John Hunter, pathologist

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The Royal College of Surgeons of England has never been accused of understating John Hunter’s contribution to the development of Surgery. In a conspicuous place of honour his statue (Figure 1), the work of an early Victorian sculptor, is there to greet all those who cross the portals at Lincoln’s Inn Fields. The famous Reynolds portrait is the centrepiece of the Council Room. Robert Home’s portrait of him as a younger man dominates the first floor landing, to be seen by all who visit the College Library or the famous Hunterian Museum. Little wonder that he is so often referred to as the patron saint of the College although such a title sits a little uneasily on one whose nature was neither patronising nor saintly. A more appropriate term of tribute is that engraved upon his tomb in Westminster Abbey (The Founder of Scientific Surgery) but, although the profession of surgery has taken the lead in paying homage to Hunter, his medical knowledge extended much more widely than the confines of surgery. No part of natural phenomena fell outside the sphere of his interest or beyond the limits of his curiosity, neither in health nor in disease, nor was his interest in the Animal Kingdom confined to humans. As a result his contributions to many areas of medical science other than surgery are legion and it is to pathology in particular that this paper refers.

Although the study of disease occupied only a small area of Hunter’s broad canvas, it was certainly one of his foremost preoccupations. Superlative dissection and insatiable curiosity were qualities that made him a morbid anatomist par excellence. From his dissections he was able to observe, to collate his manifold observations, to formulate general principles, and subsequently to draw inferences from these principles and test them. This brings to mind the comments of Henry Cohen who, in an oration to the Hunterian Society in 1956, was moved to scorn by the suggestion in Buckle’s History of civilization that Hunter’s thoughts were confused by a conflict between the deductive philosophies of his native land and the inductive methods of his adopted home. Buckle thought that, as a Scotsman, Hunter tended to reason from the general to the particular, as Plato had taught, but that in England he had become exposed to the school of thought initiated by Francis Bacon, where philosophers reason from particular facts to general principles. Lord Cohen was in no doubt that, while deduction might suffice for mathematics and some aspects of physics, the development of knowledge in biology had to depend on both deduction and induction. He believed that the search for truth required observation first, then a reactive hypothesis; then the testing of the hypothesis by controlled observation (i.e. by experiment), as a consequence of which the hypothesis, if necessary modified, could be elevated to the status of a principle.

As one attempts to survey the contributions of John Hunter to pathology, the combination of induction and deduction is conspicuously evident. The process was appositely described by Miles:

It is useful to think of the inductive-deductive processes as a staircase on which thought goes rapidly and repeatedly back and forth, upstairs inductively to the hypothesis and deductively downstairs.

Observation, and the recording thereof, was Hunter’s primary attribute. It forms the basis for most of his writings and, not least, is on display in what Wood Jones memorably described as his great unwritten book, the Hunterian Museum at the Royal College of Surgeons of England. Hunter’s museum succeeds in demonstrating how function and dysfunction can be better understood by the display of morphological features. So great a storehouse of unique specimens has inevitably attracted the attention of many
different authors. However, there is no better way of illustrating Hunter's observational powers than to cite his accounts of the dissection of human bodies. These reports, written in the immaculate hand of his devoted amanuensis, William Clift, are kept in the library of the Royal College of Surgeons of England. They indicate how meticulously this morbid anatomist carried out his work and, more than that, the thought and induction that attended his dissection. Report No. 11, for example, describes his examination of the body of a woman who died as a result of a blow to the head with an ale-house pot. The skull was not fractured but Hunter describes in detail a subdural haemorrhage. Reflecting on the victim's relatively symptom-free survival for some days after the attack he ends with a message that could well be addressed to the British Boxing Board of Control:

This shows that we are not secure though the patient is seemingly well for eight days after an accident on the head.

Perhaps the most startling account (No. 50) is that concerning a child who died of hydrocephalus at the age of 13 months:

Upon cutting through the pericranium, dura mater and . . . brain we got into a large cavity and immediately rushed out a most fine transparent fluid; rather more crystalline (sic) than pure water; and was about seven pints in quality.

