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THE CIRCLE OF WILLIS*

BY

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My first task is to thank you, Mr. President, Fellows and Members of the College, for appointing me to make this Oration according to Harvey's instructions, wherein he designed the pattern for a tradition now almost three centuries old. Whoever is charged with the duty must feel at this moment proud of the honour and humbled by the greatness of the occasion.

Of the directions given to the Orator two are simple —to commemorate the benefactors of the College, and to bid you continue in mutual love and affection among yourselves. The other is the exhortation to the Fellows and Members to search and study out the secrets of Nature by way of experiment. In this connexion we must remember that Harvey was what to-day would be called a physiologist. It is true that he practised medicine, but not very much, nor, according to one of his biographers, very well (Anon., 1830). His great discoveries, including that of the circulation of the blood, were based mainly on observations upon animals. It was natural, therefore, that he should direct the Orator to appeal for recruits to this branch of learning, and that the appeal should be addressed to the Fellows and Members of the College, for it was only physicians who were then qualified for this work. Since then the scene has changed. There is specialization of function such as Harvey could not imagine. The physiologist and physician are different persons.

The Urge to Discover

Moreover, the science of medicine, which had hardly begun in Harvey's day, now has values of its own which he would doubtless have found satisfying. He would not, I am sure, have wished you all to turn physiologists. He would none the less have urged you to prosecute research. This, I believe, is what most of us want to do when we enter the practice of consulting medicine, and for many of us the urge to discover something new is one of the motives that directs our choice of career. We start with enthusiasm, but the later results are on the whole disappointing. For this there are many reasons, of which the first and most obvious is that to want to do a thing well is not the same thing as having an aptitude for it, but I do not think this is so widely applicable as is sometimes supposed. Another reason often given is that research in medicine is a full-time employment, with the implication that a man must choose between research and practice. This idea has been fostered by the growth of units whose senior members give the whole of their time to clinical research and are not engaged in the ordinary practice of medicine.

It is true that the whole-time clinical research worker has great advantages, from which he has not been slow to profit. Witness the volume and quality of the work published from these units during the past thirty years. The practising physician also has some advantages, which are not so apparent and deserve mention. One lies in what I may call the range and intensity of his exposure to stimulus. He goes to his out-patient clinic, his wards, or his consulting-room not knowing in the morning what the day will bring to him of the phenomena of disease. No sooner has he focused his attention on one problem than it is switched to another. At the end of the day his mind carries a load of unanswered questions. This you may say is distracting and an impediment to thought, but the variety of experience has a value.

There is much darkness in the world of medicine, and light may come from an unexpected quarter, so that the man who is compelled to shift his gaze from one point of the compass to another may be better off than he who is always looking in one direction. It may happen to those wholly engaged in clinical research that they miss the opportunity of seeing in matters outside their scope something of fundamental importance to their inquiries, while to the practitioner chance may offer a new concept of disease from the observation in the same week of two cases which are clearly alike but like nothing else that has ever been seen. For the practising physician also the unanswered questions are perhaps more often invested with a sense of urgency than is the case with his whole-time research colleagues. The practitioner cannot thrust problems aside merely because they are insoluble. He cannot discard speculation because it is not susceptible to experiment. Every case he sees of motor neurone disease or disseminated sclerosis must become for the moment a personal issue wherein he has to acknowledge defeat. He is very often made to feel very uncomfortable.

Practitioners' Handicaps

In so far, then, as the impetus to research may be derived from external stimuli, the practising physician has no handicap, but he has others. First, he lacks time for quiet thought. This was what Sir Thomas Browne (1646) felt when he wrote that his work had been composed by snatches of time from his practice, envying those whose "quiet doors and unmolested hours afford no such distractions." The right man, you

*The Harveian Oration delivered at the Royal College of Physicians of London on October 18, 1954.

may say, will make time, but in the press of sessions, practice, and committees this is difficult, and is made no easier by the social conditions of our present days. I believe it right that time should be given to the consulting physician for thought, and that under present conditions it should be given by the State in the sense that some of the time he spends at his hospitals should be allowed for study and research. Provision for this has been made under the National Health Service, and it is to be hoped that the boards and committees of hospitals will make full use of their opportunity in this direction. Looking back myself, I can see how much I might have gained from an hour or two spent each week at hospital making notes of particular cases, for my own use. There is need also for a place for study, and I hope that in the building plans of our new hospitals rooms will be provided adjacent to the wards for the use of the physicians.

