Inoculation and the Decline of Smallpox Mortality in London during the Late Eighteenth and Early Nineteenth Centuries.

Summary

Davenport, Boulton and Schwarz have presented evidence for two London parishes and for Manchester to show that there was an increasing concentration of smallpox amongst young infants, arguing that this resulted from a growth in the disease's infectiousness, although this has been contested by Razzell.[1] The aim of this paper is to summarize all the existing evidence, as well as data on two other London parishes and other areas in England. The overall evidence suggests that there was no such concentration of smallpox amongst young infants. There is however agreement that adult smallpox burials largely disappeared in London at the end of the eighteenth century. It is argued here that these changes were due to the practice of inoculation (variolation) in London and its rural hinterland. It is also concluded that early vaccination was a form of attenuated inoculation, and that it was inoculation rather than classical vaccination which was responsible for the decline of smallpox mortality in London at the end of the eighteenth and beginning of the nineteenth century.

Keywords: smallpox, mortality, inoculation, London, vaccination.

Introduction

There were difficulties in the registration of smallpox in the eighteenth century, and as Dr Percival wrote in 1758:

> A considerable number of those who die of the natural disease [of smallpox], before the expulsion of the variolous eruption, are infants or very young children … Hence the convulsive paroxysms which often precede the appearance of the pustules … are always alarming, and when they happen to very young infants are frequently fatal.[23]

[1] R.J. Davenport, Leonard Schwarz and Jeremy Boutlton, 'The Decline of Adult Smallpox in Eighteenth Century London', *Economic History Review*, 64 (2011), 1289-1314; Peter Razzell, 'The Decline of Adult Smallpox in Eighteenth-Century London: a Commentary', *Economic History Review* 64 (2011), 1315-1335; R.J. Davenport, Jeremy Boulton and Leonard Schwarz, 'Urban Inoculation and the Decline of Smallpox Mortality in Eighteenth Century Cities – a Reply to Razzell', *Economic History Review*, 69 (2016), 188-214.

[2] Peter Razzell, *The Conquest of Smallpox: the Impact of Inoculation on Smallpox Mortality in Eighteenth Century Britain* (London: Caliban Books, 2003), 137.

Subsequently in 1793 Haygarth confirmed the importance of convulsions resulting from smallpox, and the way they distorted the statistics of mortality:

> The disease most fatal to infants is convulsions, arising from various causes; one of them is the small-pox. The two circumstances will explain the reason why, under one year old, the proportion of deaths by the small-pox is less than in subsequent periods…[4]

Lettsom estimated that smallpox mortality in London was twice that recorded in the Bills of Mortality, 'the generic article convulsions having swallowed up, in his opinion, a large number of smallpox deaths of infants.'[5] However, there is no evidence that the registration of convulsions associated with smallpox changed significantly in the late eighteenth century, but it does mean smallpox statistics must be treated with a degree of caution.

Migration In To London

Adults living in the hinterland of London greatly feared moving into the city, as revealed by the following account published in 1767 on the impact of inoculation on migration into London:

> Inoculation for the small-pox has so very much prevailed in the country, that thousands and ten thousands have escaped the fatal effects of that distemper in the natural way: but what are the consequences of so good an invention? No sooner are the lower sort recovered, but they aim (the women especially) to get a servitude in London, or to use their own words to better themselves; this is the only objection that can be made to inoculation, and indeed it is one, for before they did not dare to quit the place of their birth for fear of that distemper, so remained honest and useful in the country …[6]

The movement of people into London who were exempt from smallpox as a result of inoculation had a significant effect on mortality in the metropolis. In 1778 Dimsdale predicted the effect as follows:

> ... it will seem extremely probable, that the Small Pox is already arrived at its utmost pitch in respect of deaths within the Bills of Mortality, and that we can expect an abatement on this head, for the obvious reason, that one source will be stopped by the extensive practice of general Inoculations in the country, which have prevailed in

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[3] Peter Razzell, *The Conquest of Smallpox: the Impact of Inoculation on Smallpox Mortality in Eighteenth Century Britain* (London: Caliban Books, 2003), 137.
[4] J. Haygarth, *A Sketch of a Plan to Exterminate the Casual Smallpox* (London: 1793), 141.
[5] Charles Creighton, *A History of Epidemics in Britian*, 2 (Cambridge: C.U.P.,1965) 534; J.C. Lettsom, *A Letter to Sir Robert Barker and George Stacpoole Esq, upon General Inoculation* (London: 1778),5.
[6] Peter Razzell, *The Conquest of Smallpox* (London: Caliban Books, 2003), 81, 82.

