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STRESS, SUDDEN DEATH AND "HEART ATTACKS"

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The unexpected death of Ken Lay on July 5 at the age of 64 due to a "massive heart attack" illustrated the confusion and controversy over the contribution of stress to heart attacks and especially sudden death. Six weeks earlier, the former Enron CEO had been convicted of fraud and conspiracy in the largest corporate collapse and scandal in U.S. history. Although the heart attack occurred while he was vacationing in Aspen there is little doubt that he had been very distressed about the thought of spending the rest of his life in prison following his sentencing scheduled for September. Close friends said that Lay had also been subjected to severe stress because Enron's complete disintegration had cost investors billions of dollars. He was particularly devastated that four thousand employees lost not only their jobs but also all or most of their retirement savings. In addition, the four-month trial had caused additional daily stress as he was forced to repeatedly face these workers and former friends who had been ruined by his actions. To top things off, the Washington Post reported a few days earlier that federal prosecutors were seeking to force Lay and co-conspirator Jeff Skilling to turn over $182.2 million in assets that had been acquired by fraud.

Lay's pastor, Stephen P. Wende, told the *Washington Post* "He's been under extraordinary stress for five years. I don't think his spirit gave way, but his body did . . . He felt very keenly the pain of those who had lost livelihoods, life savings and lifelong jobs at Enron." Ramin Oskoui, a D.C. cardiologist said a fatal heart attack would not be surprising in a man who had watched his reputation deflate and saw his liberty vanishing before his eyes, noting that "It is well known that emotional or physical stress can precipitate a heart attack" and that for one in three men, their first cardiac symptoms resulted in death. Terry Giles, a Houston lawyer and friend who had spoken with Lay by phone the previous week, told the paper "I'm always going to believe he died of a broken heart. I think the conviction just really broke his heart." Many of the media headlines and stories also blamed his heart attack on stress, such as:

ALSO INCLUDED IN THIS ISSUE

Fox News - **"Ken Lay's Heart Attack: A Case of Death By Stress?"**

MedPage Today - **"Lay's Death Viewed as Cautionary Tale of Catastrophic Stress"**

Houston Chronicle - **"Stress of trial likely exacted a toll on Lay. Experts say the loss of control, depression, even high altitude, may have played a part"**

Slate – **"Did Stress Kill Ken Lay?"**

Others were more cautious.

MSNBC - **"Stress and Heart disease not clear cut"**

Reuters - **"Effects of stress on heart disease still unclear"**

ABC News Medical Unit - **"Lay Had History of "Heart Disease, but Did the Stress Do It? Doctors Say Stress Can Aggravate Health, but Lay's Situation Is Unclear"**.

ABC News pointed out that about ten years ago Lay was started on statins because of an elevated cholesterol and that a stent had been placed in a coronary artery in 2001 to prevent a future heart attack. The ABC Houston affiliate was told at the time that Lay had "stable coronary disease" and had also been put on aspirin and a modified diet. Lay was obviously concerned about his cardiac condition since he had installed portable heart defibrillators in his houses as well as his airplane. The ABC coverage also explored the differing opinions about the significance of stress compared to other risk factors for heart attack by asking web surfers to select which of the following statements best reflected their opinion:

- **Chronic stress is bad for you, so of course it could trigger a heart attack. (573)**
- **Heart attacks are caused by genetics and an unhealthy lifestyle, such as eating fattening foods. (55)**
- **It's a combination of the above two. (1,020)**
- **I don't know. (35)**

As can be seen by the number of responses in parentheses following each statement, the vast majority believed it was a combination of factors. However, **more than ten times as many voted for stress as opposed to heredity and eating fattening foods.** I found this quite surprising since TV advertising for statins and cholesterol-lowering products repeatedly emphasize that heart attacks are due to high cholesterol and that a high fat diet is a major contributor to both. The article went on to explain that, "The American Heart Association lists stress as a possible risk factor for heart attacks, but it's not one of the major known risk factors" and that one of the reasons is the difficulty in proving a direct cause-and-effect link. As Dr. Brian Olshansky, a University of Iowa cardiac electrophysiology specialist explained, "The reason that the American Heart Association and others have not made depression and stress a risk factor for death after myocardial infarction is that the whole concept of stress is very hard to define. What is stressful for one person may not be stressful for another person." In addition, without accurate knowledge of Lay's medical history or the post mortem findings experts would have difficulty stating how strong a role stress played in his death, especially if he had sustained a prior heart attack as the autopsy apparently suggested. Dr. Douglas Zipes, a past president of the American College of Cardiology said, "Extreme stress is recognized as a risk factor for chest pain, rapid heart beat, and sudden cardiac death. Catastrophic events over which one has no control such as loss of job, loss of spouse, loss of house, and-in this case-a felony conviction, are all examples of extreme stress that can trigger an episode of ventricular fibrillation and sudden death. We know that sudden cardiac

death increased following the events of Sept. 11, 2001 and after the Oct. 17, 1989 San Francisco earthquake." But Dr. Steven Nissen, current president of the American College of Cardiology disagreed, stating, "I don't buy the 'stress causes heart disease' paradigm. Our species is well adapted to deal with stress, and most of us don't die suddenly when life gets complicated."

