
He Hath the Falling Sickness

Few diseases arise so abruptly, speak so boldly, and define themselves so readily, as epilepsy. There is little clinical subtlety when the major form of epilepsy descends upon its victim. The unbidden affliction announces itself explosively with altered consciousness, inarticulate cries and diminished motor control, convulsions and incontinence followed by an amnesic interval of variable length.

The early Greeks called it *Herakliea nosos*, the illness of Hercules, since the legendary hero had been prone to seizures. Most commonly, however, people called it the falling sickness. The Hebrews, too, named it "the falling down" or, "one who writhes."

There are scattered references in the Scriptures to spontaneous falling down, with the victim sometimes entering a trance with his eyes open [Num 24:4.] Saul, King of the Israelites, was said to have suffered from seizures. But it awaited the apostolic writings of Mark, Luke and Matthew for a narrative description of the disease. Chapter 9 of Luke begins with Jesus assembling his twelve disciples and giving them "power and authority over all devils, and to cure diseases." And this story is then told: "And, behold, a man of the company cried out, saying, Master, I beseech thee, look upon my son: for he is my only child. And, lo, a spirit taketh him and he suddenly crieth out; and it teareth him that he foameth again, and bruising him hardly departeth from him. And I besought thy disciples to cast him out; and they could not." It is a poignant story, easily understood by any diligent parent. And it describes a disease that will not respond readily to casual therapies.

Ancient Rome had intimate knowledge of epilepsy. They called it by various names including *morbus caducus* [the falling sickness]; *morbus comitialis* [disease of the assembly hall.] It was a standing Roman custom to shut down the public assembly [*comitia*] for ritual purification whenever any legislator experienced a seizure; *morbus sacer* [the sacred sickness]; or *morbus demoniacus* [the demonic sickness.] In Act 1, scene 2 of Shakespeare's *Julius Caesar*, Casca recounts one of Caesar's many epileptic attacks: "He fell down in the market-place, and foamed at the mouth, and was speechless." Brutus responds: "'Tis very like, he hath the falling sickness." Indeed, epilepsy seemed to have been so common amongst the leaders of antiquity [eg, Caesar, Alexander the Great, even Caligula] that some thought it to be a necessary prelude to military greatness.

Both educated and uneducated have viewed this disease with horror: Many believed that the victim's body had been possessed and its control relinquished to some outside agency. A few believed that this possession was from divine sources and accordingly they rendered respect, even homage, to the epileptic; but most contended that the possessing forces were Satanic therefore requiring that they be displaced by theological rather than medical intervention.

John of Gaddesden, English court physician of the 14th Century, advised that the physician whisper into the ear of the epileptic: "Depart demon and go forth!" He commented further, "This species of devil is not cast out save by prayer and fasting. The patient should then write out this gospel and wear it about his neck and he will be cured."

Yet it was Hippocrates, writing on the island of Kos some 1,700 years earlier, who declared that epilepsy was not a spirit-possessing disease but a disorder much like any other: "And they who first referred this disease to the gods, using the divinity as a pretext and screen of their own inability to afford any assistance, have given out that the disease is sacred. . . Neither truly do I count it a worthy opinion to hold that the body of man is polluted by God."

Epilepsy was a disease which also plagued many British leaders including Alfred the Great, William III and William Pitt. Many of Queen Victoria's relatives had been epileptic and she provided funds for the National Hospital for the Paralyzed and Epileptic, in London, so that research into the cause and care of the epileptic might be furthered.

Epilepsy seemed to have been no hindrance to genius. The ranks of those prone to seizures included: Dickens, Moliere, Handel, Schumann, de Maupassant, Byron, Flaubert, Dostoyevski, Swinburne and van Gogh. Many writers incorporated their own clinical episodes into the substance of their novels. No medical text equals the sense of authenticity exhibited in Dostoyevski's vivid fictional descriptions of epileptic seizures.

Prior to the 19th Century, therapy varied from the bizarre to the ineffectually innocent. The blood of gladiators or executed prisoners was frequently recommended as a preventive measure; and Hans Christian Anderson recalls seeing parents force their epileptic children to drink the warm blood of recently beheaded criminals. A standard anti-epileptic decoction consisted of the boiled and macerated leaves of elder, garlic, peony and mistletoe. The stated rationale for the use of mistletoe was that it tenaciously clung to the upper branches of the oak tree never falling to the ground and hence must be helpful in the falling disease.

