illness grew stronger throughout the medieval period and during the Renaissance, where ideas about the "balance of the passions" were particularly popular. One marvelous example of this was Robert Burton's *The Anatomy of Melancholy* published in 1621, which included the following observations about the disastrous role of unchecked emotions, "The mind most effectually works upon the body, producing by his passions and perturbations miraculous alterations ... cruel diseases and sometimes death itself."



Quotes From ***The Anatomy of Melancholy***

The shoemaker goes bare
To Rob Peter, and pay Paul.
Penny wise and pound foolish
Women wear the pants in the house
Set a beggar on horseback and he will ride a gallop
There's many a slip between the cup and the lip
What can't be cured must be endured
Birds of a feather will flock together
The pen is mightier than the sword
Building castles in the air
Walking as if he trod upon eggs
As clear as the nose on your face
When in Rome, do as the Roman's do
Every man for himself
A good marriage is a match made in heaven
A mere madness, to live like a wretch and die rich
They do not live but linger
And hold one another's noses to the grindstone, hard
Like a dog in the manger, he only keeps so it shall do nobody else good, thus hurting himself and others
He whipped his horses and put his shoulder to the wheel
To these crocodile tears they will add sobs, fiery sighs, and a sorrowful countenance
One religion is as true as another
A dwarf standing on the shoulders of a giant may see farther than the giant himself.
The fear of death is worse than death
Some young physicians, that study to cure diseases, catch them themselves, will be sick, and appropriate all symptoms they find related of others to their own persons

As you can see, many of Burton's views and comments are still in common use almost 400 years later. It is impossible to overestimate the importance and influence of this magnum opus that is considered by some to be one of the major documents of modern European civilization. One leading literary critic called it "the greatest work of prose of the greatest period of English prose-writing."

Dr. Samuel Johnson is perhaps best remembered for providing the first authentic English dictionary in 1755. A prior attempt at a dictionary contained less than 3,000 words that were not defined but simply accompanied by a few synonyms. Johnson personally wrote the definitions of over 40,000 words, illustrating them with some 114 thousand quotations drawn from Shakespeare and great writers from every field of learning. It took him eight years to compile these two thick volumes consisting of 2300 pages and this masterpiece defined the English language for the next 150 years. As he explained, "Knowledge is of two kinds. We know a subject ourselves, or we know where we can find information about it" and his dictionary was widely relied on by all 19th century authors and poets. Johnson was also known for his wit. To buss was defined as "To kiss: to salute with the lips". Laced mutton was "an old word for a whore." He was usually very critical ("The road to Hell is paved with good intentions") and caustic when it came to authors (Your manuscript is both good and original. But the part that is good is not original, and the part that is original is not good.")

Most of what we know about Johnson comes from his biographer, James Boswell, who wrote that *Anatomy of Melancholy* delighted Johnson so much that it was "the only book that ever took him out of bed two hours sooner than he wished to rise because it gave him so much pleasure." Lord Byron wrote, "If the reader has patience to go through this volume, he will be more improved for literary conversation than by the perusal of any twenty other works with which I am acquainted." The celebrated physician Sir William Osler, who taught his students that "many times it is more important to know what kind of patient has the disease than what kind of disease the patient has" described it as "the greatest of medical treatises". He referred to Burton as, "the great authority on *morbi eruditorum*," the diseases of educated people. Burton had warned that excessive study, "dries one up, invites gouts, catarrhs, rheums . . . and all such diseases as come by overmuch sitting. Scholars emerge from their chambers lacking all social graces, and then must court ignorant patrons ('a debauched, corrupt, covetous, illiterate crew'). All that awaits is that cheerful trio, want, poverty, and beggary."

Burton referred to melancholy as "the rust of the soul"; in addition to being caused by too much black bile, it could result from an "astrological accident", heredity, a moist brain, cold stomach or hot heart. However, despite its title, the book is really not about depression or mental illness just as *Moby Dick* is not a novel about a whale. *The Anatomy of Melancholy* was really an attempt to explain how emotions and thought could contribute to a wide range of mental and physical disorders. It had a strong influence on many subsequent medical texts such as William Falconer's 1788 *Dissertation on the Influence of the Passions Upon the Disorders of the Body.* It also established a firm foothold for psychosomatic relationships in Western medicine for almost three centuries. The important effects of emotions on health progressively declined with advances in bacteriology and microscopic pathology that could accurately identify the cause of different infectious diseases and the development of vaccines to prevent them. The great 19th century French physiologist Claude Bernard, often called "The Father of Physiology" was largely responsible for Cannon's concept of homeostasis and Selye's speculations about stress and disease. Bernard engaged in frequent debates with his colleague Louis Pasteur at the prestigious *Académie Francaise,* where they sat next to one another. Pasteur, who was the prime proponent of the germ theory of disease allegedly admitted on his deathbed, "*Bernard avait raison. Le germe n'est rien, c'est le terrain qui est tout*." (Bernard was right. The microbe is nothing, the soil is everything.)