Others avoided taking sides. "People need to understand that heart disease is based on a combination of risk factors that can include your family history, your genetic risk as well as other risk factors," said Dr. Nieca Goldberg, a spokeswoman for the American Heart Association and a cardiologist at New York's Lenox Hill Hospital. "We know that stress isn't good for your health, but in terms of its relationship to heart disease, we don't know the strength of the link the way we do about cholesterol and high blood pressure and diabetes and smoking. It is not unusual when a person has a heart attack, they have it after a sudden life-changing event. It could be loss of a spouse, loss of a house, loss of a job. Stress does alter some of your risk factors for heart disease. It raises blood pressure and also makes platelets more likely to clump together ... and blood clots do cause heart attacks". Some suggested that stress could cause people to eat badly and/or avoid exercising, which might increase heart attack risk. Dr. Chip Lavie, a cardiologist at the Ochsner Health System in New Orleans asked, "Do they just have more stress and the stress causes them to do stuff that is more unhealthy ... or is it the stress directly causing the problem? The classic is a person who has a big fight with their spouse and then has a heart attack. Now that person has bad artery disease and the fight with the spouse didn't cause the bad artery disease." Dr. Redford Williams at Duke University Medical Center agreed that the stress Lay had endured "undoubtedly played a role in his premature death at age 64" and that, "Stress can play nearly as important a role in having a heart attack as high cholesterol or high blood pressure." He similarly believes that **"when people under major current life stresses die suddenly, in virtually all cases there is underlying atherosclerosis."**

The media coverage of this event was characterized by confusion as well as misinformation. One consultant asked, "Was it the stress, the thin mountain air, the juicy 4th of July steak, or a horrible prison rape nightmare perhaps?" Rather than stress being the culprit, some scenarios suggested that it was a suicide or homicide, possibly by poisoning, or that the dead person was really someone else and that Lay was on his way to some destination where he would live the rest of his life in luxury. Wikipedia, the web based encyclopedia that anyone can edit added details about Lay's death to its online biography shortly after news outlets began reporting it at around 10 a.m. EDT. At 10:06 a.m., Wikipedia's entry for Lay said he died "of an apparent suicide." At 10:08, it said he died at his Aspen, Colorado home "of an apparent [[heart attack or suicide.]." Within the same minute, it said the cause of death was "yet to be determined." At 10:09 a.m., it said, "no further details have been officially released" about the death. Two minutes later, it said: "The guilt of ruining so many lives finally led him to his suicide." At 10.12 a.m., this was replaced by: "According to Lay's pastor the cause was a 'massive coronary' heart attack." By early Wednesday afternoon, the entry said Lay was pronounced dead at Aspen Valley Hospital from a massive heart attack according to the local sheriff's department statement, but it was later learned that their information came from KHOU-TV in Houston. Wikipedia's web site warns users "newer articles may still contain significant misinformation, unencyclopedic content, or vandalism."

Exactly what constitutes a "massive coronary heart attack" is not clear since there is no such clinical or pathological diagnosis. In addition, it would not be possible to assess the extent of myocardial damage or coronary occlusion without an autopsy. It seems likely that this term was used to imply that Lay's death was so sudden that the amount of damage to the heart muscle must have been massive. What I found surprising both in my own interviews and others that were reported was the relative lack of interest in mechanisms that could explain how stress had caused Ken Lay's sudden death. One exception was Dr. Zipes, who stated

that, "the recent events of Lay's life suggest an almost textbook setup for sudden cardiac death" and, "it's also possible Lay didn't die from a heart attack but instead from heart failure." As Zipes had previously indicated, this was most likely due to ventricular fibrillation, an electrical disturbance in which the ventricles only quiver very rapidly and do not contract enough for blood to reach vital organs and death quickly follows. This is quite different than a myocardial infarction due to a coronary occlusion that cuts off blood flow to a localized area of heart muscle. This does not usually cause sudden death and most of these patients recover, whereas ventricular fibrillation is always fatal if not quickly corrected. The reporter went on to mistakenly explain," **Heart attacks are caused by the blockage of blood flow to the heart -- usually from fat clogging the arteries -- whereas heart failure is a disruption of the heart's electrical rhythm."** However, heart failure is usually a chronic condition and can occur following a heart attack or anything else that interferes with the heart's pumping ability. Heart failure, also called congestive failure, is more often due to a long-term mechanical problem rather than any acute electrical disturbance.

