

The influence of John Hunter's inoculation practice on Edward Jenner's discovery of vaccination against smallpox

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John Hunter (1728-1793) preserved a record of some of his cases in surgery in his own hand, or the hand of an assistant, in a large folio volume. This was presented by Sir Everard Home, his brother-in-law, to the Board of Trustees of the Hunterian Collection in 1825. The notes were then transcribed, between 1825 and 1828, by hand into two volumes by William Clift, formerly Hunter's assistant and first Conservator of the Museum. The two volumes contain 419 case reports, of which 53 are headed 'inoculation'. This group, by far the largest, forms 13% of the total and contains Hunter's records of his experience in the use of the technique of inoculation against smallpox. Ten of these case reports are dated (Table 1) and it can be seen that they are in chronological order starting in 1758, the last being in 1781. One may assume that the remaining 43 reports were also in chronological order.

According to John Baron¹ Edward Jenner went to London in his 21st year to study under John Hunter, with whose family he resided for 2 years. Jenner was born in May 1749. Thus, he would have been Hunter's house pupil during 1770 and 1771, the period covered by some of these case reports. Baron¹ states that Jenner was aware of the prophylactic powers of cowpox against smallpox while he was a student of Hunter and mentioned the subject to Hunter during his pupilage. George Pearson, physician and contemporary of Hunter at St George's Hospital, wrote in 1798² 'When I was in company with the late Mr John Hunter, about nine years ago, I heard him communicate the information he had received from Dr Jenner . . . and that no patient had been known to die of the cowpox, the practice of inoculation of the poison of this disease, to supersede the smallpox, might be found, on experience, to be a great improvement in physic.' Among the Hunterian Drawings at the Royal College of Surgeons there is

a coloured drawing of a finger bearing a pustule, inscribed in what appears to be Hunter's handwriting 'Cow or swine pock.' Ottley³ suggests that it was given to Hunter by Jenner in 1788. Jenner reminisced affectionately to Baron about the time he spent with Hunter during his youth. There is, however, no mention of Hunter's inoculation practice in Baron's¹ recollections or in the Hunter-Jenner letters. Baron¹ in his *Life of Edward Jenner MD LLD FRS* (1827), much of which he obtained from his close association with Jenner in his latter days, fails to mention Hunter's inoculation practice. He does, however, devote a whole section to the first publication of the practice by Timoni⁴ and its popularization by Lady Mary Wortley Montague between 1717 and 1722. He also mentions the practice of Daniel Sutton and Thomas Dimsdale.

Daniel Sutton and his brother Robert Sutton regularized the procedure of inoculation to make it safer. They worked as professional inoculators subsequent to 1765 in Suffolk and Essex, about the same time as Hunter, and concentrated on a regimen that used one puncture only, a spare diet, refrigerant drinks and fresh air⁵. They are reputed to have inoculated 17 000 people with only 5-6 deaths⁶. Their technique was followed by Thomas Dimsdale⁷ who prescribed a regimen containing no animal foods, fermented liquors, or spices during the 2 weeks before inoculation when they were given three doses of a powder containing calomel (8 g), crab's claw (8 g), and tartar emetic (1/8 g). The calomel was given to deworm the patient.

In case 200, Hunter describes a Mrs Neal inoculated by Sutton 'very full, escaped with great difficulty' indicating that she developed severe smallpox on inoculation and had a very difficult recovery. Dimsdale, who started an extensive inoculation practice in 1761, published his technique in 1766. He was well known for being invited by Catherine the Great to St Petersburg to inoculate the Imperial Russian Court, for which he was ennobled. In case 229 Hunter refers to the child of the Hon^{ble} and Rev^d Mr Harley who was inoculated by Dimsdale and did not develop smallpox in the area covered by a flannel waistcoat, but only on the exposed areas of the face, forearms, legs, etc.