Over the past five decades, there has been a resurgence of interest in psychosomatic relationships and especially the effect of emotions on the immune system. It is now well established that stress induced depression of immune system defenses can influence the incidence and severity of infectious diseases ranging from the common cold and herpes to AIDS and certain viral linked cancers. Bernard was indeed right. Most people with evidence of having been exposed to the tubercle bacillus do not develop tuberculosis. However, characteristic signs and symptoms frequently surface when their resistance is reduced by stress or the administration of stress related hormones like cortisone and related steroids.

Placebos, Great Expectations, Persuasion And Psychosomatic Medicine

"*I said that the cure itself is a certain leaf, but in addition to the drug there is a certain charm, which, if someone chants when he makes use of it, the medicine altogether restores him to health, but without the charm there is no profit from the leaf*."

~ Plato (*Charmides*, 155-6) ~

Others might know which herbs and other ingredients a tribal witch doctor put in a potion but only he could release their power. Plato recognized this 2400 years ago in what may be the first description of the placebo effect. The English word placebo is derived from the Latin verb *placere*, "to please", and *placebo* (the first person singular of the future indicative) means "I will please". It would thus seem to be the perfect term to describe anything that makes

someone feel better. There is no other word or phrase that is an adequate substitute. Synonyms like panacea, catholicon and *elixir vitae* really refer to some single substance or concoction that could cure everything. A placebo can vary from different types of sham surgical procedures to any pill, preparation or intervention that does not have a relevant pharmacological or physiologic effect.

Placebo has a very strange history since its first use seems to date back to the 13th Century as the name for one of the Vespers or Latin evening prayer services in the Roman Catholic Church. This Vesper is said or sung for the restfulness and tranquility of the soul of someone recently deceased and for all souls in Purgatory on All Souls' Day (usually November 2). Wycliffe wrote in 1380 that this traditional Office of the Dead service included a recitation of part of Psalm CXVI, "*Placebo Domine in regione vivorum*", "I will please the Lord in the land of the living". Because it was the first word, these vespers were called "placebos". However, a few hundred years later, both the English Book of Common Prayer and King James Version of the Bible translated these same words as, "I will walk before the Lord in the land of the living." This variation is believed to be stem from the use of the Hebrew word *halak* (pronounced hawlock) which means "to walk habitually" and occurs quite frequently in the Old Testament in phrases such as "he walked before God" to imply that he was therefore pleasing to God**.**

The second meaning is found in Geoffrey Chaucer's 14th century *The Canterbury Tales*, where placebo no longer signifies pleasing the Lord but rather to praise someone for the purpose of achieving some personal gain. This appears in the advice given in *The Sompnour's Tale* on how to behave when in the presence of those of a higher station, "*Beware therefore with lordes how ye play, Sing placebo*". There is also a reference to insincere Chaplains who "*syngen euere Placebo*, primarily to receive reimbursement rather than to promote the peaceful repose of someone's soul. The third meaning of a flatterer is found in *The Merchant's Tale*, where Chaucer gives the name Placebo to an obsequious, sycophantic parasite who survives only because of his profuse praise of somebody wealthy or important who will reward him for his copious compliments.

The fourth use of placebo as "an epithet given to any medicine adopted more to please rather than benefit the patient" did not surface until the nineteenth century. This definition from the 1811 edition of *Hooper's Medical Dictionary* is the first written record of placebo having such a "sugar pill" meaning according to the 20-volume *Oxford English Dictionary*, which always references the first use of a word in literature. It seems strange that this took over 500 years since the use of elixirs and medications for this purpose is as old as the history of medicine. During the late 1800's and for the next few decades, placebos were frequently prescribed and placebo had become part of common language. Nevertheless, it was never mentioned in medical texts or journals until Perry Pepper's eight paragraph "A Note On The Placebo" that appeared in a 1945 issue of *The American Journal of Pharmacy*. Pepper described his amazement that he could not find the word placebo in Wood's famous *Therapeutics* whose fourteen editions spanned the period from 1875 to 1908 when placebos were widely prescribed. Nor was placebo listed in the Index of the Surgeon General's Library or the Quarterly Cumulative Index to Medical Literature and he complained that current texts on treatment also "turn up their more scientific noses at this humble humbug." As he explained,

