THE CIRCLE OF WILLIS

For generations every medical student has been familiar with the eponym "Circle of Willis," the anastomatic connection of arteries at the base of the brain which Dr. Thomas Willis described in detail during the 17th century. But who was Willis?

Thomas Willis (1621-1675) lived in Oxford for much of his life except during its last decade that he spent in London. His reputation was based on much more than that singular vascular formation. At Oxford where he was professor of natural philosophy, he was the leader of the English iatrochemists who attempted to explain the workings of the body from current knowledge of chemical interactions. Dr. Willis established a nomenclature for cranial nerves that was the basis for modern terminology and the word "neurologie" can be attributed to him. He speculated upon the causes of sleep, insomnia, hysteria and mental retardation and observed that the medulla oblongata regulates the functions of heart, lungs and intestines and was the first to propose that higher cognitive function comes from the cerebral cortex. Willis also introduced a new etiology of hysteria, no longer attached to the central role of the uterus, but rather related to the brain and to the nervous system. However, he mistakenly believed that intercostal nerves, "the reins of the soul," by connecting the brain to the heart and lower viscera mediate bodily passions and potentiate moral virtue. Dr. Willis wrote a treatise on what he called "the pissing evil of Diabetes" and was the first to use the word "mellitus" to describe the sweet taste of diabetic urine. Also, he gave clear descriptions of myasthenia gravis, typhoid, scarlet fever, malarial and puerperal fevers Indeed, historians have described Thomas Willis as "the father of neuroanatomy" and "the father of comparative anatomy."

The mid-17th century was a time marked by scientific progress and although Dr. Willis was influenced by the emerging field of iatrochemistry, he retained deep religious beliefs and loyalty to the Crown during an era of political ferment. This was reflected by his choice to compose his medical writing in Latin, the language of scholars, religious authority and political power. Willis was described as "a plain Man, a Man of no Carriage, little discourse, Complaisance or Society...none scarce hath equal'ed, much less out-done him, how great soever." In addition to his research, Dr. Willis was a successful clinician and opened a London practice in 1666 that became the most fashionable and profitable of the period. His patients included members of wealthy elites for whom he charged the highest sums; the poor he treated for free. In his medical practice Willis combined some of the new chemical ideas with traditional Galenic principles that was informed by his own anatomic studies.

During "The Great London Plague" of 1665, Thomas Willis stayed safely out of the capital at a spa in The Midlands that was favored by the Royal family. He took advantage of the time away to write a book about proper treatment of the pestilence. In 2011 I was fortunate to discover a copy at a used book fair, bought it for a pittance, and was eager to learn what the famous doctor had to say. After all, surely no one was better qualified than Thomas Willis to comment upon the management of epidemic plague, even if he stayed out of town during the worst of it. It turned out that the book that I purchased was an English translation first published in 1692, six years after Willis's death, by a "Mr. Flemings" who identified himself as former "Amanuensis and Apothecary to the Doctor." An amanuensis is a kind of secretary who writes down what another person says and this book was based on Willis's writings in Latin as well as from lecture notes. Its full title was *The London Practice of Physick, being the Practical Part of Physick Contained in the Works of the Famous Dr. Willis; Wherein are His Definitions, Descriptions, and Methods of Curing Diseases To which is now added his plain and easie Method for the Preventing and Curing of Plague.*

In the preface Mr. Flemings acknowledged that in his dual role as translator and editor, he'd taken liberties both with content and sequence, adding that "those who understand the Latine Tongue will certainly be better pleas'd to read the Theory at large in the Original, than in the English." He explained his intent as merely to provide a synopsis of the great physician's teachings of "practical" matters, "the larg Theory being omitted." What I didn't initially realize was that in this 1692 edition Flemings had appended previously unpublished comments about plague that had been made by Willis in 1666, the year after the cataclysm, and then added these to the Latin translations that were published in 1685. It seems that after the Great Plague, Willis had composed a brief guide for general consumption which, unlike his other books, was written in plain English. In fact, these plague notes weren't published until 1690, fifteen years after Dr. Willis' death, and then by "F. Hemming" — not by "Mr. Flemings."