Then follows the ultimate in dedication to the search for knowledge: 'The fluid, when tasted, was a little brackish, and somewhat disagreeable'. When put into a spoon and held over the fire until it boiled it did not coagulate in the least . . . (and when held over the fire) till the whole was evaporated, there remained nothing in the spoon but a very little sediment that stuck to the bottom of the spoon in a very thin lamella. When I put an acid to it, it became white. . . . This, then, had none of the properties of lymph but seemed to be only simple water with a little salt which gives the brackish taste.

Hunter's consuming curiosity about biological phenomena could hardly be better exemplified; even his sense of taste was conscripted in the battle for knowledge.

The sense of hearing is of course applicable to clinical rather than post-mortem examination and is illustrated in his account of General Gage's Carcinoma of the rectum. Describing the symptoms of obstruction he refers to a vast rumbling in the bowels (and) the belly became fuller and fuller, which was principally air . . . which was easily known by the sound in patting on the belly.

The sense of touch comes into almost every dissection he described but, referring to General Gage again (this time post mortem) it is found deployed in tandem with Hunter's immense knowledge of comparative anatomy:

On slitting down the rectum . . . it was found to be . . . of a hardish gristly texture, and a good deal like the turtle's intestines.

An example of how he used his sense of smell was further demonstrated in the account of his post-mortem examination of Sir William Lee's child, who died of convulsions and fever supposed to arise from teething. In a lengthy report (No. 19) he declared his surprise at appearances entirely different from those he had expected from the clinical history but suggests a possible reason by ending 'the lungs had greatly the smell of the small-pox odour'. In addition an ingenious experimental example is provided by his demonstration that absorption from the small intestine is effected via the lymphatics, not the veins; after isolating a segment of the small intestine in a living animal he introduced musk into the gut and found that its odour was later detectable in chyle but not in venous blood.

Most of the post mortem descriptions suggest that brain injuries and disease of the alimentary tract predominated as a cause of death in eighteenth century England. There is particular interest attached to cases of cancer for it is clear that Hunter made a highly significant contribution to oncology. Some of his cases, such as No. 21 in which he describes a tumour in the neck with most of the lymphatic glands diseased could conceivably have been instances of tuberculosis; nevertheless, although life expectancy at that time would have limited the incidence of carcinoma, several dissections portray features of malignant disease readily recognizable today.

Local spread of a malignant neoplasm is the topic of No. 47. In this case Hunter described the destructive local spread of a carcinoma of the antrum and he concluded that there was nothing to be gained by attempting to remove the diseased tissue piecemeal 'because once a polypus is in the antral cavity nothing can be done'. This is the comment of one who had encountered similar conditions previously and had observed their clinical and postoperative behaviour.

There is compelling evidence that Hunter recognized the phenomenon we now refer to as metastasis. One of the dissections recorded by Clift (No. 24) deals with the body of a woman clearly suffering from a carcinoma of the breast with multiple secondary deposits. Hunter said that the growth had been initiated by a blow, but attuned for this assumption by reflecting that in its latter stages the disease was 'constitutional, for there were a great many cancerous swellings in the skin, pleura, pericardium, and diaphragm'.

Scholars are deprived of a proper insight into Hunter's knowledge of oncology because of the disastrous action of his brother-in-law, Everard Home, who burned his manuscripts, including those dealing with cancer. Opprobrium has been heaped on Home for this act of vandalism and many writers have maintained that in the years before destroying Hunter's papers he had plagiarized his brother-in-law's writings. Nevertheless, in his book entitled Observations on cancer, Home did acknowledge that not all the material information in the book should be considered as his own.

Much, certainly, originated with Mr Hunter; perhaps the greatest part . . . The general principles here stated . . . with respect to the contamination of the disease, I certainly received from Mr Hunter.

It is clear that Hunter referred to the spread of neoplasms as contamination. Home described cancers as capable of contaminating other parts, either by direct communication, or through the medium of the absorbents; and when they approach the skin, produce in it small tumours of their own nature, by a mode of contamination, with which we are, at present, unacquainted.
Later Home stated that from what he had observed in the practice of Mr Hunter . . . when the cancerous poison has acquired the power of contamination, the disease is generally too far advanced to be subdued by the extirpation of the tumour.

