John Hunter and venereal disease

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Summary

John Hunter's contribution to the understanding of venereal disease is reviewed. Hunter's evidence for the unitary nature of these diseases is examined and the advances he made in diagnosis, pathology, and management are considered.

Introduction

Nowhere in the 18th century does the conventional surgeon-anatomist merge more completely into the experimental pathologist than with the career of John Hunter. He was the inspiration for both Dr Jekyll and Mr Hyde *(1)* and according to medical folklore he inoculated himself with the 'venereal poison', becoming a 'martyr to science' *(2)*. In the Miner Library verbatim notes of Hunter's lectures on venereal disease *(3)* there is the statement, 'I produced in myself a chancre', but it is unlikely that this is reliable as it was made at least 7 years after Hunter's death by an unknown student and may be a transcription error. Whatever its historical basis, the story illustrates the fact that Hunter's scientific beliefs arose after they had been verified by personal observation and experiment. His intimate experience of the subject is found in his observations when working between 1748 and 1760 with his brother, William Hunter. These observations were extended while serving as an army surgeon on Belle Isle and later in Portugal (1761–63), and further work was based on patients at St George's Hospital and in his private practice.

Unitary nature of gonorrhoea and syphilis

John Hunter's grounds for believing that gonorrhoea and syphilis were only one malady were various. It was his settled opinion that a patient presented with only one constitutional disease at a time *(4)*. This was the reason, he suggested, that florid measles suppressed the cell-mediated reactions following smallpox inoculation *(5)*. He conceded that more than one disease could be found in the patient but asserted that if this happened the diseases would not be found in the same part of the body. So when smallpox occurred in a patient already suffering from lues both diseases did not affect the same part *(4)*. He was therefore persuaded, in the interests of economy of diagnosis, that as both syphilis and gonorrhoea could be transmitted by sexual intercourse and often occurred together they were but one malady *(4)*. He explained that the different clinical symptoms and appearances of syphilis and gonorrhoea were determined by the part of the body that was affected *(6)*. When the skin was affected ulceration resulted, while if mucous membranes such as the vagina or urethra were involved in the disease process, then a discharge developed. His post-mortem dissections of the urethrae of two corpses, retrieved from the hangman, of men who had suffered from gonorrhoea revealed signs of purulent inflammation and no ulcers or 'absorbative reaction' *(7)* characteristic of syphilis *(8)*.

That gonorrhoea and syphilis were one disease was also suggested by an experiment undertaken in 1767 in which gonococcal matter produced a chancre *(9)*. In this experiment urethral pus was inoculated by lancet on to the surface of the prepuce and glans. An ulcer, followed by buboes, gradually developed. These manifestations were partially resolved by treatment with mercury. In Hunter's detailed description of this experiment it was found that in 2 days the patient had a 'teasing irritation' which developed into a visible red preputial spot by the 4th day. Seven days after inoculation the lesion began to slough and by the 11th day had progressed so far that lunar caustic and calomel dressings had to be applied. At about this time a spot on the glans was noted. The inoculation reaction resolved and at 4 months broke down again and became indolent, taking 3 years to heal.

Hunter put forward a further argument in favour of syphilis and gonorrhoea being the same disease—their epidemiology *(10)*. He noted that by the time Captain Cook visited the island of Tahiti on his last voyage both syphilitic chancre and gonorrhoea were prevalent there. In fact Cook described 'the accursed gonorrhoea and the little yellow jaundice (infectious

hepatitis) which was hard to account for' *(11)**. The natives of the island of Tahiti dated the onset of these diseases to the visit of Bougainville, whose ship had called at the island in 1768, staying for 9 days *(10)*. The crew had developed gonorrhoea, but not syphilis, 3 weeks after leaving the island. After Bougainville left the island it is recorded that the Tahitians retired to the interior of the island where gonorrhoea, unlike the 'pox', could be cured *(10)*. An earlier explorer, Wallis, who discovered the island in 1767, made no mention of gonorrhoea, despite spending 5 months on the island *(10)*. This lends support to the suggestion that Bougainville did introduce the disease to the island. It was also known that Wallis was concerned about the health of his sailors and had his crew inspected by the ship's surgeon before going ashore to ensure that they were free from the disease *(12)*. Hunter deduced that Wallis, who had been at sea for 11 months before arriving at Tahiti *(10)*, was unlikely to have brought gonorrhoea with him as the time spent at sea was longer than the incubation period for this disease, whereas Bougainville, who had left Rio de la Plata 5 months previously *(10)*, would have noticed if his sailors had developed penile chancre en route but might have overlooked mild gonorrhoea. Hunter was convinced that syphilis must have been transmitted in the form of gonorrhoea and then developed as syphilis on the island of Tahiti *(10)*. Hunter did not know that when Wallis landed on the island a Spanish merchant ship landed, unknown to Wallis, on the other side of Tahiti *(10)* and it has been suggested that it was these sailors who spread gonorrhoea throughout the island if the disease was not already present *(14)*. Gonorrhoea has been endemic there ever since *(15)*.