Another article suggested that Lay's death was an example of the so-called "Broken Heart Syndrome." However, just a minimal amount of research would have revealed that this term refers to an unusual condition that is never fatal. It is seen almost exclusively in women who appear to be in the throes of an acute heart attack because of severe chest pressure, difficulty breathing and a sense of impending doom. Some may even show signs of heart failure and require aggressive treatment despite the lack of any evidence of cardiac damage on ECG, blood tests or coronary angiography. Symptoms frequently follow some sudden emotional trauma such as learning of the death of a loved one or even a surprise party. Patients typically recover within a few days after bed rest and reassurance that they have suffered no permanent heart damage. The disorder is also referred to as "myocardial stunning" or "stress cardiomyopathy" and has been known in Japan for years as Takotsubo Syndrome.

Nevertheless, there is little doubt that people can die from being heartbroken, and "griefe" was a well-accepted cause of death centuries ago. It has long been observed that married couples frequently die within a year or two of each other as can be readily illustrated in synagogues and temples where plaques list the date when members of the congregation have passed on. Jim Lynch demonstrated decades ago in *The Broken Heart: the Medical Consequences of Loneliness,* that widowed individuals died at significantly higher rates in the 12 months following loss of a spouse from all the leading causes of death. A subsequent study confirmed that British widowers had a 40% greater risk of death in the first year after a wife's death but not necessarily from cardiovascular disease. In one report, men whose wives had died from breast cancer experienced a sharp drop in the activity of their immune system one to two months after the loss, which could explain why widowed individuals may be more susceptible to infections and certain malignancies. Lynch also showed that a large percentage of Americans who die from heart disease had an underlying problem of lack or loss of meaningful relationships that was likely to have been a contributing factor. However, in most instances, fatalities that seem clearly linked to bereavement or loneliness are not entirely unexpected nor do they explain how stress can cause sudden death.

How Can Stress Cause Sudden Death In Perfectly Healthy People?

Sudden cardiac death can be defined as "Natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of symptoms; preexisting heart disease may have been known to be present, but the time and mode of death are unexpected. All that is known about Lay's final episode is that sheriff's deputies and an ambulance were called to his vacation home around 1 am and he was transported to the Aspen Valley Hospital where he was pronounced dead about two hours later. There is little doubt that stress is most likely to cause sudden cardiac death in people like Ken Lay with a history or evidence of coronary heart disease. However, this is not a prerequisite and there

may be scant or no coronary atherosclerosis, especially in younger patients overcome with excitement. In addition to severe fear, or overwhelming sorrow over the loss of a loved one, any intense emotional state, including extreme joy can trigger sudden death.

This was demonstrated by George Engel, a pioneer in psychosomatic medicine. In a landmark 1971 article he wrote, "**Few folklore notions have enjoyed as widespread and persistent popularity as those that ascribe sudden death to emotional shock. As far back as written records exist, people are described as dying suddenly while in the throes of fear, rage, grief, humiliation, or joy**. In the eighteenth and nineteenth centuries medical writings abounded in such accounts. Since then consideration of the relationship between emotion and sudden death has virtually disappeared from the medical literature." He attributed this to the discovery of bacteria as the cause of many diseases in the late nineteenth century, which cast doubts on all folklore explanations of medical matters. Nevertheless, he added, "Many physicians in private conversations are quite ready to recount from their own practices examples of patients who apparently died suddenly under precisely such circumstances."

Over a six-year period, Engel had carefully collected some 275 press accounts of 170 sudden deaths that were clearly connected to what he described as a "disrupting life event". Three-fifths involved men, commonly 45 to 55 years old, whereas the peak age for women was 70 to 75. There were also four teenagers and three children under ten where sudden death seemed due to some severe stressful situation. These included:

- a personal danger or threat of injury, whether real or symbolic (27%)
- the collapse or death of someone very close (21%)
- the 16-day period following acute grief (20%)
- the threat of the loss of a someone very close (9%)
- the period after danger of loss was over (7%)
- a loss of status or self-esteem (6%)
- a reunion, triumph, or "happy ending" (6%)
- a period of mourning or the anniversary of the death of a close person (3%)

In 27 percent of cases, which was the largest category, the precipitating event involved some element of fear that was either justified or imagined, such as; "A 63-year-old-security guard died after being bound by robbers. . . . A woman seeing some teenagers outside her apartment beating and robbing a bus driver died while phoning the police. . . . A 35-year-old man accused of robbery told his lawyer, 'I'm scared to death!' and then quickly collapsed and died." The most frequent type of stress seemed to stem from some sort of disruption of a very close personal relationship. Another common cause was severe emotional upset resulting from an embarrassing loss of status, humiliation or defeat. In one instance, the president of a college had been forced to retire by the Board of Trustees at the age of 59 and he collapsed with a heart attack as he was delivering his final speech. One of his best friends, a doctor, rushed to the stage to save him but the stress of losing his close companion was too much and the physician also fell to the floor of the platform and died of heart failure.