The second handicap carried by the practising physician is lack of training in methods of laboratory investigation. Time was when no more was necessary for research than the use of the five senses. Thomas Willis discovered diabetes mellitus from the observation that among those who had frequency of micturition, or what was then called the "Pissing Evil," there was a group who wasted and died, and that in them all the urine was wonderfully sweet to the taste. Discoveries of fundamental importance may still be made without recourse to the laboratory. In our own time one of the most remarkable has been the proof that what we knew as sciatica is almost invariably caused by intervertebral disk disease. It is, however, generally true that a man who would do research in these days must augment the scope of his senses by using an ever-increasing number of technical devices, the mastery of which itself consumes the months. There is no adequate provision for such training in our plan for the education of the consulting physician, but it would surely not be impossible to include a year for the senior registrar in a laboratory where he could learn the rudiments of at least one technical method of investigation, and if such experience came to be generally regarded as of advantage to the candidate for staff appointment the best men would naturally be attracted.

On the other side I would suggest that some at least of the senior appointments in full-time clinical research should be given to men who have been engaged in consulting practice. If a man had before going into practice worked long enough in a laboratory to have learned its methods he would return to it with a mind enlarged and refreshed and, what is perhaps more to the point, with enough unanswered questions to keep him busy for a long time. I believe that among those engaged in consulting practice there would be some who at the end of five years would turn with enthusiasm to whole-time research employment. Some interchange of the kind suggested seems needed to bridge the gap between practitioner and clinical research worker which now exists, to the detriment, I believe, of both parties.

Thomas Willis

Thomas Willis, born forty-three years after Harvey, was a physician who managed to combine research with a busy private practice. Willis was elected a Fellow of the College in 1664 at the age of 43. He had had an unusual career. Born at Great Bedwyn, Wiltshire, he became at the age of 15 batler to a Canon of Christ Church, Oxford, and subsequently took his B.A. On the death of his father and at the outbreak of the Civil War he went to his home at North Hinksey, but we are told by his brother-in-law, John Fell (Willis, 1684b) that, being "harased by the incursions of the Rebels, who were possessed of a Garrison strong enough Five miles from thence, and every where Plundering, he betook himself again to Oxford, being the Tents of the King as well as the Muses; where listing himself a souldier in the University Legions, he received Pay for some years, until the Cause of the Best Prince being overcome, Cromwell's tyranny afforded to this wretched nation a peace more cruel than any war." Soon after the end of the war Willis took his Bachelor of Medicine degree, and we are informed by his contemporary, Anthony Wood (1813–20), that he then "fell to the practice of it and every Monday kept Abingdon market." Thenceforward he became a busy practitioner and remained so until the end of his life, though for six years he combined with this the office of Sedleian Professor of Natural Philosophy at Oxford before moving to London in 1666. And there, Wood tells us, "in very short time after he became so noted, and so infinitely resorted to, for his practice, that never any physician before went beyond him or got more money yearly than he." He died of pneumonia in his house in St. Martin's Lane in November, 1675, and was buried in Westminster Abbey.

During the early years of his practice in Oxford Willis was one of a dozen learned men, four of them physicians, who met regularly for discussion. This was an offshoot of the invisible college, a name given by Robert Boyle to a group who before the war used to meet weekly for philosophic discourse at a London tavern. When the war broke out they split, those remaining in London meeting as before, and those at Oxford in rooms at Wadham. Some time before 1659 the meetings ceased in Oxford and were continued in London, and out of this association was born the Royal Society, of which Willis was one of the original Fellows.

Interesting Conclusions

Willis is, of course, best known for his studies of cerebral anatomy, but, besides being the first person to recognize diabetes mellitus, he was led by his reasoning from clinical observation to certain other interesting conclusions. He was, I believe, the first to envisage a hormone, arguing that "about the time of ripe age as the blood pours forth something through the Spermatic Arteries to the Genitals so also it receives a certain ferment from those parts through the veins: to wit, certain particles imbued with a seminal tincture are carried back into the blood which make it vigorous and inspire into it a new and lively virtue. Wherefore at that time . . . hairs break out, the voice becomes greater, the courses of women flow," and so on. He wrote much on epilepsy and introduced the idea of an explosion in the brain as the cause of seizures, using the analogy of gunpowder. He opposed the current view that the origin of what we call focal seizures lay in the part in which the spasm or sensation appeared, and declared his opinion that the primary cause was always in the brain, "to wit that the spirits inhabiting it being disposed to explosions, and there being exploded, bring on or cause every Falling Evil"; though he thought a peripheral stimulus might excite the explosion.