In an explanatory note Hemming/Flemings referred to Dr. Willis as "my dear *Master* and best *Friend*" and explained that a former acquaintance had asked his advice about treating plague for a friend who was traveling to Constantinople where the disease was prevalent and at the same time, there was concern that plague might be breaking out among "their Majesties Army in Ireland." Then the apothecary-secretary-translator-editor-friend recalled "this short tract, which I transcribed from the Doctor's Papers in the Year 1666, being then his Amanuensis; I knew it would far exceed whatsoever I could elsewhere obtain, or pretend to collect upon this Subject." Hemming said that he'd previously resisted suggestions to posthumously publish these plague notes because the

master had never completed them, but now he was persuaded by others who'd seen the manuscript to publish lest "that disease [in Ireland] prove Pestilential" and also as "a charitable instruction in cases of great danger, for such as cannot procure the attendance of Physicians."

What follows here are several selections in Dr. Willis's own words that although written about one year after London's Great Plague, were not published until 1690:

Title: A Plain and Easie Method for Preserving [by God's Blessing] Those That Are Well from the Infection of the Plague and For Curing such as are Infected.

In time of Pestilence, because a Physician cannot easily, or often, be consulted with; Therefore it behoveth all Persons, as well Poor as Rich, to be furnished with Remedies against that Contagious Disease; and certain Rules, or a Method how to use them: Which Method being very plain, and almost the same to all People, consists chiefly in these two Parts, viz. How to Preserve the Whole from taking Infection; and how to cure the Sick that are infected....

Touching the First; though the surest way is to fly from it, yet in regard this cannot be done by all, some Means should be us'd to secure (so far as it is possible) those that are forced to stay by it.....[Every man] may arm himself against the danger of Contagion; Which should be endeavor'd, as well by purifying the Air we breathe, as also by fortifying our selves against taking the Infection at our Nostrils, Mouth or Pores of the Body, which are the chiefest, if not the only parts the Poison creeps in That the Air we breathe in may be wholesome, all Things, that may advance or add to the corruption of it, should be diligently removed; our Houses, and Streets kept clean; all Filth and whatever may cause noisome smells, be taken away; and amongst other things, the smell of Sope-Suds, and Lye, in the washing of Clothes, be avoided....

Next to the cure of the Air...we must arm ourselves against taking in that Malignity which still remain mixt with it. Now because the Spirits are commonly the first that receive the Infection, We must fortify them, that they may not easily admit the approaches of their Enemy, which when they are in full vigor...as it were keep off at a distance. Therefore, Wine and Confidence are a good Preservative against the Plague; But when the Spirits, through fear, or want of supply, do recede and are forc'd to give back, the Enemy enters and first seizeth them and thence gets into the Blood and Humors; Therefore much fasting and emptiness are bad: But every one

should Eat and Drink at convenient Hours, in such manner and measure, as may always keep the Spirits lively and cheerful, and endeavor to compose his Mind and Affection against fears and sadness.

Also for those that live in an infected Air, that there is a suspicion that they may daily take in some pestiferous Vapours, which fermenting with the Blood and Humours, may insensibly at last break out in the Plague; it may not be amiss, once or twice a week, to take a pretty large Sweats in their Beds; And this to be done, especially if the Party has any occasion whereby he may suspect himself to have been more open to infection, or that he has taken any: After such Sweat he should keep his Chamber the forepart of the day, till the Pores are reduced to be as they were before...

Taking of Tobacco in a Pipe; the Smoke of this secures those parts which lye openest, and at once intercepts the Contagion from the Brain, Lungs and Stomach; Nay more than this, it stirs the Blood and Spirits all the Bodyover, and makes them shake off any poisonous Matter that adher'd to them...In the last great Plague, no Tobacco Shop was infected: If 'tis not of so great virtue still amongst us, the reason is, because most Men have been accustomed to take it excessively; wherefore, it is grown so familiar to them that it produceth no alteration when it should be used as an Antidote...Besides the frequent use of Tobacco, which doubtless in time of Plague may be profitable for them that can take it; others, and also Tobacconists, at sometimes should be furnished with something to smell to when they pass through infected Places. Wormwood and Rue, Galbanum, Castor and Vinegar are good....