Faced with stressful situations in which one can neither fight nor flee, people feel trapped and die, an impasse Engel had previously described as the "Giving Up-Given Up" complex. This was characterized by "an inability to cope, variously voiced as 'discouragement,' 'despair,' 'giving up, or 'depression,' accompanied typically by the affects of hopelessness and helplessness." **On the other hand, sudden death could be precipitated by extreme joy, as in the case of a healthy 18 year-old bride who was overcome by the excitement of her wedding day**. The Greek physician Galen believed that the emotion of joy was more dangerous to the heart than anger and ancient Greek and Roman accounts of sudden death cite just as many that were caused by excessive happiness as from acute grief and sorrow.

Roman historians cited the case of an aged mother, who, while mourning her son's reported death in battle, died in his arms because of extreme sudden joy at his safe return. There was also a father who died immediately after learning that his son won first prize at the Olympic games. More recently, Pyle and Gould described a case of heart rupture following an experience of sudden joy in which the pericardial sac was found to be filled with blood at autopsy.

It was generally believed that sudden death in such situations was due to some severe disturbance in heart rhythm, possibly facilitated by the increased secretion of certain hormones. As Engel commented, "We can only speculate about the mechanism of death in such cases. Most would agree that effective cardiac arrest, whether caused by ventricular asystole or by ventricular tachyarrhythmias, is probably responsible for the death of those who die within a few minutes...But such are not present in all cases...Some of the lethal influences may involve rapid shifts between sympathetic and parasympathetic cardiovascular effects. Such shifts back and forth can be invoked experimentally in animals and the usual consequence is sudden death for no other accountable reason. This has been demonstrated in squirrel monkeys. Certainly, the use of 'folklore' or 'old wives' tales' as pejorative labels, as some skeptics are wont to do, is hardly compatible with the scientific attitude requisite for the study of natural phenomena involving life and death." (Engel GL. Sudden and Rapid Death During Psychological Stress: Folklore or Folk Wisdom? *Annals of Internal Medicine* 1971; 74:771-783.)

Walter Cannon, Voodoo And Bone Pointing Deaths

As George Engel noted, the ability of severe fear and psychological stress to cause sudden death is embedded in the folklore of all ethnic groups. This was particularly common in primitive cultures following the realization that a taboo had been violated or that a powerful hex had been placed on the victim. Such fatalities represented a punishment by some deity or by a shaman who possessed similar supernatural power. As Engel had also emphasized, Western medicine tended to dismiss such stories as superstitions and "old wives' tales", especially since there was no plausible mechanism to explain how emotions could cause sudden death. Walter Cannon, Chairman of the Department of Physiology at Harvard, was fascinated by well-documented accounts of this phenomenon he had collected from all over the globe. If proven to be accurate and truthful, it would appear that this was indeed some sort of witchcraft, "black magic" or "devil worship", which he refused to accept. Cannon was determined to find the physiologic basis for what he referred to as "voodoo death", and, as he later explained,

> "In records of anthropologists and others who have lived with primitive people in widely scattered parts of the world is the testimony that when subjected to spells or sorcery or the use of "black magic" men may be brought to death. Among the natives of South America and Africa, Australia, New Zealand, and the islands of the Pacific, as well as among the Negroes of nearby Haiti, **'voodoo death' has been reported by apparently competent observers. The phenomenon is so extraordinary and so foreign to the experience of civilized people that it seems incredible; certainly if it is authentic it deserves careful consideration.** I propose to recite instances of this mode of death, to inquire whether reports of the phenomenon are trustworthy, and to examine a possible explanation of it if it should prove to be real." It was, ". . . a phenomenon characteristically noted among aborigines – among human beings so primitive, so superstitious, so ignorant, that they feel themselves bewildered strangers in an hostile world. Instead of knowledge, they have fertile and unrestricted imaginations which fill their environment with all manner of evil spirits capable of affecting their lives disastrously." (Cannon WB, "Voodoo" death. *American Anthropologist*. 1942; 44:169-181.)