He wrote well of migraine and gives us an excellent description of this malady in the case of Lady Conway, whose letters (Nicolson, 1930) leave no doubt that she found in him a better doctor than Harvey, who had previously attended her.

In his dissertation "Of the Palsie" he describes clearly the disease we now know as myasthenia gravis, observing it to be distinct from all other kinds of paralysis on account of the variability of its occurrence and the effects of fatigue. Patients with this affliction, he says, may appear well in the morning, "able to walk firmly, to fling about their arms hither and thither, or to take up any heavy thing; before noon . . . they are scarce able to move Hand or Foot." And he goes on to quote the case of a patient under his care, "a prudent and honest woman, who for many years

hath been afflicted by this sort of spurious palsy, not only in her members but in her tongue : she for some time can speak freely and readily enough, but after she hath spoken long, or hastily or eagerly, she is not able to speak a word but becomes mute as a Fish, nor can she recover the use of her voice under an hour or two."

Of his methods he wrote thus : " After I had not found in Books what might satisfy a mind desirous of Truth, I resolved with myself to reach into living and breathing examples: and therefore sitting oftentimes by the Sick, I was wont carefully to search out their cases, to weigh all the symptoms, and to put them, with exact Diaries of the Diseases, into writing ; then diligently to meditate on these ; and then began to adapt general Notions from particular events. . . ." He was first and foremost a clinician, but he was also a fine anatomist, who made great and lasting contributions to the advance of knowledge, especially of the structure of the brain and lungs, their value being enhanced by the beautiful drawings of Christopher Wren.

Association with Lower

In his work on the brain Willis was ably assisted by Richard Lower, who was later to earn fame for his work on the heart and the first blood transfusion. Lower was a younger man than Willis, and afterwards succeeded him in his practice. Wood, in his biographical sketches of the two men, suggests that Lower received too little credit for his contributions to the success of his senior. Willis, for example, was credited with the discovery of a spa, doubtless to the benefit of his practice. But Wood (1813–20) writes that in April, 1664, Lower in his travels with Dr. Willis " made a discovery of the medicinal water at East Throp . . . in Northamptonshire, the doctor being then, as usually, asleep or in a sleepy condition on horseback." Afterwards he says Lower imparted his discovery to the doctor, who claimed it for his own. Whatever may be the truth about East Throp, Willis (Franklin, 1931), in his introduction to *Cerebri Anatome,* pays handsome tribute to Lower, " a doctor," he says, " of outstanding learning and an anatomist of supreme skill. The sharpness of his scalpel and of his intellect, I readily acknowledge, enabled me to investigate better both the structure and the function of bodies, whose secrets were previously concealed." And later he writes: " When we were entering upon a much more difficult task, the dissection of the nerves, the really wonderful dexterity of this worker and his untiring perseverance were conspicuous in the extreme and no obstacle could withstand his effort."

Wood, however, could not let this pass, and, writing of Lower, tells us that after taking his degree at Christ Church he " entered upon the physic line, and practised that faculty under Dr. Tho. Willis, whom he helped, or rather instructed. in some parts of anatomy, especially when he was meditating his book *Cerebri Anatome,*" and in his list of Willis's published works (Wood, 1813–20) adds under *Cerebri Anatome* this sentence, " Whatsoever is anatomical in that book, the glory thereof belongs to the said R. Lower, whose indefatigable industry at Oxon produced that elaborate piece." Lower himself does not appear ever to have complained that he was not given his due, and his first published work was a spirited defence of Willis's treatise on fevers against the critics, which, as Fulton (1935) has observed, is testimony of the harmonious relations between the two men. Why, then, did Wood write as he did ?

Biased Opinions

Anthony Wood, who would have liked to earn fame as a historian, lived in Oxford from 1632 to 1695. His most notable work was the publication, under the title *Athenae Oxonienses* (Wood, 1813–20), of short biographies of distinguished Oxford graduates up to his time. In these his love for gossip so far outran his discretion that a copy of the second volume of the *Athenae* was burned in public by order of the Vice-Chancellor, and the author was expelled from the University. The book, however, was well received in Cambridge. Wood also kept voluminous diaries (Wood, 1891–1900), which give an entertaining account of his life and times and reveal him as a prejudiced and quarrelsome man. John Fell, the great Dean of Christ Church and later Vice-Chancellor and Bishop of Oxford, who has already been mentioned as the brother-in-law of Willis, was at the same time Wood's benefactor and one of the targets for his abuse. Fell paid for the printing of some of his books, and claimed the right to edit them. Wood could not accept criticism, grumbled, and quarrelled with him.