Many other examples of Hunter’s appreciation of malignant spread are found in Home’s book. He referred to a man between 50 and 60 years old who had, on the side of his tongue, a small foul ulcer which did not heal under any mode of treatment. Mr Hunter declared it to be cancer, and grounded his opinion upon a gland, situated behind the angle of the lower jaw, in the course of absorption, having been contaminated, and taken on the disease.

In today’s language he would have referred to a metastasis from the primary growth to a cervical lymph node; his opinion was not accepted at that time but within the next year or two it had been proved correct. Post mortem examination showed the tongue and pharynx to be ‘the chief seat of the disease’ while ‘the lymphatic glands, in general, of the neck were diseased’. An interesting example of Hunter’s experience of similar lesions comes in a reference by Home to a ‘tumour in the neck of Mr Gainsborough, the painter, which was too far advanced before Mr Hunter saw him, to admit of any operation.’

Hunter had learned to recognize inoperable neoplasia and it seems probable that he had learned the hard way. Home described a case of carcinoma of the breast with axillary metastases that was seen in 1775, a period at which surgeons were more sanguine than at present, and ventured to perform it in cases which now would be considered too far advanced to admit of it. Mr Hunter performed the operation, and found a greater number of glands diseased than had been expected: he however was able to remove all that had undergone any alteration in their structure, which included the whole axillary cluster. To come at them, he dissected round the axillary artery, which was laid bare for an inch in length.

Despite this surgical feat, the patient survived only 3 months in very considerable pain and after her death the disease was found to have spread to the ribs and muscles of the chest.

In respect of the surgery and surgical pathology of breast cancer, Hunter’s achievements were preceded by those of the Frenchman, Henri Francois Le Dran. In 1757, while Hunter was still working in his brother’s School of Anatomy, Le Dran published a description of the dissemination of breast cancer to the regional lymph nodes and even to the lungs. He recognized the crucial importance of treating the disease before involvement of lymph nodes and condemned the use of non-surgical methods such as the application of caustics. Le Dran’s monograph established his position as one of the most remarkable surgeons of the eighteenth century and a leader in the surgical treatment of breast cancer.

Despite Le Dran’s pre-eminence in regard to breast cancer there is, within the Hunterian Museum, a specimen of priceless significance in the history of Oncology. This is a specimen from a man who came into St George’s Hospital in November 1786, with a hard swelling of the lower part of the thigh. About five months previously he had experienced shooting pains in his thigh and a month later he had noticed some swelling. Latterly it began increasing in size very rapidly and had become so large as to interfere with movement of the knee joint.

The pain was now exhausting him much, increasing nearly in proportion to the size; and it was thought advisable to remove the whole, which was done.

He recovered well after the amputation but after four weeks began to complain of difficulty in breathing. ‘From this time he began to lose his flesh and sink gradually’ and died only 7 weeks after the operation. When Hunter examined the amputated femur he found that the swelling was composed of a soft substance which seemed to originate from the bone itself and within which ossification was taking place. One of the bottled specimens shows a vertical section of the lower part of the femur while another is a section of one of the condyles showing part of its articular cartilage, apparently intact, and the medullary space replaced by solid bone (Figure 2). These are features, especially when taken together with the clinical history, of a highly malignant osteosarcoma. In Hunter’s day it was, of course, not yet possible to seek histological corroboration.

What makes this specimen so noteworthy, however, is the co-existence of a dried specimen of the lungs and trachea of the same patient. This preparation, like those of the femur, is preserved for grateful posterity in thick glass jars now some 200 years old - part of the attraction of these remarkable specimens but hardly conducive to sharp photography (Figure 3). Nevertheless one must agree with Hunter’s description:

At the roots of both lungs, and apparently formed in their substance, are large nodulated and rough masses of spongy, but hard and heavy, bone.