Hunter describes 10 deaths out of the 89 individual patients recorded, two of these were not in his own cases. In one case there was an intercurrent infection with measles and in another, a child at the breast, that had difficulty in breathing and sucking. The other eight died of an overwhelming infection with smallpox. All the fatal cases were in small children. Fifty-nine of the patients recorded were children,

Table 1. Dated cases

Case number	Date
188	1758
215	1767
221	1774
225	1775
227	1776
230	Feb 1777
231	Feb 1777
237	1779
247	May 1781
249	Nov 1781

Table 2. Age of children inoculated (where given)

	Number
Under 1 year old	15
Over 1 year under 2 years old	5
Over 2 years under 11 years old	25

many of whose ages are given (Table 2). As 20 were under 2 years old, the youngest was 6 weeks, it is interesting to note that Dimsdale⁷ declined to inoculate children under two years of age unless pressed. However, he states that those he inoculated under this age did well. The proportion of fatal cases described by Hunter does not give an indication of the mortality rate in his hands. Hunter describes only cases of interest in his reports and, thus, they cannot be used as statistical evidence for disease incidence in his practice. Sutton's reputation has been mentioned above. A truer incidence is that of Benjamin Franklin⁸ who cites two deaths out of 338 inoculated, one of whom died of 'worm fever'; this is an incidence of 0.6%. The incidence with different operators would depend upon case selection and those with an upper and middle class practice might be expected to have had better results. There is no doubt that malnutrition would produce a higher mortality rate. However, with mortality figures under 1%, inoculation could be considered to be a relatively safe procedure for its time.

The technique of inoculation used by John Hunter was not dissimilar to that described by Timoni⁴. He made a scratch on each arm and inserted a thread steeped in material from a smallpox or inoculation pustule. The threads stuck to the scratch and he did not remove them until the second or third day. This technique differed from that of the Suttons who used one incision; Dimsdale⁷ used one incision to both arms, or two incisions in one arm. The incision was usually made with a lancet. The pock usually took about a week to develop. Between 10 and 14 days after inoculation, the patient might develop a generalized eruption, often preceded by fever and constitutional symptoms. Hunter describes a generalized eruption in 52 cases and constitutional disturbance of varying degrees in 57. Seven children had epileptiform fits during the febrile phase. These occurred in children up to 3 years of age.

In a few cases there was no generalized eruption and the site of inoculation became inflamed between 2 and 3 days after inoculation, but did not 'fill up', and became a true pock between 7 and 14 days. This type of reaction was, no doubt, the 'accelerated reaction' or 'reaction of immunity' investigated in depth by Von Pirquet⁹ in relation to cowpox vaccination and shown to be an allergic reaction of the form known now as delayed type hypersensitivity. This type of hypersensitivity reaction can frequently be correlated with the development of resistance to further infection.

It would appear that the fever was no worse following inoculation than that which later occurred with vaccination, nor was the risk of an epileptiform fit any greater. These complications are mentioned by Hunter because they were events that needed to be emphasized as being noteworthy. The main difference between vaccination and inoculation, which led to the former technique superseding the latter, was

not a decreased mortality rate, nor even morbidity, but the virtual absence of dissemination of the lesions so that there was no risk of the subjects developing unsightly pock marks, particularly on the face.

Finally, there is evidence in a number of case reports of Hunter as the experimental scientist. In one series of cases inoculated with material from the same source, he showed that the course of the disease produced was not affected by diet, drugs, or the use of one as opposed to two incisions. In another case he observed that material from a smallpox pock that developed after inoculation was more effective than material taken directly from the lesion forming at an inoculation site in a subject who developed only a local lesion. He observed that the lesion that developed from the material derived from the smallpox pock developed faster than that which developed from material derived from the inoculation site. On other occasions he noted that material from the same source could produce a severe effect in one individual and a mild effect in another. In a further case Hunter noted that material from the same individual from a pock, produced a local lesion, whereas material from the inoculation site of the same donor produced no lesion in the same recipient.

In conclusion, there seems to be no doubt that Edward Jenner must have observed John Hunter's inoculation practice and discussions between them on the use of cowpox are on record. The overriding question is as to why Jenner waited until 1798 to complete his experiments and publish his results - 5 years after Hunter's death? In view of the low mortality rate of the procedure of inoculation, which in the hands of the Suttons was reputed to be only five out of 40 000¹⁰, one wonders whether Hunter might possibly have been a little less than enthusiastic about the introduction of this new procedure. Moreover, there is the possibility that the virus strain used in inoculation had become to some degree attenuated by intradermal inoculation and, thus, was producing a milder effect in the individual¹¹.

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