Inconsistencies in the theory that syphilis and gonorrhea were a common disease

The separate identities of syphilis and gonorrhoea were not settled until Ricord's experiments in 1837, when he inoculated 2500 'human volunteers' with gonorrhoea, none of whom developed syphilis *(16)*. Even today, nearly 200 years later, Koch's postulates for syphilis and gonorrhoea have not been fulfilled. Jesse Foot, a contemporary of Hunter's who criticised much of his work, accepted the theory of the single nature of the diseases without question *(17)*. Apart from the clinical differences between syphilis and gonorrhoea, Hunter also chose to ignore that their incubation periods were different and that mercury treatment discriminated between the two diseases, gonorrhoea being resistant and syphilis susceptible to this treatment. Hunter even argued that the specificity of mercury in the treatment of syphilis was evidence for the syphilitic nature of rheumatism *(18)*, which may have been bone gummata or periostitis, as the condition was subdued by treatment with mercury. Hunter recognised that immunity to reinoculation was a feature of syphilis *(19)*, while repeated episodes of gonorrhoea were frequent occurrences, implying that immunity to the gonococcal component of the disease did not develop.

When Hunter's inoculation experiment mentioned above was considered it was suggested by d'Arcy Power *(2)* that, as the lesion following inoculation of syphilitic material developed so quickly, the initial lesion might be chancroid. It is possible that the infection might have resulted from lack of aseptic precautions and the disease may have been rendered chronic by the application of topical medication. Furthermore, there is no evidence that the person inoculated refrained from sexual intercourse in the 3 years of observation and might well have contracted syphilis at a later date. It is unlikely that Hunter missed the diagnosis of an intraurethral chancre in the patient who was the source of gonococcal material for the inoculation experiment. He advocated the diagnosis of cowperitis by the clinical technique of palpation of the base of the penis *(20)*. If he had followed his own directions before beginning the experiment he would have detected the diagnostic intraurethral mass in the donor's urethra *(20)*. Lastly, it seems unlikely that Hunter experimented on himself since if he had inoculated himself with syphilis he surely would have treated himself with mercurials, which might have caused skin discoloration, and it is difficult to imagine that even if this treatment was taken in secret it would not have come to light. The postmortem reports on him indicate no pathological changes attributable to syphilis *(22)*. In addition, all his other inoculation experiments were on patients on whom he attended *(23)*. He was not, however, averse to self-experimentation and was known to have given himself madder root to discover whether his urine changed colour, which it did *(24)*.

Immunological observations

Hunter made a number of interesting observations on the immunology of syphilis. He was unable to produce lesions by inoculating the disease in patients with secondary syphilis, but he could do so during the primary stage *(19)*.

*Cook voyaged to Tahiti to observe the transit of Venus, not the transmission of her diseases.

He attempted a variety of challenge experiments: he was unable to produce syphilitic ulcers if material for autoinoculation was derived from patients with late secondary lesions but could invariably succeed if material from a chancre was used *(19)*. This may imply that fewer bacteria were present in the late secondary rashes, but Hunter believed that the inability to reinoculate was due to constitutional resistance *(19)*. In fact his view has been borne out by modern work which demonstrates that in secondary syphilis there is not only a suppression of cellular immunity in the infectious stage, which makes tuberculin-type (luetin) reactions unlikely to occur *(25)*, but even if a lesion does occur it would mimic the minimal lesions of secondary syphilis, the stage of the disease that the patient has reached. In contrast, during primary syphilis the luetin test tends to give a positive reaction and inoculation ulcers are produced *(25)*. Following Hunter, from the early 19th century until relatively recently, physicians regarded the lack of multiple autoinoculation lesions in syphilis as a diagnostic test for syphilis as compared with chancroid *(26)*. Hunter considered that the agent of syphilis was a morbid toxin which multiplied within the host *(27)*. Jesse Foot drew the analogy between this venereal toxin and snake venoms; snake venoms, although harmful to other species, never harm the snake *(28)*; so once the venereal toxin was present in the patient no further lesions would be produced in the event of a fresh infection.

Hunter's concept of the functions of lymphoid tissue was that lymph nodes might also be a barrier to further infection, especially as he conceived that skin ulcers resulted from absorption of noxious foreign matter *(29)*. Some of the lymph-node enlargements might also follow a reaction to infection *(30)*. Arguing that the syphilitic virus might pass up the lymphatics to the lymph node, Hunter applied mercury to the skin of the thigh adjacent to the enlarged syphilitic inguinal lymph node, which then regressed in size *(31)*. Hunter argued that this followed the local absorption of mercury to the lymph node. He may have been influenced in these experiments by the postmortem findings of Sheldon, who had delineated the lacteals by injection of mercury *(32)*. Hunter had already demonstrated the lacteals, with his brother William, by using indigo incorporated into milk which was then fed to animals. These animals, when killed, had blue-stained lacteals, having absorbed the coloured milk *(33)*. The analogy suggested by these experiments was that infectious agents might be removed and subsequently absorbed in the lymph nodes.