He then cited examples of death due to fright in the Tupinambás Indians of South America when they were condemned and sentenced by the "medicine man." In Africa, a young tribesman had unknowingly eaten the forbidden wild hen when visiting a friend who lived far away. When informed of this unintended violation a few years later, he was overcome by fear, started to shake and died within 24 hours. A Maori New Zealand woman who had eaten some fruit was later told that it had been taken from a tabooed place and that the spirit whose sanctity had been profaned would kill her. She similarly died suddenly less than 24 hours later. Some shamans and sorcerers used props. African witch doctors had knucklebones, European witches carved wooden dolls and Australian aborigine sorcerers used bones extracted from the flesh of giant lizards. In Haiti, where voodoo was a religion, there were dozens of different dolls and methods of maiming or sticking pins in them to inflict harm on victims, which may be why Cannon decided to label the entire phenomenon "voodoo death". Some of the best-authenticated and most dramatic examples were the bone pointing deaths from Australia. When the bone slivers were pointed at a person while the sorcerer simultaneously recited a death spell, the victim invariably became very ill and almost always died. Dr. Herbert Basedow's personal description of this in the early 1900's was as follows:

> "The man who discovers that he is being 'boned' is a pitiable sight. He stands aghast, with his eyes staring at the treacherous pointer, and with his hands lifted as though to ward off the lethal medium, which he imagines is pouring into his body. His cheeks blanch and his eyes become glassy and the expression on his face becomes horribly distorted. He attempts to shriek but usually the sound chokes in his throat, and all that one might see is froth at his mouth. He sways backwards and soon falls to the ground, and after a short time appears to be in a swoon: but, soon after he writhes as if in mortal agony, and, covering his face with his hands, begins to moan. After a while he becomes very composed and crawls to his wurley [hut]. From this time onwards he sickens and frets, refusing to eat and keeping aloof from the daily affairs of the tribe. Unless help is forthcoming in the shape of a counter-charm administered by the hands of the Nangarri, or medicine man, his death is only a matter of a comparatively short time."

Cannon collected numerous reports from Hawaii, Haiti, Trinidad, Guyana other primitive societies and painstakingly investigated over 30 before becoming convinced that "voodoo death" was indeed valid. However, since there were no connections or links between most of these very different and geographically separated cultures, what common denominator was responsible for this peculiar type of "death by decree". Cannon concluded that three components were required.

1. The victim and all family and friends must believe that the ability and power of the hexer or medicine man is genuine and will indeed cause death.
2. All previously known victims of the hexing or curse must have died unless the punishment had been removed.
3. Every person known to the victim must behave toward him as if his death in a short period of time was a certainty. This meant that everyone would leave him alone and isolated, including family and friends.

Death was inevitable if these three criteria were met. The absence of social support was just as important as withholding food, water and any physical aid. Relatives also began chanting and mourning rituals that reinforced in them, the bone pointing victim and the rest of the tribe the belief that death was imminent. The victim was still physically alive, but dying psychologically and was already dead socially. The psychologist William James had previously emphasized, **"the catastrophic emotional effect we all would suffer if everyone around us suddenly acted as if we had ceased to exist."**

Few people were better equipped than Walter Cannon to elucidate the mechanisms of stress induced sudden death. His earliest research in 1897 had focused on the physiology of emotions following the observation that fear and other stressful states disrupted normal peristaltic waves in the esophagus and stomach. He subsequently showed that when experimental animals were strongly aroused, increased stimulation of the sympathetic nervous system and a surge in adrenaline secretion resulted in numerous "flight or fight responses" that could be life saving in emergency situations. These changes in blood flow, muscle tension, blood sugar, blood clotting etc. were summarized in his 1915 book, *Bodily Changes in Pain, Hunger, Fear and Rage*. Over the next few years, Cannon devoted his physiological expertise to studying the problem of persistent shock due to low blood pressure that occurred in badly wounded men from blood loss during World War I. Working in field hospitals, he became aware of peculiar cases of battlefield casualties who were also in shock but had not suffered any injury or bleeding, and whose critical and sometimes fatal low blood pressure seemed to be due to extreme fear. Some of these soldiers who were literally scared to death were reminiscent of the terrified natives who eventually succumbed to some sorcerer's spell. Cannon believed that in both instances, persistent and lethal shock was due to increased stimulation of "the sympathico-adrenal system" which caused a constant constriction of small arterioles that also lowered blood volume. As he explained,

> "If adrenaline, which constricts the blood vessels precisely as nerve impulses constrict them, is continuously injected at a rate which produces the vasoconstriction of strong emotional states, the blood volume is reduced. The foregoing paragraphs have revealed how a persistent and profound emotional state may induce a disastrous fall of blood pressure, ending in death. Lack of food and drink would collaborate with the damaging emotional effects, to induce the fatal outcome. These are the conditions, which, as we have seen, are prevalent in persons who have been reported as dying as a consequence of sorcery. They go without food or water as they, in their isolation, wait in fear for their impending death. In these circumstances they might well die from a true state of shock, in the surgical sense—a shock induced by prolonged and tense emotion. **The suggestion which I offer, therefore, is that 'voodoo death' may be real, and that it may be explained as due to shocking emotional stress—to obvious or repressed terror**."