Richard Lower appears from the diaries to have been one of Wood's intimate friends. During the years 1658 to 1662 Lower's name appears frequently as a companion in the taverns of Oxford. The entries begin with the mention of Mr. Lower, who later becomes Mr. Richard Lower until July 28, 1660, when the entry reads " Spent on Dick Lower at the Mermaid Tavern one shilling." Of Thomas Willis there is no mention in the diaries until 1664, when there is a note of the discovery—by Lower—of the healing well at East Throp. The omission is curious, for Willis was not a negligible person, and it is hardly to be supposed that in a city the size of Oxford the two men never met. That they must in fact have been known to one another is proved by a passage in a letter written in 1725 by Browne Willis, Thomas's grandson, to Bishop Kennett, and preserved in the Bishop's copy of the *Athenae.*

Browne Willis was a scholar and antiquarian of repute, and the purpose of his letter was to refute the statement made by Wood in the *Athenae* that Thomas Willis's grandfather was a tailor. This letter begins, " I most readily obey your lordshipp's commands in communicating something of my good grandfather Dr. Willis. A. Wood, who was his next neighbour in St. John Baptist's parish Oxon, and had a disagreement with the family, says several things untrue of his descent." From these observations it seems likely that Wood had a prejudice against Willis and a favourable inclination towards Lower, and it is certain that as a historian he would have been influenced by whatever prejudices he may have had.

There is, moreover, evidence that Wood's account of the relative contributions of Willis and Lower to *Cerebri Anatome* was derived from a source already biased. Henry Stubbe, philosopher and physician, published (Stubbe, 1670) a series of papers the sole object of which was to discredit the Fellows of the Royal Society (whom he called contemptuously the Virtuosi), and he attacked Willis among others. He alleges that Willis could not have spared the time from his great practice to compose *Cerebri Anatome,* and writes, " Whatsoever there is in that Piece, which is Anatomical, the glory thereof belongs to Dr. Lower, whose indefatigable industry produced that elaborate Treatise " (p. 95). We know from Wood's diary that he had purchased Stubbe's book, and his comment in the *Athenae,* published many years later, is an almost exact transcription of the sentence I have just quoted ; but what he ignored, or perhaps had never read, was a postscript. This is to be found out of its context at the end of Stubbe's little volume. It begins " I think myself obliged to adde one thing more where I speak as if Dr. Willis had had little to do in the discoveries of Dr. Lower about anatomy," and goes on to say that, although Lower did the dissections, Willis's was the master mind which inspired and directed the work. The last sentence of this recantation is revealing: " Thus much I thought fitting to annex, lest the Virtuosi should censure me as partial to my old School-fellow, Dr. Lower, or swayed by any regard then that of Truth " (p. 178).

It is due to Willis that this story should be told in full, for some of those who have written about him have followed Wood, including Michael Foster (1901), who tells us that Lower was " the henchman of the fashionable Willis whose false fame in large measure rested on Lower's careful, unacknowledged. work." In this I scent something of the odour in which the physiologist held the successful practitioner 50 years ago.

Willis's "Cerebri Anatome"

Cerebri Anatome was published in 1664 and is chiefly distinguished for the description of the cranial nerves, but better known for the dissertation upon the arteries at the base of the brain. Wren's drawing shows the anterior cerebral arteries joining where the anterior communicating artery should be and bifurcating a little further forward, but, apart from this, there is no fault. Willis, however, saw that there was a circle and that it must have some physiological significance. In discussing this he first suggests that the function of the circle is to mix the blood before its distribution to the brain, but on a later page adds:

"But there is another reason far greater than this of these manifold ingraftings of the Vessels, to wit, that there may be a manifold way, and that more certain, for the blood about to go into divers Regions of the Brain, laid open for each; so that if by chance one or two should be stopt, there might easily be found another passage instead of them: as for example, if the Caroüd of one side should be obstructed, then the Vessels of the other side might provide for either Province. . . . Further, if both the Carotids should be stopt, the offices of each might be supplied through the Vertebrals" (Willis, 1684a).