> The giving of a placebo — when, how, what — seems to be the function of the physician which, like certain functions of the body, is not to be mentioned in polite society. Yet there is a certain amount of skill in the choice and administration of a placebo. In the first place, it must be nothing more than what the name implies — a medicine without any pharmacologic action whatever. Even a mild sedative is not a true placebo. Secondly, its name must

> be unknown to even the most inveterate patient who knows most drugs by name and is always quick to read the prescription. If the medicines named are familiar the type of patient who needs a placebo will promptly explain that this or that drug had been tried and "had not helped me" or "had upset my stomach. It is well if the drug have a Latin and polysyllabic name; it is wise if it be prescribed with some assurance and emphasis for psychotherapeutic effect. The older physicians each had his favorite placeboic prescriptions — one chose Tincture of Condurango, another Fluidextract of *Cimicifuga nigra*. Certainly, the latter by its Latin name might be expected to have more supratentorial action than if one merely wrote for the Black Cohosh and Condurango would be more efficacious than sugar of milk.

I became well aware of this when I first entered practice. Few prescriptions containing multiple ingredients for pharmacists to compound were being written, especially for presumably inert ingredients, and older physicians would frequently prescribe Latibrabonehp for anxious patients because all the local druggists knew that this was Phenobarbital spelled backwards. Another favorite was periodic injections of vitamin B_{12} for fatigue and lack of energy since this impressive looking red fluid had no side effects and the designation 12 suggested it was much more potent than B vitamins with lower numbers. As Pepper points out, these were not true placebos and it may well be that vitamin B_{12} did provide benefits for some patients even though there was then no indication for its use other than for pernicious anemia or other B_{12} deficiency disorder. If you wrote a prescription for a true placebo or one of the old favorites noted above today, it might be quite difficult to find a pharmacist with the ability to fill it. And even if you could, there would also be the risk of being sued for malpractice.

Nevertheless, placebos are in widespread use in clinical trials to determine the efficacy of new drugs in what are referred to as "double blind" studies in which neither the patient or physician knows what is being administered. This is largely due to a 1955 article entitled "The Powerful Placebo" published in the *Journal of the American Medical Association* by Henry Beecher. This distinguished Harvard anesthesiologist evaluated over two-dozen studies and calculated that between 30 and 40 percent of any treated group would respond to a placebo. However, subsequent research has shown that placebos are effective in closer to 50 or 60 percent of subjects and in some instances can be greater than the active drug. This is particularly true for subjective complaints such as pain and depression. In a popular 1998 book, one researcher cited studies showing that the multibillion-dollar success of Prozac and similar antidepressants was almost entirely due to placebo effects. In a more recent article, he and coworkers analyzed 19 double blind antidepressant clinical trials and concluded that the expectation of improvement, not any changes in brain chemistry, accounted for 75 percent of the drugs' effectiveness. Placebo effects can be so strong in depression that some double blind studies now often compare a new antidepressant with an existing approved drug rather than a placebo to demonstrate that they are equally or hopefully more effective.

In addition to the condition being treated, many other factors influence the success of placebo therapy, including the nature of the placebo. Placebo injections are more potent than placebo pills, and capsules are more potent than tablets. Placebo effects are dose related since two placebo pills have a greater effect than one, and large pills are more powerful than smaller ones. Sixty years ago, almost all pills were white and round. Today, an entire industry is devoted to determining what color, size and shape is preferable for a particular product. A dynamic red is thought to suggest rapid action whereas a calm blue is better for a good night's sleep. One experiment in medical students confirmed that blue placebo capsules were more likely to produce sedation than pink capsules. The diamond-shaped blue pill Viagra introduced in 1997 became an overnight sensation with sales of $1.74 billion in one year alone. Several years later, the marketing mavens for a rival product, Levitra, conducted

extensive market research and concluded that many consumers didn't "resonate with the imagery" of Viagra because the blue color was too cool and some equated it with being sick. Their goal was to develop something more enticing for Levitra and they came up with a vibrant and energetic orange color and an orange and purple flame logo. Surprisingly, there is no evidence that a patient's response to placebos is related to his or her personality, sex, or even suggestibility. In addition to benefits, placebos can also have significant adverse reactions, including *dermatitis medicamentosa* and angioneurotic edema and there are even reports of people becoming addicted to placebos. The most common side effects are drowsiness, headaches, nervousness, insomnia, nausea and constipation. Nocebos, which produce negative placebo effects, can also be powerful. In one report, researchers told psychology students who had volunteered for a study that a mild electric current would be passed through their skulls, and that they might experience a headache. Although there was in fact no such current, more than two-thirds of the students reported that they felt head pain.