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**Figure 2.** Hunter’s specimen of an osteosarcoma from an amputation carried out at St George’s Hospital in 1786. (Courtesy of The Trustees of the Hunterian Collection)

**Figure 3.** Dried specimen of lungs and trachea, overrun by mineralized deposits, taken post mortem from the patient whose primary osteosarcoma is shown in Figure 2. (Courtesy of The Trustees of the Hunterian Collection)
In short, the clinical description of respiratory difficulty is readily understood, and the appearances strikingly demonstrate metastatic osteosarcoma in the lungs.

Before finishing the description of this unique specimen by relating Hunter’s interpretation it is necessary to digress in order to place it in its historical context. It is noticeable that Hunter has not specifically mentioned metastatic neoplasia, which raises the question of who first recognized this phenomenon. According to Tarin a formation of secondary tumour colonies in distant organs by dissemination from a primary tumour was first termed metastasis by Recamier in 1829. Recamier discussed the case of a woman in her late forties with a carcinoma of the breast, who died of a cerebral tumour. Cerebral symptoms appeared contemporaneously with a considerable reduction in the size of the breast tumour. The detailed case history records the onset of the menopause a few months previously. A post mortem examination revealed the presence within the cerebrum of a firm greyish tumour having the appearance of a carcinoma and confirmed that the breast tumour, although still adherent to skin, had (conceivably as a consequence of hormonal changes associated with menopause) diminished in size and was surrounded by fibrosis. It was the coincidental shrinkage of the lesion in the breast and the development of a cerebral tumour that led Recamier to postulate a cancerous metastasis, a change of place of the cancer. It is as though he was thinking of some inexplicable transference of the neoplastic growth in toto from one part of the body to another. Clearly he was not conversant with the work of his compatriot Le Dran, some 70 years earlier.

Hunter, when he spoke of multiple secondary deposits as a ‘constitutional’ phenomenon, and in many of his remarks about contamination, was certainly approaching the true concept of metastasis and when he described this osteosarcoma more than 40 years before Recamier’s paper) his prescience is conspicuous:

On examining the body it was found that the same disposition to form bone, which had taken place in the thigh-bone, had also affected the thorax and its contents. The cartilages of the trachea were opaque, and in some places ossified: bony tumours were found in the cellular membrane of the lungs, upon the pericardium, and some very large ones on the pleura, adhering to the ribs, and upon the anterior surface of the vertebrae of the back. These tumours, or diseased appearances, were all the different states between soft parts and bones, so that they had not been originally formed into bone; but had been formed first of soft substance, which had afterwards been removed for osseous matter.

After discussing the rapidity of growth in the lungs, as judged by clinical signs and symptoms, and commenting on its similarity to the progressive increase in size of the swelling in the thigh, Hunter concluded with a momentous reflection:

One can figure to themselves a reason why the tumour which formed on the outer surface of the thigh-bone might become bony, because it might acquire that disposition from the bone itself; but, from these tumours formed in the chest becoming bone, shows it was the nature of the tumours themselves.

Even without the benefits of histopathology, Hunter recognized that the nature of the tumours in the chest matched that of the preceding growth in the femur; he was clearly moving towards the concept of metastatic neoplasia. This is reminiscent of the comment of Adams6 who wrote in 1818:

When we make a discovery in Pathology we only learn what we have overlooked in his (Hunter’s) writings or forgotten in his lectures.

In the case of this osteosarcoma, he provided a striking illustration of a phenomenon to describe which Recamier, some 50 years afterwards, coined the term ‘metastasis’ - albeit for the wrong reason.

In his studies of bone Hunter made important observations and inferences relating to both the physiological and the pathological. One of the descriptive catalogues of the Hunterian Museum includes ‘Mr Hunter’s classification of absorption’ a remarkably orderly categorization that recognized the distinction between absorption connected with growth and that which was a consequence of disease. Even without the benefit of microscopy Hunter was alert to the labile nature of bone. He referred to ‘modelling absorption’ - a concept we are inclined to think of as relatively modern - and said that ‘a bone cannot be formed without it, the new osseous part cannot be added ‘till some of the old is taken away’. Of particular interest to Dentistry is that Hunter’s curiosity was first aroused by features observed during the 6 years he spent working in dental practice with James Spence, a fellow Scot. In later years he said that the phenomenon of absorption first suggested itself to me in observing the waste of the sockets of the teeth, as also of the fangs of the shedding teeth, which was in the year 1754 and 1755.