He goes on to say:

"It is not long since we dissected the dead body of a certain man, whom a great Scirrhus or hard Swelling within the Mesentery, growing at last ulcerous, had killed. When his Skull was opened, we beheld those things belonging to the Head, and found the right Carotid, rising within the Skull plainly bony or rather stony, its cavity being almost wholly shut up; so that the influx of the blood being denied by this passage, it seemed wonderful, wherefore this sick person had not dyed before of an Apoplexy: which indeed he was so far from, that he enjoyed to the last moment of his life, the free exercise of his mind and animal function . . . This Gentleman, about the beginning of his sickness, was tormented with a cruel pain of the Head towards the left side. The cause whereof I know not how better to explain, than that the blood excluded from the right Carotid Artery, when at first it rushed more impetuously in the left, had distended the Membrane" (Willis, 1684a).

Dissertations on the Circle

It is perhaps remarkable that Willis nearly three hundred years ago asked himself why this man did not have a hemiplegia, and perceived from his dissections of the circle that anatomy might supply the answer, but it is even more to his credit that he should have remembered the episode of headache and found what was probably the correct explanation for it. Willis was an indefatigable student of symptoms. This is apparent in the case histories illustrating his clinical writings, and when he was at his dissections he was ever thinking not only of the function of the structures he laid bare but of the disorder of function that might result from their disease. This, you may say, is the way any liberal-minded anatomist thinks, but Willis was a busy practitioner, able to draw upon his own experience of symptoms unexplained. We may be sure that he would have been interested in what we now think about the functions of his circle, and the symptoms that occur when one of the internal carotid arteries is occluded. His observation that this may happen without hemiplegia has, of course, been amply confirmed, and also the appearance of headache as a symptom of the event. That it may be the only symptom we know from an example in which headache in a young woman without other symptoms was investigated by arteriography and internal carotid occlusion demonstrated; and in patients with hemiplegia headache as a preliminary symptom is not uncommon. The explanation we believe to be correct is that which occurred to Willis—distension of other vessels—for we know that when the wall of an artery of the head is stretched beyond physiological limits headache results.

Recent Experimental Work

As to what happens in the circle after occlusion we can only speculate, but our speculations may be guided by methods of observation and experimental records which were not available to Willis. The experiments in which he would have delighted most are those in which a dye or other visible substance is injected into one of the afferent arteries of the circle, for such experiments he performed himself in the cadaver. Cerebral arteriography has now enabled us to see in man the course of radio-opaque solutions injected into the internal carotid and vertebral arteries, both in the normal state of the circulation and when one or both internal carotids are occluded. What we see in the arteriograms cannot be an accurate picture, for the opaque solution is injected under pressure, but arteriography has taught us a great deal. Provided that the anterior communicating artery is of fair calibre, fluid injected into one internal carotid artery, when the other is occluded by digital compression, flows into both hemispheres, and if there is bilateral carotid occlusion proximal to the circle a vertebral injection enters the branches of the internal carotid arteries by way of the posterior communicating branches, as Willis imagined.

A way of learning what happens in the normal circle is to watch the flow of injected dye in a living animal, the brain being exposed by operation. This had been done before, but not with the essential precaution of introducing the solution of dye into a vertebral or carotid artery without disturbing the normal pressure. McDonald and Potter (1951), observing this precaution, have shown that the dye entering a vertebral artery flows into the basilar and posterior cerebral arteries and forward into each posterior communicating artery up to a point about midway along its length. Conversely, dye injected into a carotid artery passes into the anterior and middle cerebral arteries of that side and the anterior cerebral artery, and backwards into the posterior communicating artery up to a point halfway along its length. At this point injection into either the vertebral or the carotid artery results in an interface of blood and dye, a dead point, at which the pressure of the two opposing streams is balanced. There is in fact no flow of blood through the posterior communicating arteries at all.

In the rabbit, which was used for these experiments, there is a single anterior cerebral artery and therefore no anterior communicating artery, but, having regard to the observation that in man a radio-opaque solution injected into one internal carotid ordinarily fills only the anterior cerebral of the same side, it is probable that in the normal circle of Willis there is another dead point at the mid-point of the anterior communicating artery. Thus there are virtually three separate streams of arterial blood supplying the brain, one from the basilar and one from each internal carotid artery, separated from one another not by any physical barrier, but by the dead points in the posterior and anterior communicating arteries, the position of each of these dead points depending upon the balance of pressure in the opposing streams.

