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REFLECTIONS ON THE HUNTERIAN METHOD*

BY

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To be invited to deliver the Hunterian Oration is for anyone a great privilege, but it is enhanced for the recipient if he be a physician, since John Hunter is acclaimed as the founder of scientific surgery. No one questions that it was his teaching and example which transformed surgery from a craft guided by the primitive precept, "If thy right hand offend thee, cut it off," to an art and science which he recognized must be based on a sound knowledge of anatomy and physiology. Yet it is superlatively proper that the physician in the twentieth century should share in these commemorative orations, since for Hunter surgery differed from medicine only in that surgery stressed the treatment of wounds and injuries, and included in its scope their operative treatment and such therapeutic procedures as the excision of tumours and cutting for stone. But for the rest the surgeon of the late eighteenth century practised in the same fields as his physician colleagues. Though Moynihan can claim to have defined the surgeon as "a physician doomed to the practice of surgery," no surgeon has better exemplified its truth in himself than John Hunter.

Much modern surgery, in precept if not in practice, is beginning to emerge from its earlier preoccupation with operative techniques. Yet nearly two centuries ago Hunter was writing: "This last part of surgery, namely, operations, is a reflection on the healing art; it is a tacit acknowledgement of the insufficiency of surgery. It is like an armed savage who attempts to get that by force, which a civilized man would get by stratagem. No surgeon should approach the victim of his operation without a sacred dread and reluctance, and should be superior to that popular éclat generally attending painful operations, often only because they are so, or because they are expensive to the patient." (*P.*, Vol. I, p. 210.)† And Drewry Ottley in his "Life" remarks that Hunter used frequently to say, "To perform an operation is to mutilate a patient we cannot cure; it should, therefore, be considered as an acknowledgement of the imperfection of our art."

But this honour which you have done me has brought with it a rare pleasure, for it sent me to Hunter's works in search of a topic which might permit me some novelty in the presentation if not in the content of my Oration. For when we recall the hundreds of orations which have been delivered, we may be disposed to agree with James Palmer, the editor of Hunter's collected works, who, referring to the commemorative orations, wrote 120

years ago: "It may be worthy of consideration whether it would not be better that these orations should occur less frequently. It is a hopeless task to seek for something new every year on so limited a subject."

I had earlier read the many lives of Hunter which concentrated on his character, his querulous, rude, and overbearing manner, combined with an affectionate loyalty to those for whom he cared; his relations with his brother William, and the rest. I had learnt from these and such extracts of his works which I had read of his unrivalled contributions to surgery, and of his great museum, and I had accepted the all but universal encomiums on him, and of his pre-eminence in the history of surgery (Jesse Foot's *Life of John Hunter* provides the sole exception). But until I read John Hunter's works at first hand, and in their entirety, I had failed to realize how wide was the canvas on which he painted. For he covered all aspects of physiology and, in its narrower sense, medicine, and he brought to bear on them an industry, zest, imagination, and genius which could yield enough interesting material for innumerable orations if only the speakers could make it so.

Workings of Nature

I propose to discuss the method by which Hunter sought to understand the workings of Nature so that he could interpret, use, and control them for the beneficent aims of medicine. Before his time medicine was shackled in the fetters, firstly, of authority, and, secondly, of the concept of diseases, which had been enunciated by Sydenham, as separate and distinguishable entities. The manuals of the time were still teaching the medicine of Hippocrates, Celsus, and Galen, and contributions to learned societies and monographs were prefaced at length by extensive references to ancient writers and their views. Hunter eschewed this and was indeed contemptuous of book-learning and of the dead languages, unlike his brother William, who was a good classical scholar. You will recall how Hunter spent a brief period at St. Mary's Hall, Oxford, and that many years later he spoke of this to Sir Anthony Carlisle—"They wanted to make an old woman of me; or that I should stuff Latin and Greek at the University, but," he added, significantly pressing his thumbnail on the table, "these schemes I cracked like so many vermin as they came before me."

Of all his writings, his *Observations on Digestion* is the only major work in which any comprehensive reference to the history of his subject is introduced. For Hunter, "it was not enough that Galen said so." His book was Nature herself and he sought her message by observation and experiment, the method by which Harvey a century

*The Hunterian Oration of the Hunterian Society delivered at the Mansion House, London, on February 20, 1956.