> a remarkable manner within the last two years in the counties of Bedford, Bucks, Herts, and Cambridge, and others contiguous to London; and these patients have been generally such inferior persons as may be supposed to supply London. To such an extent has this practice been carried, that I imagine the number must amount to many thousands...[7]

The age profile of these immigrants is suggested by the proportion of adults over the age of twenty-one dying from smallpox in these rural hinterlands.

Table 1: The Proportion of Adult Smallpox Deaths in the South of England.[8]

Place	*Period*	*Proportion of Adult Smallpox Deaths*
Basingstoke, Hampshire	1675-1803	56%
Riseley, Bedfordshire	1690-1742	44%
Godalming, Surrey	1701-23	50%
Calne, Wiltshire	1704-58	39%
Tenterden, Kent	1712-41	78%
Banbury, Oxfordshire	1718-19	40%
Breamore, Hampshire	1720-1803	83%
Aynho, Northamptonshire	1723-24	69%
Great Shefford, Berkshire	1751-67	34%
Rayleigh, Essex	1753	72%
Southampton, Hampshire	1753-61	54%
Bury St. Edmunds, Suffolk	1756-57	42%
Burford, Oxfordshire	1758	46%
Cuxham, Oxfordshire	1772	75%
Horton Kerbie Kent	1772-1801	100%
Thanet, Kent	1774-89	2%
Sutton Courtenay, Berkshire	1782-1811	67%

About a half of all smallpox deaths in the south of England were of adults. The disease was widely avoided when present in market towns and other places of high visibility in these areas,[9] and this may have been one of the reasons why it was a disease of both adults and children in these rural and provincial southern districts.

The practice of general inoculations confirms the age profile of smallpox in the south. For example, in Diss Norfolk in 1784 the people inoculated ranged from 'one month to between eighty and ninety years'; in Brighton Sussex in 1786 'One to Near Four Score

[7] Thomas Dimsdale, *Observations on the Introduction of the Plan of the Dispensary for General Inoculation* (London: W.Owen, 1778), 125, 126.
[8] Razzell, *The Conquest of Smallpox*, xii, xiii.
[9] *Ibid*, 145, 146.

Years'; in Weston Norfolk in 1788 'old folks, and even women with child, have been inoculated'; and in Dursley, Gloucestershire in 1797 the inoculated were 'of all ages, from a fortnight old to seventy years.'[10] Likewise, many members of the militia and the army in the South of England were inoculated in the 1790s, confirming the presence of smallpox amongst adults at this time.[11]

These populations were of all ages, and formed the basis of the migrants entering London at the end of the eighteenth century. After they had been inoculated they were exempt from the disease, partly accounting for the disappearance of adult smallpox deaths in the metropolis during this period.

Age Profile of Smallpox Deaths in London and Manchester.

Davenport et.al. have used data from the St. Martin's Burial Register and Stepney's Sexton's Register to argue that there was increasing endemicization of smallpox in London. Both registers suffer from poor registration. In St. Martin's there was a gap between 1766 and 1775, an important period for the author's thesis on increasing infectiousness. In Stepney's register, there was no information on children dying under the age of two before 1774, or any information age and the child/adult status of smallpox victims in the period 1757-73, a central period for their argument. The following is an analysis of smallpox burial ages in Stepney for the post-1774 period when such data is available.

Table 2: Distribution by Age of Smallpox Burials (Per Cent) in St. Dunstan's Stepney, 1774-1808.[12]

Age Group	Period			
	1774-79	1780-89	1790-99	1800-08
≤1	22.3	21.7	24.2	22.8
≤2	21.8	17.3	17.4	24.4
≤3	18.9	16.8	17.7	16.8
≤4	12.4	14.2	13.7	10.8
≤5	16.2	6.7	9.3	9.2
≤10	9.6	13.0	12.1	10.0
0<20	2.0	2.3	1.6	2.8
0+	2.8	8.1	4.0	3.2
Total Number of Cases	354	346	322	250

There is no significant change in the proportions of infants dying from smallpox, and except some decline in adult smallpox, Table 2 does not support the endemicization

[10] *Ibid*, 118, 122.
[11] Razzell, 'The decline', 1319, 1320.
[12] The source of this table is the St. Dunstan Stepney Sexton's Burial Register.

thesis. Data for another London parish with continuous data from 1760 to 1812 – St. Mary Whitechapel – also shows no increase in infant smallpox burials, although there was a significant fall in adult burials.[13]

Additional evidence on age incidence is now available for another London parish. The burial register of St. John's Wapping provides a complete list of the ages of smallpox burials in the period 1763-1802 – with nearly 100% coverage – listing ages to the nearest month, which when analysed yields the following results.