He went on to say that any such hypothesis is not satisfactory or useful unless it "allows observations to be made which may determine whether or not it is correct." Since Cannon believed that death was due to the continuous outpouring of adrenaline, he predicted that doomed individuals would exhibit fast and shallow respirations, the pulse toward the end would be rapid and "thready", the skin would be "cool and moist", there would be hemoconcentration due to low blood volume and the heart would beat faster and faster until it was in a state of constant contraction and failed. He was anxious for someone to confirm his theory and concluded with this request. "If in the future, however, any observer has opportunity to see an instance of 'voodoo death', it is to be hoped that he will conduct the simpler tests before the victim's last gasp."

Cannon's paper was published in 1942 and a year or two later, Stewart Wolf did observe such a death while serving as a consultant for a native general hospital in New Guinea during World War II. He told me that he had been asked to see if he could do anything to help a healthy 30 year-old man who was convinced he would soon die as a result of a powerful hex or death spell called puri-puri. Stewart could find nothing wrong on physical examination and said the patient was very cooperative and surprisingly congenial despite the death sentence. He was transferred to Stewart's Army hospital, which was staffed by other professors, physicians, technicians and nurses from Cornell Medical School and Hospital in New York, where a very thorough workup also revealed no significant

abnormality. Despite reassurance from Stewart and all the other consultants, the patient remained convinced that death was imminent because of the puri-puri hex and was resigned to the fact that nothing could counteract it. Stewart continued to follow the patient whose condition remained stable until he suddenly died a few days later. While New Guinea laws did not permit post mortem examinations authorities agreed to make an exception in this unusual case. The procedure was performed by skilled pathologists who were unable to find any abnormality or cause of death. What was particularly puzzling was that neither the autopsy findings nor the patient's final hours resembled Cannon's "voodoo" death scenario. Indeed, rather than stimulation of sympathetic nervous system activity and adrenaline secretion, it appeared that death occurred because the heart had just suddenly stopped beating. **The most likely explanation for this was parasympathetic and vagus nerve hyperactivity, the exact opposite of Cannon's hypothesis.**

Richter's Rats, Low HRV, The Evil Eye And Modern Hexes

Stewart was disappointed since Walter Cannon had been instrumental in obtaining support for his research on stress and ulcers. Cannon also wrote a very gracious Foreword to his book *Human Gastric Function* that was published the previous year. Stewart's inability to confirm his friend's sudden death theory probably stimulated his own interest and subsequent contributions to this subject. By the time George Engel's article on sudden death in humans appeared three decades later it had been proven that increased parasympathetic activity could indeed be the culprit. By coincidence, George Engel was Stewart's classmate at Johns Hopkins and it was Curt Richter, another Hopkins friend who first demonstrated how stress induced parasympathetic stimulation could cause sudden death. Richter, who directed the Psychobiological Laboratory at Johns Hopkins for six decades, is best known for discovering the body's biorhythms and identifying the brain sites that control sleeping, waking and other daily cycles. He had been concerned that the progressive inbreeding of his laboratory rats had rendered them too weak to serve as accurate models for his research on biological clocks and spontaneous activities. To evaluate this he developed an endurance test in which the animals were place in a circular glass tank of water with a whirlpool device that forced them to constantly swim to avoid drowning. While most lasted for 60 to 80 hours before becoming exhausted, a few sank to the bottom in ten minutes. The reason for these deaths was not clear but he recalled that in a prior experiment in which the rat's whiskers (vibrissae) had been clipped, the animals started to behave strangely and often died for no apparent reason a few hours later. He decided to clip the whiskers of 12 rats and when the swim test was repeated, three rats died within a few minutes and none of the remainder were able to last nearly as long as the original group.

Richter then studied a few dozen wild rats, most of which he had personally trapped in the streets and sewers of Baltimore. These animals tended to be much fiercer, more aggressive and suspicious than their laboratory cousins. They constantly searched for some means of escape and strongly resisted any type of restraint. Although much stronger than laboratory rats he was surprised that they usually lasted less than 15 minutes in the swim test. Some even dove straight to the bottom of the tank and died immediately. And when he trimmed their whiskers, they all sank within a few minutes and some died while being held firmly to prevent escape prior to immersion. Richter reasoned that trimming the snout hairs destroyed the rat's most important means of contact with its environment. Under certain circumstances, this could be sufficiently stressful to cause death, much like the hex victims that were suddenly deprived of all social support. To confirm Cannon's theory that death was due to intense sympathetic nervous system stimulation he devised a crude ECG to monitor cardiac events. He was surprised to find that sudden death was preceded by a drop in heart rate as well as a slowing in respiration and lowering of body temperature. These were all indicative of parasympathetic stimulation. He confirmed this by showing that injecting the rats with atropine, a parasympathetic blocking drug, prevented sudden death in his swim test.