†The references are to *The Works of John Hunter*, 1835, edited by James F. Palmer (*P.*). The italics in the quotations are mine.—H. C.

and a half earlier had not, as is sometimes stated, *discovered* that the blood circulates, but had *demonstrated* beyond all reasonable doubt that the blood circulates. But it is interesting to reflect that Harvey did not translate his observations into the practice of medicine. Indeed, there is no evidence to suggest that he realized their clinical import. Harvey had forgotten the doctrines of Plato, who in his *Timaeus* had regarded health as the harmonious balance of the body's elements, and disease as discord and imbalance, and he was, as were his successors, wedded to the concept of diseases as specific entities. But Hunter, possibly because he had little book learning, clearly saw in Ottley's words "that in order to obtain just conceptions of the nature of these aberrations from healthy actions which constitute disease, it was necessary first to understand well the healthy actions themselves; and these required to be studied, not in man alone, but throughout the whole animal series, and even to receive further elucidation by comparison with the functions of vegetable life. It was no less an undertaking, then, than the study of the phenomena of life, in health and disease, throughout the whole range of organized beings, in which Hunter proposed to engage; an undertaking which required a genius like his to plan, and from the difficulties of executing which any mind less energetic, less industrious, and less devoted to science than his own would have shrunk."

Hunter's method of trying to arrive at truth was that of reflective inquiry—the method of science. In its simplest and perhaps over-simplified form, four stages can be discerned—first, the accurate observation and recording of significant facts; secondly, grouping them on the basis of similarity; thirdly, formulating a hypothesis to account for the facts—the Baconian method of induction; and, fourthly, deducing from this hypothesis consequences whose validity could be tested by further observation or experiment. I say *over-simplification* because these four stages neglect to emphasize the part played by chance observation in discovery. From Archimedes' law to Fleming's discovery of penicillin the history of science is replete with the fruits of accidental observations. It was, for example, William Hunter's chance finding of both testicles (of a 7- or 8-months stillborn child) lying in the abdomen which led to John Hunter's work on the descent of the testis and scrotal hernia, and indeed it was John Hunter's chance observation on the flushing of the deer's antler which led him to his operation for the treatment of aneurysms. But we must remember with Pasteur that "chance only visits the mind that is prepared." And it is perhaps necessary to stress the error of the Baconian view that the mere orderly arrangement of data makes the right hypothesis obvious. At each stage of induction ability (it may be intuition) is indispensable; indeed, some steps in induction can be taken only by those endowed with genius. My purpose is to recall some of the less well known of Hunter's contributions to biology and medicine which illustrate his outstanding genius.

A Wide Field

Since the days of Hippocrates no clinician has made so many observations in disease over so wide a field. Indeed, many of Hunter's aphorisms have a Hippocratic flavour. He had, for example, noted the more positive feeling of robust health which precedes the onset of acute disease. He writes: "Often the internal feeling of health is the forerunner of disease. People just before a disease shall be in better spirits, and feel strong, so as to take notice of it

themselves. A gentleman had better health before a spitting of blood came on. A boy had more spirits than usual the night before he was attacked with the cold fit of fever." (P., I, 311.)

He was well aware of the age incidence of disease: "The young subject and old," he writes, "are more susceptible of many diseases than the full-grown, or stationary, but they are not subject to the same diseases. The young are more susceptible of scrofula than the middle-aged, but particularly more than the old; and this scrofula may produce consumption, which we know is peculiar to youth. Children are more disposed to have affections of the bowels, and worms, perhaps, from a peculiarity in their way of life. They are also more subject to water in the head than those who are older. The young have few affections of the mind, excepting those arising from natural passions, or immediate sensations of the body. The middle age would appear to have but few diseases peculiar to it, excepting nervous affections and hypochondriasis, etc. The middle age gets into an imaginary region, a region of romance, which produces diseases of the mind, and also affects the body. However, it is, as it were, accidentally affected with the diseases both of youth and age, with which it is gradually intermixed. The foundations for the diseases of old age are often laid by intemperance during the middle age. In the old we have perhaps as great a variety of diseases as in the young. . . . In the old we have the gout, which seldom takes place in the young. Cancer is peculiar to the latter part of the middle age, and still more to the old. Gall-stones are to be found chiefly in the middle-aged and old. Ossifications of arteries are rarely found in young persons. The bladder becomes less disposed to stretch, and more irritable; hence old people make water oftener than young. The prostate gland is more subject to indurations." (P., I, 343-4.)