The 19th Century physician, baffled and humbled by epilepsy, believed that it was of unknown cause, inscrutable and, alas, incurable. But gradually the neurophysiologists explored the nature of normal brain impulses and the manner in which certain portions of the cerebrum held dominion over motor activity in the limbs. Epilepsy was then conceived of as an explosive happening in which uncontrolled impulses were initiated from an abnormal cerebral locus. The idea of supracorporeal possession was now replaced by the more secular concept of abnormal excitation arising from a pathological segment of cerebral cortex. And gradually, too, effective therapies such as the bromides, barbiturates and dilantin were discovered.

This current century has witnessed significant inroads in the understanding, diagnosis, treatment and even prevention of the epilepsies. Studies have determined that there are many forms of epilepsies: some awesomely dramatic such as the *grand mal* seizures; but others with neither convulsive movements nor other visible abnormalities; and with, at most, a brief spell of detached staring [*petit mal*.] The epileptic diseases have been shown to be caused by a spectrum of unrelated ills including birth injury, toxins,

metabolic insults, vascular disorders, heritable neurological lesions, even brain tumors. And current treatment has evolved to a stage where the great majority of epileptics may now lead productive lives unburdened by the threat of seizures. But society's memory is long; and there are still those who think of epilepsy as possession by demonic forces.

– Stanley M. Aronson, MD

Medical Genetics: Past, Present and Future

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EARLY HISTORY OF HUMAN GENETICS

From a historical point of view, knowledge of human genetics has its roots in antiquity; the ancient Hebrews were aware of the natural history and mechanism of inheritance of the disease we now call hemophilia, as they omitted the obligatory ritual circumcision in male infants whose brothers or maternal uncles had bleeding disorders. Many centuries later, in the mid-1800s, Gregor Mendel deduced the basic rules of inheritance from his experiments on garden peas; before that time, inheritance was thought to be a merging of characteristics of both parents. Mendel realized that there were discrete units of heredity which were passed to offspring in a predictable manner. Unappreciated until early in this century, his observations became the cornerstones of modern genetics when the inheritance of inborn errors of metabolism was studied and found to fit his rules.

MODERN HISTORY OF MEDICAL GENETICS

As a medical subspecialty, genetics is quite young; knowledge necessary for its recognition began to accumulate in 1956, when we learned that the normal number of chromosomes in humans is 46, not 48 per cell, as had been previously thought. Geneticists discovered the chromosomal origins of Down syndrome, Turner syndrome and Klinefelter syndrome during the next few years. Watson and Crick deciphered the genetic code in the 1960s, and around that time, prenatal diagnosis by amniocentesis was developed. Techniques for differential staining of chromosomes led to the mapping of genes on their chromosomes during the 1970s, and cloning of human genes began in the 1980s. In this decade, new molecular technologies have elucidated the actual structure of many disease-causing genes and, with that knowledge, the ability to test patients for these genetic disorders has increased markedly.

New mechanisms for genetic disorders that do not follow Mendel's rules have recently been identified; for example, trinucleotide expansion syndromes (from repetitive stretches of DNA triplets) that cause Fragile X Syndrome,

Abbreviations Used:

CF	cystic fibrosis
ELSI	Ethical Legal and Social Implications
FISH	fluorescent in situ hybridization
PCR	polymerase chain reaction
PKU	phenylketonuria

Huntington's disease, and several other CNS disorders. Microdeletions (tiny missing pieces of chromosomes detectable with fluorescent techniques) can lead to Prader-Willi Syndrome and interestingly can cause altogether different syndromes, depending on whether the microdeletion has been inherited from the father or the mother (referred to as genetic imprinting).

The Human Genome Project, a coordinated international initiative, will produce detailed maps of each human chromosome and determine the base sequence of all approximately 100,000 human genes. Molecular geneticists are discovering new techniques as part of this endeavor, and the Project is running ahead of schedule. One arm of the Project focuses on the Ethical, Legal and Social Implications (ELSI). Interestingly, Frances Alexakos surveyed Rhode Island primary care physicians, asking their attitudes on ordering genetic testing for breast cancer. Those results, abstracted in this issue, indicate strong interest in testing as well as concerns about informed consent, emotional stress and medical-legal considerations. Public education is also a priority of the Genome Project. The above endeavors should allow individuals to make informed decisions on their health and reproduction. Results are also expected to enhance the practice of medicine in general, and more specifically, the development of gene therapy in the future.

GENETICS IN SUBSPECIALTIES

Clinical geneticists care for patients with various types of birth defects and genetic disorders. Most activity currently takes place in academic departments of pediatrics and obstetrics. However, genetic knowledge has begun to dif-