The origins of inoculation

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DECLARATIONS

Competing interests
None declared

Funding
None

Ethical approval
Written informed consent was obtained from the patient or next of kin

Guarantor
AB

Contributorship
AB is the sole contributor

Acknowledgements
Additional material is available from the James Lind Library website (http://www.jameslindlibrary.org), where it was originally published

Early in the 18th century, variolation (referred to then as 'inoculation') was introduced to Britain and New England to protect people likely to be at risk of infection with smallpox. This triggered a number of important developments. Among them were early examples of what we refer to today as 'evidence-based medicine' – immunization, and quantitative measures of disease severity.

Establishing the protective effects and subsequent spread of variolation paved the way for recognition that inoculation with cowpox (vaccination) also conferred protection. The definitive experiments that established that vaccination was protective showed that variolation did not 'take' following vaccination, thus confirming that immunity had been achieved. Vaccination led ultimately to the eradication of smallpox, one of the great achievements of medicine. Given the central role of variolation in these significant events, it is worth investigating where the practice originated.

Inoculation in parts of the Ottoman Empire and Europe

Working backwards in time from the first variolations in Britain and colonial Massachusetts in 1721, it is possible to trace the practice back for at least a century in parts of the Ottoman Empire and Europe. In 1714, a letter written by Emanuel Timonius at Constaninople was circulated around Europe and read to the Royal Society by John Woodward.

> *'The writer of this ingenious discourse observes, in the first place, that the Circassians, Georgians, and other Asiatics, have introduced this practice of procuring the smallpox by a sort of inoculation, for about the space of forty years, among the Turks and others at Constantinople.'*
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> *'That although at first the more prudent were very cautious in the use of this practice; yet the happy success it has found to have in thousands of subjects for these eight years past, has put it out of all suspicion and doubt; since the operation, having been performed on persons of all ages, sexes, and different temperaments…none have been found to die of the smallpox.'*
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> *…They that have this inoculation practised upon them are subject to very slight symptoms, some being scarce sensible they are ill or sick: and what is valued by the fair, it never leaves and scars or pits in the face.'*[1]

When this was published in the Philosophical Transactions of the Royal Society it triggered a reply from Cotton Mather, a minister in Boston, Massachusetts.

> *'I am willing to confirm to you, in a favourable opinion, of Dr. Timonius' communication; and therefore, I do assure you, that many months before I met with any intimations of treating the smallpox with the method of inoculation, anywhere in Europe; I had from a servant of my own an account of its being practised in Africa. Enquiring of my Negro man, Onesimus, who is a pretty intelligent fellow, whether he had ever had the smallpox, he answered, both yes and no; and then told me that he had undergone an operation, which had given him something of the smallpox and would forever preserve him from it; adding that it was often used among the Guramantese and whoever had the courage to use it was forever free of the fear of contagion. He described the operation to me, and showed me in his arm the scar which it had left upon him; and*

his description of it made it the same that afterwards I found related unto you by your Timonius.'[2]

Onesimus was a Guaramante from what is now southern Libya, who had been given to Mather by his parishioners in 1707. Mather said that he had had this conversation with Onesimus many months before he read the Timonius report. Mather's comments were amplified by another minister, Benjamin Colman, who described his conversations with several negroes who had also been inoculated in Africa.[3] Subsequently, in 1716, a well respected physician, Jacob Pylarinius, also writing from Turkey, reported that inoculation had been introduced into Constatinople by a Greek woman about 1660. It had been widely used by poor Christians until, during a severe smallpox epidemic in 1700, the practice spread throughout the Christian community more generally.

Pylarinius claimed that variolation was not used by Muslims because it was believed by them to interfere with divine providence.[4] However, this cannot have been a universal belief because it was being used by Arabs in North Africa before 1700, as recorded in a letter originally written in Arabic by Cassem Algaida Aga, the ambassador from Tripoli to the Court of St James. His letter was translated and subsequently published in a book by John Gaspar Scheuchzer, Foreign Secretary of the Royal Society[5]:

My opinion being asked relating to the Inoculation of the Small-Pox, I will mention in a few Words what I know of it. If anyone hath a Mind to have his Children inoculated, he carries them to one that lies ill of the Small-Pox, at the Time when the Pustules are come to full Maturity. Then the Surgeon makes an incision upon the Back of the Hand, between the Thumb and Fore-finger, and puts a little of the Matter, squeezed out of the largest and fullest Pustules, into the Wound. This done, the Child's Hand is wrapp'd up with a Handkerchief to keep it from the Air, and he is left to his liberty 'till the Fever arising confines him to his Bed, which commonly happens at the End of three or four Days. After that, by God's Permission, a few Pustules of the Small-Pox break out upon the Child. All this I can confirm by a domestick Proof: For my father carried us, five Brothers and three Sisters, to the House of a Girl that lay ill of the Small-Pox, and had us all inoculated the same Day. Now he that had most of us all, had not above twenty Pustules. Otherwise this Practice is so innocent, and so sure, that out of a hundred Persons inoculated not two die; whereas on the contrary, out of a hundred Persons that are infected with the Small-Pox the natural Way, there die commonly about thirty. It is withal so ancient in the Kingdoms of Tripoli, Tunis and Algier, that no body remembers its first rise: and it is generally practised not only by the Inhabitants of the Towns, but also by the wild Arabs.'[5]

Lady Mary Wortley Montague, the wife of a British diplomat in Constantinople, discovered that variolation was widely practised in Turkey and that it was considered safe and effective in preventing fatal smallpox. She had her son inoculated by an old Greek practitioner, and in April 1721, back in England, she asked Charles Maitland, a Scottish surgeon who had been with her in Constantinople, to inoculate her daughter.[6,7] This prompted intense interest in inoculation in England, and, in 1723, James Jurin, Secretary to the Royal Society, published the results of his multinational survey of mortality rates following variolated and natural smallpox.[8]

The most surprising evidence was submitted by two Welsh doctors, Perrot Williams and Richard Wright, who wrote that the practice was well known and had been used over many years by many individuals in and around the port of Haverford West.[8] Richard Wright reported that many among the common people in the region considered variolation an ancient practice, and that he knew a man aged about 90 who had been variolated as a child, as had his mother before him, who had told him that variolation was a common practice throughout her time. Since Wright's letter had been written in 1722, and assuming the 90-year old had been inoculated as a child, variolation appears to have been in use in Wales since at least as early as 1600.

In many cases the operation was performed by buying a few scabs or pus from someone suffering from natural smallpox and then puncturing the skin with a needle which had been contaminated with the smallpox matter. Some individuals just rubbed the scabs on their own skin, and in at least one case (Williams, in Jurin 1723) a school

boy had scraped the back of his hand with a penknife until it bled and then rubbed the scabs into the wound. All witnesses agreed that they had had mild smallpox and had never had the infection a second time. A midwife said that, during the previous fifty years, she had only heard of one person who had died following the operation. A similarly low mortality was reported from Constantinople where multiple shallow needle punctures were used to transmit the infection.[1]

Several other descriptions of a practice known as 'buying the pocks' exist and record its use in Scotland and mainland Europe.[9] While they all agree that money or goods were exchanged for the pocks, the descriptions of how the operation was carried out are inconsistent. In Scotland, wool contaminated with smallpox material was wrapped around a child's wrist. Elsewhere, smallpox scabs were held for some time in the child's hand.[9] Still others had the child wear smallpox-infected clothes. Despite evidence that 'buying the pocks' was widespread in Europe, inoculation did not penetrate deeply into life before it was introduced from Constantinople early in the 18th century.

A comprehensive investigation of the practice and spread of inoculation in the Ottoman Empire was carried out by Patrick Russell, an English doctor living in Aleppo.[10] By interviewing women in harems, their bedouin servants, and many merchants from as far east as what is now Iraq, Russell established that inoculation was used almost everywhere outside the bigger cities such as Constantinople and Aleppo. It was proscribed in the cities by the Turks, whom Russell dubbed 'fatalists' because they believed that providence forbade them to interfere in divine intentions.

Russell also requested help from several doctors and historians to discover whether they could find evidence of the first use of inoculation, and where it had originated. They all agreed that, while the practice was thought to be very old, there was no mention of it in any medical or historical works. Russell had produced an interesting puzzle. Why was something so beneficial, which was employed throughout much of the Ottoman Empire, completely missing from written records of the time?

Combining these various accounts of inoculation in several a parts of Europe, Africa, and Asia reveals another curiosity. The practice was known widely as 'buying the pocks', regardless of the technique actually used to transmit the disease. Whether the skin was broken, or the pocks just held in the hand, or even, when a 'pocky thread' was tied around a child's wrist, the same words were used. Although pocks were usually 'bought' – that is, paid for with money or small gifts – this was not always the case and yet the same terms were used to refer to the process.[8–11] A second common feature is that, with few exceptions, a needle was used to prick the skin, often in a circular pattern. Such common features suggest that inoculation (the term was applied when the practice was introduced into England and America) probably had a single origin and that the name and technique spread with it.