Views on Hereditary Nature of Disease

Hunter made several acute observations on genetic aspects of diseases. He noted, for example, that certain features such as a large nose or a peculiar gait might continue in a family for several generations and then become extinct, but he postulates, what we know now to be true of recessives, "that if such children were to inter-marry with one another, the hereditary disposition would never be lost." And he quotes the case of a white negress with woolly hair (evidently an albino) who "married a white man and had three children, one quite black and the others tawny." But for Hunter, Nature could not be divorced from nurture. He recognized that in some diseases the hereditary factors played a more dominant part in pathogenesis than in others; yet even in these, which had not earlier been looked upon as depending on any hereditary factor, Hunter believed that it was present. And he noted also that what was attributed to heredity was sometimes due to exposure to a similar environment as the parent.

In gout, for example, he anticipated the modern view that what is inherited is a gouty diathesis which, he writes, "never takes on action of itself; it must have the immediate cause to excite it, which is a stimulus of a particular kind. We find gout attacking people whose parents for many generations have not had it, and often never. We see it starting up in countries where luxury is introduced, where it was never known before. However, there are many instances where it would appear to be hereditary, as in the case of young men of fifteen, the sons of gouty men. But I suspect that *this does not arise simply from the father's having had the gout, but from the circumstance that most people who have had the gout severely have deserved it, and that children have inherited the disposition for the way of living as well as the susceptibility for the disease, and will therefore be more liable to fall into the disease than children at large.* On this principle of the hereditary nature of diseases, if it be just, every disease under the sun will be hereditary; but many diseases having a stronger visible cause has made the hereditary susceptibility in them to be overlooked. Thus, the smallpox is as much hereditary as scrofula or

gout, but from its arising in all cases from poison communicated, and evidently not in a spontaneous manner. is the reason why the hereditary susceptibility has been overlooked. But on our principle the smallpox is as hereditary as any other, only requiring the immediate cause to act to produce it as in any other disease. We may make the same observation with regard to the venereal disease, for we see some persons much more susceptible of this disease than others are, and suffering more severely from it when they get it." (P., I, 358.)

Importance of the Syndrome

Again, Hunter knew as did few of his contemporaries the greater importance in diagnosis of the constantly recurring pattern of symptoms and signs—the syndrome—than the isolated symptom or sign. He writes of renal calculus: "Suppose a stone in the kidney; it may produce three symptoms: 1st, Pain in the part; 2nd, Vomiting, which is symptomatic; 3rd, Bloody urine. Now these symptoms may occur in other diseases, independently of stone; if they are combined, they afford a pretty certain diagnosis of the presence of stone, but any one or two of them leaves it doubtful. These symptoms attend the passing of a stone through the ureter, as when in the kidney; and when a stone gets from the ureter into the bladder the symptoms abate, and a different pain is felt, and this chance occurring confirms us in the opinion we had before formed of the existence of a stone." (P., I, 363.)

His writings abound in these discerning clinical pictures, accurately observed and correctly interpreted. These owe much to his habit of keeping careful and detailed case records. He exhorts others to do likewise. At the conclusion of his "Proposals for the recovery of persons apparently drowned" (P., IV, 165) he suggests that "all who are employed in this practice (that is, of treating the apparently drowned) be particularly required to keep an accurate journal of the means used, and the degree of success attending them; whence we may be furnished with facts sufficient to enable us to draw conclusions, on which a certain practice may hereafter be established."

Hunter proves no exception to the dictum of Aeschylus that the wisest of the wise may err. His views on the unity of gonorrhoea and chancre and the effect of the moon on disease were wrong. He completely misunderstood what was happening during his first heart attack, during which, because he could feel no pulse in either arm for 45 minutes, he believed that "no circulation was going on" during this period. But this was yet another example of the perils which flow from subjective observation and the interpretation of one's own symptoms. Again he misinterpreted many of his experiments on digestion, on the blood, and on the "living principle." But these errors must in part be related to the limitations imposed by the knowledge of the times. And though Hunter's general obstinacy might well have favoured tenacity even of false beliefs, in the field of science he exemplified Cicero's conclusion that "it is in the nature of every man to err, but only the fool perseveres in error." When Astley Cooper, then one of Hunter's pupils, asked Hunter if an opinion he was then expressing was not directly at variance with one stated a year before, he replied, "Very likely; I hope I grow wiser every year"; and to another of his pupils he said, "Never ask me what I have said, or what I have written; but if you ask me what my present opinions are, I will tell you."