The placebo effect is not limited to subjective sensations since some studies show actual physiological changes as a result of sham treatments. Doctors were able to eliminate specific warts by painting them with a brightly colored, inert dye and promising patients that the warts would be gone when the color wore off. Significant dilation of the airways has been achieved in asthmatics by simply telling them they were inhaling a bronchodilator even though the inhaler had no active ingredients. Relief of pain following a wisdom-tooth extraction was just as great from a fake application of ultrasound as from a real one, but only when both the patient and therapist thought the machine was on. More than half of colitis patients treated with a placebo in 11 different trials reported feeling better and in 50 percent of these, sigmoidoscopic examination confirmed a reduction in bowel inflammation.

Some of the most impressive results of placebos have come from sham surgeries. Five decades ago, ligation of the mammary arteries to increase blood flow to the heart was a common surgical treatment for angina because 90 percent of patients reported benefits. However, it was abandoned after a young cardiologist demonstrated that he could obtain the same results with placebo surgery, in which the same small incisions of the chest were made, but the arteries were not tied off. A recent randomized study of laser surgery to improve blood flow to the heart showed that patients who underwent the procedure reported significantly less pain and showed improved cardiac function. However, so did the patients who were not aware they had a sham procedure and this placebo effect persisted. Two and a half years later, scans and other tests showed improvement in blood flow only in those patients who thought they had been operated on. In another report on 180 patients with osteoarthritis of the knee, those who received sham arthroscopic surgery in which only an incision was made had as much pain relief and improved mobility as patients who actually underwent the entire procedure. After 2 weeks, the sham surgery patients were actually doing better than those who underwent the procedure, possibly because they had been subjected to less trauma. And there was no difference between the two groups two years later with respect to improvement in walking, stair climbing and pain relief. In another study to evaluate the effectiveness of transplantation of human embryonic dopamine neurons into the brains of advanced Parkinson's disease patients, 20 were randomly assigned to receive the transplant and 20 had sham surgery. One year later, those who thought they had received the transplant reported better quality of life than those who thought they had received the sham surgery, regardless of which surgery they actually received. However, objective assessment of neurological function by specialists who did not know which treatment any patient had received also found more differences in improvement based on perceived rather than actual treatment. One patient reported that she was physically inactive for several years due to her disability but had resumed hiking and ice-skating in the year following the procedure. When the double blind details were revealed, she was shocked to find that she had received the sham surgery.

Other examples include glomectomy (the surgical removal of a small, normal mass of tissue called the carotid body that is found on the carotid artery) for the treatment of asthma and freezing the stomach for duodenal ulcers. **These were associated with 70 percent improvement described as excellent or very good because in all cases, doctors as well as patients expected them to work.** These procedures were largely discontinued following controlled studies that showed them to be of little value. The importance of great expectations cannot be underemphasized. Investigators studied 103 patients who underwent total hip replacement surgery and another 89 who had a knee replacement. Participants completed pre-operative questionnaires about overall health, physical functioning, level of pain, and their expectations about the success of surgery. When evaluated 6 months later, all patients reported a reduction in pain and improved physical function. However, three out of four patients who had expected complete pain relief had much less pain and much better functioning than those who had the identical procedure but lower expectations about its success. Other studies have also shown that except for pre-operative health status, the most important predictor of success following surgery was the patient's expectation of success.

All of this is consistent with the research of Jerome Frank, a psychotherapy scholar and Professor of Psychiatry at Johns Hopkins whom I had the privilege of knowing and studying under. In his remarkable book, *Persuasion and Healing*, Frank summed it all up by explaining that **the curative effects of placebo treatments have the four features that are shared by all psychotherapies: a person in distress; an expert; an explanation for the condition; and some sort of intervention or healing ritual.** He believed that this combination of elements reversed demoralization and promoted the expectation of recovery, but exactly how this is achieved is still a subject of much debate. A recent positive emission tomography study showed that placebos could increase the concentration of endorphin activity in key areas of the brain that could account for relief of pain or significant improvement in mood. Robert Ader, who coined the term psychoneuroimmunology, has presented a convincing argument that placebo effects can be largely due to conditioned responses. We hope to address these and other theories in a future Newsletter devoted to the evolution of Psychosomatic Medicine — so stay tuned.

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