In contrast to animals born and reared in the laboratory, the wild rats were not used to being handled or being restrained and confined to different experimental settings. They died because without their whiskers to supply information in a hostile environment they felt helpless and hopeless, which was believed to be a powerful parasympathetic stimulus. To test this, he allowed several to sink to the bottom of the tank, quickly retrieved them from almost certain drowning, and then put them back in the tank when they had recovered. After repeating this several times the wild rats no longer died following immersion and could swim for hours, simply because they had learned that their situation was really not hopeless after all. As Richter noted in a breakthrough 1957 article, this was similar to the voodoo victims, who, when freed of their hex, were also observed to "recover instantaneously, even after appearing more dead than alive." **Like his wild rats, voodoo victims perished because of overwhelming feelings of hopelessness and helplessness that caused a progressive slowing of cardiac contractions and eventually their cessation**. In summarizing his paper Richter wrote "A phenomenon of sudden death has been described that occurs in man, rats, and many other animals apparently as a result of hopelessness; this seems to involve over activity primarily of the parasympathetic system. In this instance as in many others, the ideas of Walter Cannon opened up a new area of interesting, exciting research." (Richter R. On the Phenomenon of Sudden Death in Animals and Man. *Psychosomatic Medicine* 1957; 19:191-198)

Walter Cannon had introduced the concept of homeostasis and described the coordinated responses responsible for insuring this hallmark of health in his 1932 book, *The Wisdom of the Body*. Cannon and Claude Bernard before him had focused entirely on physiological mechanisms responsible for maintaining this "steady state". Richter expanded this to include behavioral factors that could influence these adaptive responses and were equally important in maintaining the stability of the internal environment. It was not that Richter had proved that Cannon was wrong. The laboratory rats had indeed died from exhaustion and sympathetic stimulation whereas the wild rats showed a very different pattern. They reverted to a very primitive survival strategy in which they "played dead" and their hearts slowed up to the point where they actually stopped. In retrospect, Cannon's persistence in verifying and attempting to explain how stress could cause sudden death was indeed a remarkable achievement. When the article was written in 1942, the term "stress" popularized by Cannon's admirer Hans Selye was not in general use and little was known about pituitary and adrenal cortex hormones that participated in the response to stress. CRH (corticotropin releasing hormone) from the hypothalamus was not fully identified until four decades later nor was it immediately apparent that CRH was activated by signals from the amygdala, the brain's fear center. It was thus impossible for Cannon to anticipate the cascade of hormones and chemicals released in situations of severe fear that would be more likely to produce the cardiac arrhythmias and vascular collapse than his simplistic explanation of arteriolar constriction and reduction of blood volume. Yet, he anticipated this by emphasizing that his hypothesis would be of value only if it could be tested. He clearly recognized that theories don't have to be correct, only facts do. Theories that don't pan out can prove very valuable because they encourage others to find new facts that lead to better theories, which is exactly what happened here.

In commenting on the difference of opinion about "voodoo death" between Cannon and Richter, Stewart Wolf concluded that both were correct. In a 1960 article, he cited supportive clinical illustrations of both, including a patient who could induce complete cardiac arrest at will. He concluded, however, that, "The evidence relating psychological phenomena to disease of the heart and blood vessels is fragmentary and at this stage altogether inconclusive. It is sufficiently promising, however, to warrant a great deal more systematic study and serious interest on the part of physiologists and clinicians." (Wolf S. Stress and Heart Disease. *Modern Concepts of Cardiovascular Disease,* 1960; 29:No.7, July) Stewart and his neurocardiology team were the first to recognize that diminished HRV (heart

rate variability) was a more important predictor of sudden death and heart attacks than standard risk factors such as hypertension, cholesterol or smoking. However, it took three decades for the clinical significance of this to be fully appreciated and for the complete results of his research to be published in a paper entitled, "Oscillatory Functions Affecting Outcome of Coronary Heart Disease: The Hazard of Too Much or Too Little Stability". Stewart went on to make further contributions in this area, some of the most notable stemming from his studies of Roseto showing the cardioprotective and stress reducing effects of strong social support.