Achievements in Comparative Anatomy and Physiology

None will deny the pre-eminence of Hunter in comparative anatomy. Richard Owen, whose own achievements in biology add weight to his judgment, wrote: "... The historian of the natural sciences has just and sufficient grounds for regarding Hunter as the first of the moderns who treated of the organs of the animal body under their most general relations, and who pointed out the anatomical conditions which were characteristic of great groups or classes of animals; as one, in short, throughout whose works

we meet with general propositions in comparative anatomy, the like of which exist not in the writings of any of his contemporaries or predecessors, save in those of Aristotle"—an unparalleled and unprecedented panegyric. Yet a close study of his work convinces me, and I trust I shall carry that conviction to you, that he merits also an honoured niche in the physiological Valhalla. True, some of his experiments were simple and direct, showing no great ingenuity of design or interpretation. For example, he carried out intravenous injections of a variety of drugs—opium, ether, borax, Glauber's salts, etc., to observe their effects. Of one, he records: "I threw into the veins of a dog two teaspoonfuls of common gin. He showed no sense of uneasiness, but became soon vastly quiet, and not in the least irritable, showing no signs of fear when touched. He seemed wholly relaxed; his breathing was easy, and his pulse slow. He continued about an hour in this way and then began to recover" (P., I, 349). A proof by animal experiment of what is commonly observed in man.

Other experiments were, however, of a complexity which matched their purpose. I will quote one in some detail, because it reveals more than most of Hunter's experiments a modernity of design which gives him as a physiologist an unchallengeable superiority to his contemporaries. In this experiment he sought the effect of extirpating one ovary upon the number of young produced; his paper was originally published in the *Philosophical Transactions* (vol. 77, p. 233) and read on March 22, 1787.

Here can be seen clearly Hunter's appreciation, firstly, of the crucial experiment designed to establish one of two conflicting hypotheses; secondly, of the importance of accurate quantitative recording and analysis; and thirdly, of the need for controls.

He refers to the presence of two ovaries and paired oviducts in the female and to "the limited portion of the middle stage of life allotted" for reproduction, and he then asks himself if this reproductive period is shortened by repeated acts of propagation. In the human species Hunter observed that a "woman who begins to breed at an early period, as at fifteen, and has her children fast . . . seldom breeds longer than the age of thirty or thirty-five"; but if she begins later she continues to breed later. A similar phenomenon, he says, is seen in most animals.

Is this limited propagation period due to the ovary or is it the outcome of general constitutional factors? Hunter writes: "As the female, in most classes of animals, has two ovaria, I imagined that by removing one it might be possible to determine how far their actions were reciprocally influenced by each other, from the changes which by comparison might be observed to take place, either by the breeding-period being shortened, or perhaps, in those animals whose nature it is to bring forth more than one at a time, by the number produced at each birth being diminished. There are two views in which this subject may be considered. The first, that the ovaria, when properly employed, may be bodies determined and unalterable respecting the number of young to be produced. In this case we can readily imagine that, when one ovary is removed, the other may be capable of producing its determined number in two different ways: one, when the remaining ovary, not influenced by the loss of the other, will produce its allotted number, and in the same time; the other, when affected by the loss, yet the constitution demanding the same number of young each time of breeding, as if there were still two ovaria; it must furnish double the number it would have been required to supply had both been allowed to remain, but must consequently cease from the performance of its function in half the time. The second view of the subject is, by supposing that there is not originally any fixed number which the ovary must produce, but that the number is increased or diminished according to circumstances; that it is rather the constitution at large that determines the number; and that if one ovary is removed, the other will be called upon by the constitution to perform the operations of both, by which means the animal should produce with one

ovarium the same number of young as would have been produced if both had remained." (P., IV, 51.)