Internal Carotid Occlusion

The most frequent cause of internal carotid occlusion is atherosclerosis, and the site is usually in the neck within a centimetre of the origin of the artery. Before the advent of total obstruction there must be a gradual narrowing of the lumen, which favours the establishment of collateral circulation. We may compare this with what happens when there is atherosclerosis of a coronary artery, for in the heart as in the brain occlusion may occur without infarction if the process of narrowing is slow and there is time for a good collateral circulation to develop. In the brain there is opportunity for widening of anastomotic channels between the superficial branches of the posterior and middle cerebral arteries, and, as we know from arteriography, the communication in the orbit between branches of the external carotid and the ophthalmic branch of the internal carotid can short-circuit the obstruction in the neck. The direction of flow in the ophthalmic artery being then reversed, it receives blood from the external carotid which, entering the lumen of the internal carotid above the obstruction, fills the middle cerebral artery. But the circle of Willis must

provide the most important source of compensatory flow. When pressure falls on the obstructed side there must be a shift of the dead point in the anterior communicating artery and a flow of blood from the unobstructed side to fill the anterior and probably the middle cerebral arteries on the obstructed side. Both hemispheres must then obtain their main blood supply from the unobstructed internal carotid, which, being in a part of its course enclosed within a bony canal, cannot be capable of any great dilatation, though even a small increase in its diameter would be an important contribution, since the volume of fluid passing through a tube varies with the fourth power of its radius. It is probable that under these conditions the maintenance of cerebral blood flow in patients who do not develop hemiplegia as an immediate effect of carotid occlusion depends mainly upon a rise of mean arterial blood pressure, for this has been observed as an effect of carotid ligation.

The equitable distribution of blood to the two hemispheres after occlusion of one internal carotid artery requires an anterior communicating artery of adequate diameter, but it seems probable that alterations of calibre in the peripheral vessels of the two hemispheres must play a part. The local effect of cerebral ischaemia is vasodilatation from the accumulation of CO_2. The hemisphere on the obstructed side, therefore, at any rate for a time, may claim more than an equal share of blood with a corresponding vasoconstriction in the hemisphere on the unobstructed side. This surmise finds support in the observation immediately after common carotid ligation of abnormal waves in the electroencephalogram in both hemispheres and occasionally only in that supplied by the unobstructed artery (P. Schurr, personal communication). If after internal carotid occlusion by disease, the total cerebral blood flow is at times less than normal and the hemisphere on the obstructed side simultaneously demands more than its fair share, this might explain the occurrence of transient loss of function in the limbs on the ipsilateral or obstructed side of the body in certain cases.

Compensatory Mechanisms

When cerebral function remains intact after internal carotid occlusion we may assume that the various compensatory mechanisms have come into action, but the situation must still be precarious. The haemodynamic crisis that has occurred is not a transient affair. There is a perpetual struggle both for the maintenance of the total cerebral blood flow and for its equitable distribution; and loss of blood volume, a fall of blood pressure, or a temporary upset of the balance between vasoconstriction and vasodilatation may cause local ischaemia or infarction with reversible or irreversible loss of function. An irreversible hemiplegia is the commonest ending, and is indeed often the first event, but it is the preliminary symptoms occurring in certain cases which invite explanation. Headache, as Willis first observed, may be one. Hemiplegia may be preceded by episodes of weakness or numbness over a period which may extend from a few hours to several years. The loss of function in these episodes may be severe, with rapid and complete recovery, and this may recur so often that occlusion of peripheral branches, by extension of clot from the site of the original obstruction, or by detached emboli, can hardly explain them. I suggest that this episodic loss of function, which must be ischaemic, is not due to any fresh vascular obstruction, but to a temporary failure of the compensatory mechanisms.

I shall venture, following the example of Willis, to relate some particulars of a patient in whom the brain was finally inspected.