He pointed out in his first book, Natural history of the human teeth7, that the absorption of alveoli in the elderly and of the roots of temporary teeth in children is not a change produced by pressure but is ‘a particular process in the animal oeconomy’. Resorption of transplanted teeth, like that of temporary teeth, was a subject of great interest to him. He described in detail how teeth that he had re-implanted underwent pitting and resorption (Figure 4).

The understanding of bone resorption was central to the concept of bone growth and must be accounted one of Hunter’s important contributions to pathology, no less than it is to physiology. Before Hunter, bone growth was assumed to be a general expansion either in length or girth - or both. Hunter, however explained that

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Figure 4. Hunterian specimens of transplanted teeth that had undergone different degrees of resorption. B was a premolar that had been extracted and a cavity filled before being reimplanted; the root then underwent complete resorption. (Courtesy of The Trustees of the Hunterian Collection)
bones do not grow by having new particles put into the interstices of previously formed parts... as, for instance, if I put a sponge into water, the water getting into all the interstices makes it larger.

The story behind Hunter's discoveries in this field are well known and need no detailed recapitulation here. In 1736 John Belchier, a surgeon at Guy's Hospital, first observed that the bones of pigs fed on madder, a vegetable dye used in the cloth industry, appeared to be stained. Hunter used this as a marker, his first experiment comparing the bones of two pigs fed with madder for 2 weeks. One of the animals, killed immediately thereafter, showed more staining periosteally than endosteally; the other, maintained for a further period without madder in the diet, showed staining endosteally but not periosteally.

This, and other experiments, convinced Hunter that combined resorption and deposition was the only mechanism by which bones could enlarge in size whilst maintaining their original shape. Apart from using madder as a marker of bone growth, Hunter devised a method of monitoring linear increase by implanting lead shot, the surviving specimen testifying to his ingenuity and his surgical skill (Figure 5).

It is worth mentioning, perhaps, that although Hunter's grasp of the principles underlying bone turnover was remarkably complete, there remained many unsolved mysteries. Abernethy, one of his devoted pupils, related that when the master was once asked how he could suppose it possible for abscesses to produce their effects, he replied 'Nay, I know not, unless they possess powers similar to those which a caterpillar exerts when feeding on a leaf'. This was a characteristically truthful response and Qvist has listed a series of instances in which Hunter has been at pains to expose his own mistakes.

Although the territories of physiology and pathology overlap to a considerable extent in Hunter's work on bone, it is evident that Hunter was constantly applying his new knowledge of deposition and resorption towards the understanding of disease. One such example from his dental experience is embodied in his advice to remove very loose or decayed teeth rather than anchoring them to adjacent teeth, in order to prevent absorption from spreading to their supporting bone. This was deductive reasoning arising from all the inductive philosophy embodied in his Classification of absorption. His understanding of the aetiology of both periodontal disease and dental caries was negligible, but his description of the clinical appearance of both these diseases from their inception to their outcome is wholly admirable. The very earliest sign of caries, a minute area of altered translucency in enamel, did not escape those aquiline powers of observation.

A good insight into his research activities is provided by Hunter's correspondence with his close friend, Edward Jenner, renowned for his work on vaccination against smallpox. Jenner lived in Gloucestershire and was a valuable source of wildlife of all descriptions. He and Hunter corresponded and exchanged views, specimens and works of art over a period of more than 20 years. Perhaps the most quoted phrase in this correspondence is Hunter's famous suggestion - 'try the experiment' - an exhortation to forego further speculation and put the hypothesis to the test.