Briefly, then, Hunter surmises that removal of one ovary may halve the number of offspring produced at each birth, or shorten by half the breeding period. To test by experiment which of these hypotheses is valid he chose pigs, "as being easily managed, producing several at a litter, and breeding perfectly well under the confinement necessary for experiments." He selected two females of the same colour and size, and likewise a boar, all of the same farrow. He removed an ovary from one of the females and marked this by slitting its ear. Both pigs were kept warm and well fed. The spayed animal bred from December, 1779, till September, 1783—from 2 years old to 6 years old—that is, for nearly four years; during this time she had eight farrows and 76 pigs (Table I). The control animal continued breeding for two years longer—till December, 1785—a period of six years, during which time she had 13 farrows and 162 pigs (Table II). Both were with the boar later but without effect, from which circumstance Hunter concludes that "it appears

TABLE I.—*Spayed Sow*

Farrows	Number of Young	Time
1	6	December, 1779
2	8	July, 1780
3	6	January, 1781
4	10	August, 1781
5	10	March, 1782
6	9	September, 1782
7	14	May, 1783
8	13	September, 1783
	76	

TABLE II.—*Perfect Sow*

Farrows	Number of Young	Time
1	9	
2	6	
3	8	
4	13	December, 1781
5	10	June, 1782
6	16	December, 1782
7	13	June, 1783
8	12	October, 1783
9	17	February, 1784
10	16	June, 1784
11	12	December, 1784
12	16	May, 1785
13	19	December, 1785
	162	

that the desire for the male continues after the power of breeding is exhausted in the female; and therefore does not altogether depend on the powers of the ovaria to propagate, although it may probably be influenced by the existence of such parts." He noted also that "both sows rather increased their number each time as they grew older, although not uniformly." Hunter's conclusion is, then, that "the ovaria are from the beginning destined to produce a fixed number, beyond which they cannot go . . . but that the constitution at large has no power of giving to one ovarium the power of propagating equal to both."

A Footnote by Hunter

Hunter was aware of the hazards of drawing conclusions from a single experiment, though he adds that "the difference in the number of pigs produced by each was greater than can be justly imputed to accident," or, as we should say in modern jargon—the result is statistically significant. And as a final footnote, Hunter bemoans the limitations imposed by time and money on experimental investigations. "It may be thought by some," he writes, "that I should have repeated this experiment; but an annual expense of twenty pounds for ten years, and the necessary attention to make the experiment complete, will be sufficient reason for my not having done it."

He refers to this again in his *Observations on Digestion*, when he writes of the difficulty of carrying the burden both

of practice and of research, and has a characteristic gibe at the clergy, which is patently unjustified in the light of Stephen Hales's investigations on the circulation, a generation or two earlier. He observes: "It happens, unfortunately, that those who from the nature of their education are best qualified to investigate the intricacies, and improve our knowledge of the animal economy, are compelled to get their living by the practice of a profession which is constant employment. The only educated men who have leisure are those of the Church, some of whom we frequently find commencing philosophers and physiologists, though they have not had that kind of education which would best direct their pursuits. Experiments, it is true, may be made by men of their description; but these must neither be much complicated, nor have any immediate relation to those branches of knowledge with which they have had few opportunities of being acquainted: at best, they will seldom go further than to explain a single fact. To look through a microscope and examine the red globules of blood, to view animalculae, and give a candid account of what they see, are points on which such inquirers may be allowed to indulge themselves; but it is presumption in them to affect to reason of a science in which they can have but a very superficial knowledge, or to expect to throw light on subjects that they have not taken the previous steps to understand. It should be remembered that nothing in Nature stands alone; but that every art and science has a relation to some other art or science, and that it requires a knowledge of these others, as far as this connexion takes place, to enable us to become perfect in that which engages our particular attention." (P., IV, 83.)

Perhaps the most frequent criticism which has been levelled against Hunter as a scientist is that, like the Greeks, he was prone to generalize from insufficient data. Indeed, it was written of Hunter that "from the specimens we have of his hypothetical reasoning, we have no reason to regret that he did not oftener indulge in it." I believe these criticisms to be ill-founded. There are many instances of brilliant observations and inductions in which Hunter was half a century or more ahead of his time, and in support I will quote but four examples of Hunter's prior claim to important physiological truths.