This patient was a woman aged 53, known to have had mitral stenosis with auricular fibrillation for several years. The first symptom of cerebral disorder was headache, which had begun to trouble her three years previously. Its first onset was sudden, and thereafter it occurred almost daily for several hours and continued thus for six months, after which it became much less frequent and severe. Eighteen months before I saw her she had transient loss of vision in the right eye, shortly followed by numbness and weakness of the right limbs with recovery in 24 hours. A month later there was another episode of transient right hemiparesis. A few days after she had recovered from this she had a left hemiparesis, from which recovery was complete in 48 hours. From this time onwards she had frequent attacks of a similar nature in which sometimes the right limbs were affected, sometimes the left. On the last occasion, six weeks before I saw her, she suddenly found her left hand weak and tremulous and then her right leg. This was accompanied by right-sided headache. Recovery occurred as usual in 24 hours. These episodes had been attributed to cerebral emboli, but when she came to see me in my consulting-room she was active and well, apart from the complaint of general tiredness, and on examination showed no trace of weakness or loss of sensation nor any abnormality of the reflexes apart from a relative briskness of the left arm jerks. She was admitted to hospital a few days later and died from the effects of an embolus in her left internal carotid artery. At the post-mortem inspection the findings relevant to this story were an old organized embolic occlusion in the right internal carotid artery just proximal to the circle of Willis, and two small areas of infarction of old standing, one in each hemisphere in the neighbourhood of the internal capsule.

I suggest that the occlusion of the right internal carotid artery was responsible for the phase of headache, which became less as anastomosis improved. At some time thereafter she had a small embolic infarction in each hemisphere. Each of these lesions could have caused a transient hemiparesis but could not have accounted for the very frequent attacks that have been related. Each, however, may well have resulted in a special local demand for compensatory circulation, and so have added to the effect of temporary failure of the compensatory mechanism as a whole in determining transient weakness and numbness of the limbs.

Only in one other patient have I encountered the story of transient loss of function in the limbs on the same side as the carotid obstruction, a woman who finally developed a left hemiplegia with arteriographic proof of occlusion of the right internal carotid artery in the neck. She had first attended hospital six years previously for attacks which were then regarded as hysterical. They continued up to the time of the hemiplegia. They never occurred except during menstruation, and then quite often. The onset was rapid, with a feeling she described as that of going under ether, and this feeling persisted throughout the attack. The next sensation was that of weakness and numbness experienced in those parts of her body which were in use—the arm or leg on one side of the body, never on both sides, but as often on the right as the left. If she were talking at the onset of an attack indistinct speech would be the first evidence of weakness. The whole episode lasted about five minutes, and with it she would have a bursting sensation in the neck. She had very occasionally lost her senses briefly at the height of the attack. There may be in this case some anomaly of the circle of Willis. I mention it as an example of symptoms which seem to depend upon some recurrent haemodynamic crisis following internal carotid occlusion, for I suppose this existed from the first and that the hemiplegia was the final result of a complete failure of compensation.

A Well-recognized Symptom

Transient blindness on the same side as the obstructed internal carotid is now a well-recognized symptom, though by no means common. These attacks, usually occurring at irregular intervals of days or weeks, are of a fairly constant pattern, of sudden onset and lasting from one to five minutes. As a rule they precede hemiplegia, often by many months, and frequently cease before that event. There is no doubt that the blindness is due to transient retinal ischaemia, for the retinal arteries have been observed in an attack and are bloodless. I suspect this is an example of what may be happening elsewhere in the cerebral circulation, but here with a more impressive clinical effect, for the reason that the retinal arteries have no anastomosis. The cessation of these attacks of blindness some time after internal carotid occlusion may be due to an increase of the flow from the external carotid side as anastomotic channels widen.

Conclusion

I imagine it may have been the lot of more than one Harveian Orator, as he comes to the end of his discourse, to fear that he has disappointed expectation and fallen short in the performance of an honourable duty. I have taken the name of Thomas Willis for commemoration as one of the Benefactors of the College. He gave well of the fruits of his labours preserved in those many pages which even Anthony Wood (1813–20) praised for the "natural smoothness, pure elegancy, [and] delightful, unaffected neatness" of their Latin style. I have occupied some part of your time with speculation about the cause of symptoms resulting from occlusion of the internal carotid artery. If there be anything in this of the least value let me exhort you, as I have the right, to search and study out these secrets of nature by way of experiment. Willis would have approved this exhortation and perhaps have thought us laggards. He foresaw great works. The ancients, he said, bound to false suppositions, might be excused the faulty structure of their reasoning, but "those who come after should take care for the Re-edifying of the Building even from the ground, on which our most famous Harvey hath laid the Circulation of the Blood as a new Foundation in Medicine."