Observations on transmission of disease

Hunter had no doubt that the mode of transmission common to both syphilis and gonorrhoea was venereal. He deduced that gonococcal pus was infectious because if the pus was removed by washing from the urethra of the patient with gonorrhoea the sexual contact of that patient was less likely to acquire the disease *(34)*. It followed that if venereal disease were to be prevented it was preferable that onanism rather than natural sexual intercourse should be practised by infected partners *(35)*. Hunter also observed that syringes employed to treat gonorrhea transmitted the disease when used for rectal washouts, causing gonococcal proctitis in those patients *(36)*. After studying syphilis in infants he thought that the disease could not be transmitted congenitally *(37)*, although he was not unaware of transplacental transmission of disease since he had described a case of congenital smallpox *(38)*. Hunter was also accused of transmitting syphilis by tooth transplantation *(39)*. However, the reactions which resulted from this procedure were more likely to have been caused by the rejection of a small part of the tissue removed with the transplanted tooth, perhaps complicated by a foreign body reaction, than by syphilis. He was unable to transmit venereal diseases to animals, but his experiments were limited to asses and dogs *(40)*.

Clinical observations

Hunter described the relapsing nature of syphilis, loss of hair, and the palmar and plantar syphilides as well as the 'transparent' early (roseolar) skin rash *(41)*. He thought the distribution of lesions was enhanced in the colder parts of the body *(42)*; preference for lower temperatures may partially explain the distribution in man of the late secondary lesion such as condyloma. The ease with which the spirochaete is cultivated in the laboratory by inoculation into the rabbit testis may also be related to the testis being slightly cooler than other parts of the rabbit, enhancing the survival of *Treponema pallidum* at the site *(43)*. Hunter noted that deafness *(44)*, involvement of the eye *(45)*, and periostitis *(44)* might be caused by syphilis. He did not believe that the viscera and brain were affected *(46)*.

Hunter's postmortem investigations showed that although the terminal inch and a half of urethra might be free from the disease, lacunae were full of pus and might give rise to the sinuses at these sites *(8)*. He contrasted the lack of infection by gonorrhoea in the ovaries with the disease in the testes *(47)* but was acute enough to note that the testicular disease was an

epididymitis rather than an orchitis *(48)*; he failed to look for evidence of salpingitis. Hunter did not understand how gonorrhoea, which started in the urethra, spread to the testes. He proposed that 'sympathetic inflammation' accounted for the syndrome *(49)*. It is not surprising that Hunter recognised that urethritis could be associated with arthritis, 'the seat of rheumatism' *(50)*, as the syndrome was suspected by Hippocrates *(51)*. He described weakness and fainting following urethral instrumentation, which resembles the changes found in endotoxic shock *(52)*. He suggested that chordee followed dilatation (thrombosis) of the vessels of the corpora cavernosa penis *(53)*; Hunter thought that these changes were analogous to those described by Cuvier of dilated penile vessels of elephants after erection *(54)*. A dried preparation of an elephant's penis existed in the original Hunterian Collection at the Royal College of Surgeons of England. Everard Home, 22 years later, drew the analogy between these vessels and the dilated vascular network in the spleen *(55)*.

Guidance for treatment

Hunter's attitude towards treatment was very conservative. He observed that gonorrhoea was a self-limiting disease that resolved in 1 in 5 cases within 2 weeks and in 4 out of 5 cases within 2 months *(56)*. There was therefore no need to give any treatment other than supportive measures in the uncomplicated case. He was thus led to abjure the use of topical applications such as astringents, turpentine, vitriols, evacuants, and other nostrums such as 'dragon's blood' *(57)*. He arranged a clinical trial in which he showed that only 1 in 10 patients with gonorrhoea was helped by the treatment then available; his control group was given bread pills *(58)*. However, he lacked a statistical training and therefore did not hold with 'multiplying experiments to prove an already "obvious" proposition' *(59)*. Treatment should not be withheld if gonorrhoea was complicated by stricture of the urethra; dilatation was then recommended *(60)*. If dilatation of the urethra by bougies was ineffectual Hunter then advised that the urethra be opened above the level of the stricture and a probe be inserted to dilate the stricture from above rather than from below *(61)*. He knew that syphilis could not be cured without mercury, the specific antidote, but warned against toxic effects such as soreness of the mouth or discoloration of the skin *(62)*. He was aware of the Herxheimer reaction as he described a case with 'great debility, hectic heat and colliquative sweats' which occurred when treatment of a patient with buboes was begun, but if the mercurial treatment was continued rapid healing resulted without any constitutional disturbance *(63)*.

Conclusion

In the latter part of the 18th century venereal disease was managed with a mixture of hope, wild guesswork, and traditional ignorance. Hunter, with his passion for observing natural phenomena ranging from geology to comparative anatomy, included all disease, and particularly venereal disease, in this category. Hunter found venereal disease was a subject that merited study, making discussion of such diseases respectable in medical circles. The absorption and digestion of his pioneer research freed the subject from indifferent observation despite the efforts of argumentative if not perverse opponents. He is remembered for his rational technique in investigating venereal disease based on observation and experiment.

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