Instances of Hunter's Prescience

First, the *Law of Specific Nerve Energies*, called Müller's law after Johannes Müller (1801–58), the greatest German physiologist of his day, and, like Hunter, an all-round medical naturalist. This law or doctrine was published in 1826. It states that the subjective response of a sense organ is the same whatever the nature of the exciting stimulus. Thus if the visual system be excited by pressure on the eye, an electrical stimulus, irritation, or section of the optic nerve, the resulting sensation is *visual* only. The character of sensation resulting from a stimulus depends on *what* nerve fibres are stimulated, not on *how* they are stimulated. Hunter had in his "Principles of Surgery" many decades earlier observed and recorded the same phenomenon. He makes, as Owen points out, "the ingenious remark that the nerves which are specially designed to receive peculiar impressions convey the ideas of such impressions to the brain, in whatever way they may be affected or stimulated." Thus he says, "A mechanical impression on the retina produces an impression of light; a blow on the ear the sensation of sound."

Again, Johann Friedrich Meckel, the younger, of Halle (1781–1833), is credited with the earliest expression of the view that the development of a higher animal recapitulates the life history of lower animals; it is an epitome of the ancestral stages which preceded it. Yet Hunter's studies on monsters and of the developing chick had led him to write: "If we were capable of following the progress of increase of the number of the parts of the most perfect animal, as they first formed in succession from the very first, to its state of full perfections, we should probably be able to compare it with some one of the incomplete animals themselves, of every order of animals in the creation,

being at no stage different from some of those inferior orders; or in other words, if we were to take a series of animals from the more imperfect to the perfect, we should probably find an imperfect animal corresponding with some stage of the most perfect." It may be that the later recapitulation theory impressed itself by the pithy phrase—"Ontogeny repeats phylogeny," but the central theme had been discerned by Hunter in an earlier century.

Hunter's views on muscular contraction are also worthy of mention, for in these he anticipated not only that inhibition is a positive process but also the law of reciprocal innervation of antagonistic muscles—which Sherrington was to demonstrate over a century later. Moreover, he postulated the law of intestinal peristalsis. He is writing of muscular contraction being generally supposed to arise from some impression, called a stimulus, and continues: "I can even conceive that a cessation of action requires its stimulus to produce it. . . . Whatever becomes a stimulus to one set of muscles becomes a cause of relaxation to those which act in a contrary direction; and whatever becomes a stimulus to one part of a muscular canal, where a succession of actions is to take place, becomes also a cause of relaxation in the part beyond it, as in the intestine." (P., III, 146.)

My last illustration of Hunter's sagacity and prescience in generalizing hypotheses from groups of analogous phenomena is drawn from his observations on referred pain.

For many—and until I read the complete works of John Hunter I was one of them—theories of the mechanism of referred pain stem from Martyn's paper, "On the Physiological Meaning of Inframammary Pain," published in 1864.

Hunter recognized (P., I, 363) that there are in disease many anomalous symptoms which make the diagnosis doubtful, and of these there are, he writes: "*Delusive Symptoms respecting Sensation*." This delusion of the senses makes disease seem where it really is not, from the different seat of the symptoms and of the diseased part. Thus, diseases of the liver are referred to the shoulder, of the testicles to the back, of the hip to the knee. When the trunk of the nerve is injured, the pain is referred to the termination of it, as, after amputation of the leg, pain is felt in the toes. When pressure is made on a large nerve, the most acute sensation will be at some distance below the part pressed on."

Earlier writers had been aware that the site of pain and the site of the disease causing it did not always correspond, but, as Hunter observed (P., I, 331 *et seq.*), this had always been attributed to the principle of "sympathy." "Thus," he writes, "sensation of pain in the shoulder from disease in the liver has been always supposed to arise from the shoulder sympathizing with the liver. But I believe it is a delusion in the mind; for the nerves of the part are not the seat of the disease, and irritation could not communicate to the mind the sensation of pain in the part affected excepting they (the nerves) take on the same action, which they must do when they produce the sensation of pain of that part."