Concerning Rules of Diet, I need not say much, because such Precepts are commonly known: 'Tis to be observ'd in general, that only wholesome Food should be taken: Very salt Meats, as hang'd Beef, Bacon, Pork, salt Fish, also shell-Fish, most kind of Herbage and raw Fruit should be avoided. The Meals should be moderate, and eaten in due season....These kind of Remedies, and manner of living, ought chiefly to be insisted on as Preservatives against the Plague. Those that are timorous and of tender Constitutions require a support from the use of more means, whereas Persons that are strong, and of a bold temper, have need of the less Remedies. But 'tis not safe for any to be so confident as to dare to converse with infected People, or live in the midst of Contagion without any Antidote at all...

In the use of means, caution is to be had, that strong and hot Cordials be not too often taken, not yet indifferently by all People; for that will inflame the Blood, and make it apt to kindle a Fever, which at such times soon turns to the Plague. The like caution is to be had against immoderate drinking of Wine; though moderate proportion chears and fortifies the Spirits, yet too much greatly disorders them and thereby People are more expos'd to take Infection.

Letting of Blood in time of Plague has been observ'd to be very pernicious; so also oft or strong Purging; or the Veins being emptied either way, will readily suck in whatever poisonous Atoms lurk in the outward Pores of the Body, which being admitted become the more prevalent, because the Spirits being depauperated, are less able to subdue or repel them.

Although having been published five years after the Great Plague, Thomas Willis's abbreviated manual on plague was intended for popular consumption. Flemings/ Hemming, writing two years later, added his own more expansive recording of his master's words about plague in a second edition of *The London Practice of Physick* (the first was published in 1685.) This book was intended to be a practical guide for physicians and, although devoid of theory, it had a different tone and emphasis than Willis's earlier manual. According to his "amanuensis," Dr. Willis observed that it wasn't easy to make accurate examinations of plague victims, "for these kinds of sickness do not happen every year, nor when they are rife, is it free for every Physician, who minds his own Health, to visit the Sick with a curious Eye, or to stay long with them, that he may diligently observe every Accident and carefully weigh the Reason of them."

Dr. Willis concluded his chapter on plague by citing the unfortunate example of Henry Sayer, "a Physician very learned and fortunate in Practice," who during a milder epidemic in 1645 "boldly went to visit all sorts of Sick Persons, both poor and rich, any others refusing this Undertaking":

He daily gave them Medicines, touching Buboes and virulent Ulcers with his own Hand; and so by a diligent, tho dangerous means, cured many of the Diseased. To fortifie himself against the Contagion, before he went to infected Houses, he was want to drink a good Draught of Generous Wine, and after he had gone his Circuit, to repeat the same Antidote. After that he had taken Care a long time of the Sick in this City, without receiving any Injury, as tho he were Plague free; he was sent to Wallingford Castle, where this Contagion violently raged....and there, in a short space, having dared to lye in the same Bed with a

certain Officer felled with the Plague, whose Society he very much delighted in, he took the Infection of the same disease. Nor could then those Arts prove of use to their Master, which had been beneficial to all others {and} did he perish of that Disease.

Amulets were among various prophylactics favored by Dr. Willis which when "hung about the Neck, or worn about the Arm-Wrists, are thought to have a wonderful Force against the Pestilence." He suggested that "atomical" bodies emerging from the amulets had the same shape as pestilential particles, "by reason of a Similitude of Partsdrawing the same from our Body to their Embraces, they to some free the Infected from the Mailignity." Dr. Willis advised using amulets made from arsenic, quicksilver, powdered toad and other "venomous Things." Indeed, toads had a special place in the 17th century pharmacopoeia and their tuberous and swollen skin seemed to correspond to the lesions and carbuncles of plague victims. Indeed, the miraculous appearance of large numbers of toads, alleged to have been seen immediately before the outbreak of a plague epidemic, was thought to have been a sign of the toad's special affinity for pestilence.

The disappearance of toad amulets and other strange remedies for preventing or treating plague owed more to the disappearance of epidemic plague itself during the late 17th century than to scientific efficacy. In our own time, plague is considered to be a rare disease of rats and bats which when transmitted to man is easily treated with broad spectrum antibiotics. Although sporadic cases continue to be reported in the United States, I'm not aware that powdered toad has come back into fashion. Nevertheless, concerning COVID-19, I suspect that a former resident of the White House might have found it to be an "interesting" remedy.