Roseto also confirmed that belief in hexes still persisted, as in the curse of the *mal occhio*, or "evil eye". This could be offset by a twisted horn shaped amulet made of gold or silver or carved out of red coral, called a *cornicello* (little horn). These are still popular, particularly in people of Italian ancestry and are readily available in most jewelry stores. Belief in similar evil eye curses abounds in every culture and is especially prevalent today in Mediterranean countries. In Spain it is *mal ojo* or *el ojo* (the bad eye or just the eye), in Sicily it is *jettatore* (the projection from the eye) and in Greece it is called *kako mati*. In Greece and Turkey, glass blue eye charms to ward against the evil eye are still regularly sold and are often pinned on a baby's clothing. The Greek Orthodox Church takes this very seriously and has a special *Vaskania* prayer to help those who have been cursed. Other preventive or helpful measures are to wear a cross, blue glass eye or garlic on a necklace or to spit three times. (If you are in a situation where you can't spit, making a "tuh, tuh, tuh" sound that mimics expectoration will suffice). These latter maneuvers are particularly useful for the envious eye, which can be invoked by saying something complimentary. In Yiddish this evil eye is ayn hora, hence the common expression *keinaynahorah* for "no evil eye", (from kein, no; ayin, eye; and harah evil) This must be said immediately after any flattering statement, such as "'I hear your son just got into medical school, *keinaynahorah*" or "I have such a beautiful granddaughter, *keinaynahorah*". This is sometimes abbreviated as *kaynahorah* or is further shortened to "canary". Jews and individuals of any faith are often apt to remark, "Don't give me a canary" when something praiseworthy is said.

Voodoo deaths and spells are also still with us as evidenced by a 1992 case report of a 60 year-old Alabama man who was wasting away and near death. He was convinced that a voodoo priest had put a curse on him and an extensive workup revealed no other explanation for his progressive debilitation and failure to respond to treatment. As the situation seemed terminal, his frustrated physician ceremoniously gathered the dying man's relatives around his hospital bed and authoritatively announced that he had finally solved the problem by frightening the priest into telling him how he could remove the hex. He told the astonished patient, "The voodoo priest made you breathe in some lizard eggs and they climbed down into your stomach and hatched out some small lizards. All but one of them died leaving a larger one, which is eating up all of your food and the lining of your body. I will now get that lizard out of your system and cure you of this horrible curse." He administered a strong emetic and when the patient had vomited into a basin several times, surreptitiously slid in a green lizard. He then held it up for everyone to see and authoritatively announced the curse had now been lifted. The patient rapidly regained his appetite and strength, was discharged, and lived another ten years. In analyzing the case, the author asked, "Are we so different from our ancient and primitive witch doctor colleagues? . . . . **Is death from hexing a strange and bizarre phenomenon limited to ignorant and superstitious tribes, or is it part of some phenomenon basic to many forms of human communication?**" (Meador CK. Hex Death: Voodoo Magic or Persuasion? *Southern Medical Journal*, 1992; 85:244-247.)

And in November 1988, Florida Republican Senator Alberto Gutman charged his opponent with using voodoo against him in an election. As the police officer who investigated the charge commented, "It's not a common thing but it's not a rare thing, especially down here

in Miami." More recently, superstar Jennifer Lopez was accused in a court deposition of casting "voodoo" spells on all her lovers past and present. One of her past husbands claimed the singer practices Santeria, a Cuban version of voodoo brought to the Americas by West African slaves. Lopez has also been accused of being responsible for hurricane Katrina, which destroyed a rival form of voodoo that previously flourished in New Orleans. Many believe there will be a resurgence of interest in voodoo as a result of increased immigration from countries where this and allied practices are common. Santeria, Brujerio from Puerto Rico and other Caribbean voodoo variants are currently flourishing in the Bronx, as well as Miami. Some Yankee fans are convinced that the team's good fortunes are due to voodoo type hexes that have been directed at their opposition or specific players. That's not surprising since baseball has a long history of superstition from the "Curse of the Bambino" to some players' refusal to wash their clothes or bodies after a win. The desire to keep a number you have been successful with, faith in a lucky bat or glove, particular pre game or pre batting rituals are common. One of the most serious superstitions is never to talk about a no-hitter or perfect game in progress, since this will surely give the pitcher "a canary".

We hear a great deal about the ability of placebos (Latin for "I will please") to relieve complaints and promote health. Voodoo, bone pointing and other hexes are examples of nocebos (Latin for "I will harm"). A nocebo response is any ill effect caused by suggestion or the belief that something is harmful, and contemporary medicine is replete with illustrations of this. **For example, routine preoperative warnings of a host of potential serious hazards to avoid medico-legal problems can become a self-fulfilling prophecy for susceptible individuals.** The same is true when well-intentioned physicians advise patients that they have only so many weeks or months left to get their affairs in order. These nocebos can be the modern equivalent of a bone pointing decree for those who expect the worse to happen or promptly give up all hope of recovery and succumb much sooner than predicted. The power of suggestion, faith and belief to promote health is widely acknowledged. However, we often fail to appreciate that this is a two-edged sword that can also cause harm. Although such nocebos may be unintentional, they can be just as potent as a primitive hex specifically designed to be damaging or deadly.

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