He then proceeds to formulate a hypothesis which anticipates many which appeared over a century later. "To account for this delusion in sensation in ourselves may be difficult, but we may conceive it to be in this way. We may suppose that when the seat of sensation in the brain only takes on part of the action of sensation in the brain, it may be in this way. Suppose E, (Pl. XVII, f.3) [see accompanying Diagram], the brain; AB, two portions of the brain; G, H, two nerves; F, communication between these two nerves; CD, two different parts of the body. The nerve G is inserted into part of the brain A; the nerve H into the other part B. F is a communicating nerve between G and H. A and B are the two parts of the brain to which sensation from C and D is conducted. C is the disease or part impressed. But from the connexion between C and D, by means of the nerves G F H, B will become the seat of action of the nerve G as well as of the nerve H, and the sensation be in part referred to D as well as to C. For if the nerve H is stimulated, in consequence of these

connexions, to take up part of the action of the nerve G, and B is sensible of it as well as A is of the sensation of C, then the sensitive principle of the nerve A B is made sensible of both the disease of the part of impression as also of the sympathizer D, which become the two impressions in the sensorium. If anything stimulates G, part of the action is communicated to H; this goes on with the action to B, so that both A and B become sensible of the disease C. If there is disease in C, the mind is made sensible of it, because G always communicates the sense of C to A; but if a small portion of it is brought over to H, and this nerve carries on the action to B, B becomes sensible of it also, and B refers it not to C, but to D, because it is to that point that it has been accustomed to refer all its sensations."

"I do not know," he writes, "whether this explanation may be the true one or no, but it is one mode of explaining how we may feel both the disease and the part of sympathy." But Hunter went further. "How is it," he asks, "in those cases where the sympathizer takes on the whole action, affection, or sensation? In this case we must suppose that not only a part but the whole of the sensation passes by the communicating nerve F to B, and thus the disease appears to be in D only. But it is possible that nervous sympathy is not affected by the nerves communicating with one another in the body, but from their connexions in the brain; as from the point B sympathizing with the point A, taking on the whole of its action, and referring its sensation to D."

This is a noteworthy example of Hunter's outstanding powers of induction. To too many the oft-quoted excerpt from his letter to Jenner (P., I, 56)—"But why think? Why not try the experiment? Repeat all the experiments . . . and they will give you the solution"—has suggested that Hunter frowned on hypothesis. But this is far from the truth. He followed the scientific method—he sought to interpret observed facts by a hypothesis which he then proceeded to test, and if necessary modify, by further observation and experiment. He believed with Henle that "a hypothesis which becomes dispossessed by new facts dies an honourable death; and if it has already called up for examination those truths by which it was annihilated, it deserves a moment of gratitude."

The Path to Truth

In an excess of taxonomic zeal critics have often regarded the great thinkers of the past as exemplifying either the Platonic method of deduction or the Baconian method of induction. But Hunter uses both. Not because, as Buckle suggests in his *History of Civilization in England*, Hunter was born and remained for the first 20 years of his life in Scotland and passed the rest in London. "Hence," writes Buckle (vol. III, p. 423) "the early associations of his mind were formed in the midst of a deductive nation, the later associations in the midst of an inductive one. The country of his birth made him deductive, the country of his adoption made him inductive. As a Scotsman he preferred reasoning from generals to particular facts; as an inhabitant of England he became inured to the opposite plan of reasoning from particular facts to general principles." And Buckle adds, "I make no doubt that one of the reasons why Hunter in investigating a subject is often obscure, is that on such occasions his mind was divided between these two hostile methods."

Few more nonsensical statements can ever have been penned. I suspect that had Hunter been told that he was combining two philosophic methods he would have felt like M. Jourdain. The method of natural science must combine both induction and deduction, though the latter

may suffice for mathematics and some aspects of theoretical physics. For the path of truth, even though the ultimate goal is never attained, is by observation, classification, and a reactive hypothesis; then comes the search for significant facts by further directed and controlled observation (which is experiment) which will support, modify, or refute this initial hypothesis; this leads to further hypotheses (induction) which are again tested by observation and experiment (deduction). Of this and of the unexpected result of experiments Hunter was well aware. "Many things," he observes, "arise out of investigation which were not at first conceived; and even misfortunes in experiments have brought things to our knowledge that were not, and probably could not have been, previously conceived. On the other hand, I have often devised experiments by the fire-side or in my carriage, and have also conceived the result; but when I tried the experiment the result was different, or I found the experiment could not be attended with all the circumstances that were suggested." (P., IV, IX.)