There are many other gems but perhaps as good an example as any of Hunter's approach to biological enquiry is his correspondence with Jenner asking for specimens of hedgehogs and observations on their natural habits. This is an illustration of Hunter's inductive approach. Faced with the problem that hedgehogs sent by Jenner did not survive at his farm at Earl's Court, he first wished to ensure that they were properly fed. That having failed he sought to ascertain details of their body heat in Gloucestershire and bombarded Jenner with requests and suggestions. His next move, certainly, would be to cajole Jenner to send additional hedgehogs so that he could make similar measurements in Earl's Court. By these means he would hope to identify whatever factor might be making Earl's Court so much less suitable than Gloucestershire as a home for hedgehogs. We can be sure it would not have stopped there; just as General Gage's rectum came to be likened to the intestines of a turtle, so he would have envisaged that the lessons learned from Jenner's hedgehogs would come to be applied to his dissection of other animals - including humans. A later letter depicts that inatiable urge to satisfy his curiosity about the metabolism of hedgehogs. 'Dear Jenner' it begins, 'I received yours by Dr Hicks, with the hedgehog alive. I put it in the garden: but I want more."

Although Francis Bacon, the founder of the inductive approach, died about 100 years before Hunter was born, it is extremely unlikely that Hunter was influenced by his writings. He was positively averse to devoting time to the works of others and in view of his own vast output it is understandable that a review of the literature could not have commanded high priority. If it were not for this one might have thought that Hunter was strongly influenced by Bacon, so close is the parallel between Hunter's philosophy and Bacon's approach to natural science. Bacon took the view that scholasticism of the day, nourished on religious dogma, failed to explain natural phenomena and he initiated experimentation as the alternative. Hunter had an exactly similar distaste for enshrined pronouncements and Edward Jenner, for one, would surely attest to his addiction to experimentation. Bacon said that he thought his mind was nimble and versatile enough to seek out resemblances (such as a turtle's intestines and General Gage's rectum, perhaps) and that he had...
a desire to seek, patience to doubt, fondness to meditate, slowness to assert, readiness to consider, carefulness to dispose and set in order.

All of these attributes are uncannily similar to those that emerge from a study of Hunter's work and the evidence of his contemporaries; such as Abernethy\(^9\), for example, who said

In the whole of his labours and reasonings we may perceive a most diligent search for every fact belonging to the subject he was investigating and the most anxious solicitude to avoid the least misrepresentation of them.

Bacon may well have been the herald of modern science; Hunter, assuredly, announced the dawn of modern pathology.

These two great innovators share an interesting distinction. Hunter is portrayed for posternity at the Royal College of Surgeons of England in marble. The artist, George Weekes, a noted Victorian sculptor is, curiously enough, also the creator of Francis Bacon's marble image at Trinity College, Cambridge. In both statues the sculptor has succeeded in portraying an aura of contemplation that must have governed the lives of both these great men.

If a moment of fantasy can be permitted it is tempting to compare George Weekes' statue of Hunter with two other world renowned statues of thinkers. Michelangelo's Lorenzo di Medici (Il Penseroso) must surely be the greatest of them all and Rodin's *Thinker* perhaps the most widely known. Looking at the three together, I find little difficulty in imagining what Lorenzo and Rodin's *Man* were thinking of: Lorenzo, surely, was scheming two moves ahead of his current enemy's next ploy; Rodin's *Man* was brooding on whom or what he would kill for his next meal. Guessing Hunter's thoughts is a much more difficult problem. George Qvist\(^8\), in his valuable biography of Hunter, commenting on his versatility, said

At one moment he might be dissecting a bee and at the next, a whale. On one occasion he might be studying the insect larva on an oak leaf and the next, speculating on the age of the earth.

His insatiable curiosity might have been concentrated on a myriad of different biological phenomena.

A final thought should be devoted to motivation. What was it that persuaded this prodigious genius to devote his intellectual energies so unsparingly towards unravelling riddles of Nature? Perhaps a very simple answer comes in a phrase from one of his many letters to Jenner. He had, it seems, received in the post a parcel containing a cheese and a fish - but no letter to indicate the identity of the sender.

Dear Jenner he wrote, I beg for the future you will always write when you send me anything. Somebody sent me a cheese, with a fish upon it; perhaps it was you; *you know how I hate to be puzzled*.

It must indeed have been a powerful emotion to have launched and sustained studies of disease so far-reaching that their contribution to pathology persists to this day.

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