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PANCREATITIS FOLLOWING PREGNANCY

BY

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The relation between pregnancy and pancreatitis is little discussed in the literature, although many reports of pregnancy complicated by pancreatitis have been published (Kingsley, 1934; Cassel and Malewitz, 1950; Burger, 1952) since the cases of Schmitt (1818) and of Lawrence (1831) early last century. Langmade and Edmondson (1951) collected 53 cases from the literature and reported nine more of their own.

The earliest report of pancreatitis occurring in the post-partum period seems to be that of Haidlen (1884). Watts (1918) and Fallis and Plain (1939) have each reported two cases, and others have been described or mentioned by Deaver (1918), Paxton and Payne (1948), Roberts *et al.* (1950), Rose (1951), and Comfort and Steinberg (1952). McWhorter (1932) reported 64 cases of pancreatitis in two of which "the onset of pancreatitis occurred shortly after childbirth." Langmade and Edmondson (1951) noted that, in pancreatitis complicating pregnancy, liability to an exacerbation during the puerperium was an outstanding characteristic.

Nevertheless, most recent writers do not stress pregnancy as an aetiological factor in pancreatitis (Paxton and Payne, 1948; Warren, 1948; Macnab, 1949; Fallis, 1951; Saint and Weiden, 1953). There is, however, increasing evidence to support the idea of Whipple (1907) that "acute" and "chronic" pancreatitis are differing phases of the same disease process (Comfort *et al.*, 1946), while Saint has rightly emphasized that "pancreatitis" is a general term covering several diseases which have in common only the feature of localization to the pancreas (Saint and Weiden, 1953).

This paper reports six patients with pancreatitis, in all of whom the disease was first manifest a few weeks or months after completion of pregnancy, in whom the clinical and laboratory findings were similar, and none of whom presented any evidence of the known causes of pancreatitis. It is suggested that these patients may be representative of one type of pancreatitis which forms a distinctive syndrome, to be separated from the large group of patients with "pancreatitis of unknown aetiology." For convenience, some of the features of these cases are given in Table I.

Case 1

A woman aged 20 was admitted on May 29, 1954. One year before admission she had been delivered of a stillborn child. Six weeks after this she developed flatulent dyspepsia and intermittent epigastric distress, later followed by severe constant epigastric pain radiating through to the back on the left side. She vomited occasionally. The pain was worse after fatty foods. Two weeks before admission she had more severe pain than previously, and this was followed by persistent vomiting and then jaundice with dark urine and pale stools.

On examination she was jaundiced. Her temperature was 99.8° F. (37.7° C.), pulse 80, blood pressure 120/90 mm. Hg. There was rigidity and guarding over her abdomen, but she was more tender in the epigastrium. The liver and gall-bladder were impalpable. The diagnosis of obstructive jaundice due to pancreatitis was made. The urinary diastase level was 400 units.

Laparotomy was performed on June 1. The gall-bladder was normal and contained no calculi, while the pancreas was irregularly enlarged and thickened. The common bile duct was drained and a pancreatic biopsy was performed; this showed pancreatitis (Fig. 1).

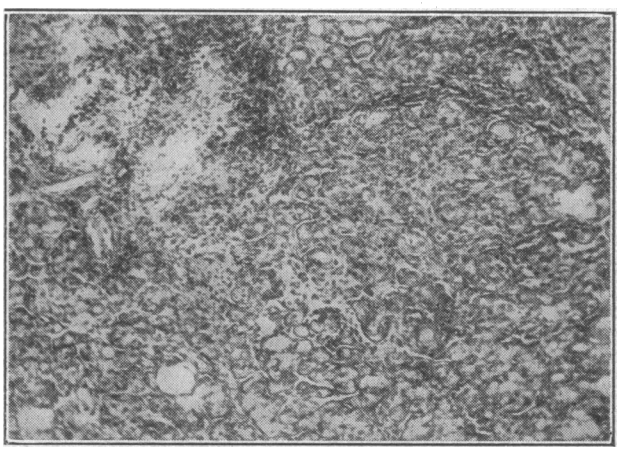

FIG. 1.—Pancreatic specimen taken for biopsy at operation in Case 1. At this stage the patient was still jaundiced and the urinary diastase elevated. The specimen shows increased fibrous tissue and cellular infiltration without necrosis of the parenchymal cells; the pancreatic ducts are slightly dilated. (Van Gieson. ×144.)

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