Conclusion

Other orators, both of this Society and of the Royal College of Surgeons, have dealt in detail with Hunter's contributions to pathology and to the craft of surgery, and we do right to honour him with Ambroise Paré and Lister as one of the three greatest surgeons the world has known. But he surpasses them both, for he was one of the greatest experimental biologists of all time, who brought to the study of medicine not only an unrivalled knowledge of anatomy and physiology, and an unmatched industry and zest in unmasking Nature's secrets, but a supreme intellect and creative imagination yoked to the scientific method of reflective inquiry.

It has been for me a privilege, for which I am truly grateful, to convey to you my reflections on the working of John Hunter's mind. And if in expressing opinions and formulating judgments I have erred on the side of dogmatism, I pray that you will remember, what I certainly do not forget, that these reflections are those of an amateur medical historian whose interest in the genius of ancient masters, even when labelled surgeons, has never abated.

ACETAZOLAMIDE IN TREATMENT OF EPILEPSY

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It has long been known that starvation may help in reducing the frequency of epileptic seizures (Guelpa and Marie, 1911). On the assumption that ketosis and acidosis were responsible, the ketogenic diet was introduced and in some hands proved of value (Barborka, 1930; Keith, 1947). Cohen and Cobb (1941) had similar success with a sulphonamide used for the same purpose on the grounds that it inhibited the enzyme carbonic anhydrase, which catalyses the reversible reaction $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3$. The main result of the inhibition is an inability to form an acid urine because of reduction in the availability of the hydrogen ion, thus producing an alkaline urine containing increased amounts of sodium. The loss of fixed base results in the production of a metabolic acidosis. Recently a much more potent carbonic anhydrase inhibitor—acetazolamide ("diamox")

—has been introduced, and it seemed reasonable to attempt an evaluation of its anticonvulsant properties in view of its ability to produce an acidosis.

Bergstrom *et al.* (1952), Merlis (1954), Pero (1955), Vivien (1955), Ferroni *et al.* (1955), Munoz and Gomenzoro (to be published), and Lombroso *et al.* (1956) have already reported its effects in epilepsy, and the present study is a further attempt to assess its value.

Material

Twenty-six patients were treated with acetazolamide. Of these, 23 were of the idiopathic or "centrencephalic" type of epilepsy. The definitions proposed by Symonds (1954, 1955) have been employed. Thus major epilepsy included all those with grand-mal seizures, and minimal those having the classical petit-mal attack or "blank spell" as defined by Gowers (1881) as well as the akinetic and myoclonic types. Between these two extremes were a variety of seizure patterns that are best termed "minor."

There were six patients (three male and three female) aged between 12 and 31 years, suffering from major epilepsy. Five (four female and one male), aged from 5 to 36, had the minimal type. In the minor group there were four females aged from 13 to 34 years. Those with mixed idiopathic epilepsy were aged from 14 to 38 years and comprised seven females and one male; they had all been difficult to control with known anticonvulsants during the preceding year. The remaining three patients had symptomatic epilepsy of varying aetiologies, and had resisted all therapy. Initially, only those patients who were not responding to known medications were given the drug, but later it was used from the onset in nine cases. Altogether 15 patients had acetazolamide alone over periods ranging from 4 weeks to 18 months.

Method

The majority of cases were studied as out-patients, although a few began treatment while in hospital. The frequency of seizures was recorded by the patient or a relative. There was first a preliminary control period of never less than one month, during which time nine patients had no treatment, while the remaining 17 continued previous therapy which had been inadequate to control their attacks. The following rough grouping of patients was possible:—Grade I: infrequent attacks, less than one a month; Grade II: moderately frequent attacks, more frequent than in Grade I but not more than one a week; and Grade III: frequent attacks, more frequent than one a week.

Assessment of the minimal cases was more difficult, and here Grade I contained those patients who were aware of occasional attacks, Grade II those whose attacks were frequent enough to interrupt speech and other activities, and Grade III those with continuous attacks producing a state of confusion and lengthy amnesia.

Out-patients were assessed approximately once a month and in-patients once a week. If an E.E.G. had not already been carried out a recording was made before acetazolamide therapy was begun, and another during the course of treatment. The plasma bicarbonate level was estimated before and during therapy, and in many cases it was done each month.

A dose of 125 mg. of acetazolamide twice a day was added to the previous medications in the first few cases. If improvement occurred and was sustained the other drugs were gradually eliminated. In most of those deriving no benefit the dose of acetazolamide was progressively increased and adapted to the individual until it was approximately 10 mg. per kg. of body weight.