Inoculation in China and India

Inoculation had become established in the Ottoman Empire and Wales since 'time immemorial', and had reached Constantinople by about 1650. But where had it come from? Two possible origins have been suggested: China or India. The earliest written discussion of variolation in China is found in a book first published in 1549.[12] Joseph Needham, who investigated the origins of inoculation in China, believed that, because the author commented on the possibility that variolation induced menstruation, the practice must have already been well known, if little written about. Several other slightly later Chinese authors complain that many inoculators would not reveal their secrets. As a result, it is difficult to establish exactly what was happening and when it had begun in China. One of Needham's texts reports that variolation was first practised between 1567 and 1572, and that it had been invented by an 'extraordinary man' who had based it on alchemical principles. Thereafter several families became hereditary inoculators but, for commercial reasons, refused to reveal their secrets.

In the second half of the 17th century, the Khang-his emperor boasted that he had inoculated his whole family, his army, and other groups, and that they had all passed through mild smallpox. Also, at about this time, manuals

setting out the techniques of inoculation were published. Remarkably they all were based on blowing smallpox material up the nose of the child being inoculated (insufflation). Sometimes dry scabs were ground to powder; at other times the scabs were extracted into water, and yet another approach was to collect fluid from a pustule onto a cotton plug and place that up the nose.

Needham also describes an even older, but much less well documented, tradition of inoculation in China.[12] In this version it was invented by a Taoist or Buddhist monk, or possibly a nun, about 1000 AD and practiced by Taoists as a mixture of medicine, technique, magic, and spells which were transmitted orally and which were covered by a taboo so that they were never written down. Needham can give no firmer evidence for this version than the fact that it was a widely accepted tradition. An editorial commentator wonders whether it is realistic to believe that something with the importance of inoculation would have remained completely secret for over 500 years.[12] The only certainty is that there were written accounts of inoculation by the mid 1500s. At all events, although a description of the Chinese method of insufflation of smallpox material up the nose had reached England in 1700, it appears to have had little practical impact.[6]

India is an alternative to China as the origin of the spread of inoculation to the Ottoman Empire and Europe. Two 18th century accounts by early English residents in India give descriptions of inoculations done by itinerant Brahmins.[13,14] Their technique involved dipping a sharp iron needle into a smallpox pustule and then puncturing the skin repeatedly in a small circle, usually on the upper arm. Writing in 1731, Oliver Coult reported that the operation had been 'first performed by Dununtary, a physician of Champanagar', about 150 years previously (that is, about 1580), and that Dununtary had learned of the secret in a dream.[13] However, this story may be problematical because a Dutch correspondent reported that inoculation was not used in Bihar, the Indian province which includes the city of Champanagar.[11] All three commentators on Indian practice agree that inoculation was used in Bengal, the region that includes modern West Bengal in India and Bangladesh. Howell, thought that it had been used there for many hundreds of years.

Many modern texts claim that inoculation had been practised in India for thousands of years .[15] These accounts are based on claims that the practice is described in ancient Sanskrit texts. However, although there are detailed descriptions of smallpox and its treatment in ancient Indian texts, there is no evidence in these that prophylactic measures were used. [16,17]

Conclusions

There are two accounts of inoculation in the middle of the 16th century, one Chinese and one Indian, and each gives a specific place and name to the initial inoculators. Whether it was in use before about 1550 is entirely speculative. So from where and how did inoculation arrive in parts of the Ottoman Empire and Europe during the 17th century?

The Chinese method involved blowing smallpox matter up the nose. Extant recipes[12] show that the 'pocky matter' should be carried at body temperature for a month before it is used. If that was not possible then it could be exposed to hot steam and various herbs. Both these processes would have damaged many of the smallpox virus particles, thus greatly reducing the infectious load transmitted. Without them the process was probably dangerous and little different from a natural infection. On the one recorded occasion when the Chinese method was tried in London, the recipient had severe headaches and the experiment was never repeated.[6]

On the other hand, the marked similarity of the methods used in India and in many parts of the Ottoman Empire, argue that they share a common origin. It is difficult to see how the Chinese method could have been modified to produce it. But this still does not tell us where or how it was first developed. Since the claim that it was an ancient practice in India has been rejected, there is no reason to assume that it began there. Perhaps the traditions of the Ottoman Empire are correct: it was invented by the Arabs[11] at some unknown time before about 1550, and then spread along trade routes through Africa and the Middle East to reach India.

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