Table 3: Distribution by Age of Smallpox Burials (Per Cent) in St. John Wapping, 1763-1802.[14]

Age Group	Period				
	1763-67	1768-72	1773-82	1783-92	1793-1802
≤1	19.9	22.1	9.1	0.5	1.2
≤2	15.7	20.0	7.2	7.8	3.6
≤3	18.7	10.0	0.6	5.2	3.6
≤4	8.4	15.0	7.2	.3	7.8
≤5	9.6	8.6	.3	.9	.8
≤10	9.0	9.3	.3	.3	0.2
0<20	3.0	3.6	.0	.0	.7
0+	15.7	11.4	.4	.9	.1
Total Number of Cases	166	140	04	51	18

There was a long-term fall in the number of adult smallpox burials between 1768-72 and 1793-1802, largely confirming earlier evidence on the subject. There was however no linear trend in the concentration of smallpox burials amongst infants under the age of one, and no significant change before and after 1770, which the authors argue was the watershed for increasing infectiousness. Overall, Table 3 does not suggest a significant change in the age incidence of children dying from smallpox, although it confirms the sharp decline in adult burials between 1763 and 1802.

Davenport et.al. produce evidence to show that there was increasing concentration of smallpox deaths in infants under the age of one in St. Marys, St Denys and St. George Collegiate Church Manchester. Their figures are as follows: 1753-61: 18.9%; 1772-8: 32.7%; 1785-91: 29.2%; 1803-7: 32.3%.[15] There is a sharp rise between 1753-61 and 1785-91, and after that latter period the proportion of young infants dying of smallpox remains stable. It is possible that the increase between 1753-61 and 1772-8 is a result of growing mortality due to the increasing virulence of the disease, as the disease was

[13] Razzell, 'The decline', 1316.
[14] The source for this table is the St. John Wapping Burial Register. I would like to thank Ramola Davenport for sending me the raw data on which this table is based.
[15] 'Davenport et.al., 'Urban inoculation', 195.

particularly lethal to young infants.[16] The authors also produce figures for St. John Deansgate Manchester which show no long-term increase in infectiousness – from 23.4% in 1769-99 to 22.9% in 1800-12.[17]

There is other evidence to indicate that smallpox did not become more concentrated in very young infants in other urban areas at the end of the eighteenth century. The burial register of Holy Trinity Whitehaven – a town with a population of 8,712 in 1801 – recorded the ages of smallpox burials in the period 1751-81.

Table 4: Distribution by Age of Smallpox Burials (per cent) in Holy Trinity Whitehaven, 1751-81. [18]

ge Group	*eriod*			
	751-58	759-68	769-75	776-81
≤1	6.0	6.7	.4	.2
≤2	9.1	1.7	6.3	6.9
≤3	7.9	2.4	3.0	3.5
≤4	9.1	6.1	0.0	4.6
≤5	1.7	.6	.2	.4
≤10	7.5	.5	.9	.5
0+	.5	.9	.2	.8
Total number of cases	62	61	35	30

There was a significant decrease in the proportion of young infants under one dying from smallpox between 1759-68 and 1776-81, although this was counter-balanced by an increase in the percentage of children dying aged from one to two between 1751-58 and 1776-81. Table 4 does not indicate an overall increase in infectiousness of smallpox in the period after the 1760s.

The authors have argued that Swedish data that does not refute the endemicization thesis as it covers the period 1776-1805, and their argument is that the concentration of smallpox amongst young infants took place from the 1760s onwards.[19] However, there is evidence that age incidence was constant in Sweden during the period 1756-60 to 1788-92.

[16] For growing mortality in Manchester see Davenport et.al., 'Urban inoculation', 199;for increasing virulence see Razzell, *The Conquest*, 175-179; for case-fatality rates amongst children see *Ibid*, xviii.
[17] Davenport et.al., 'Urban inoculation', 195.
[18] The source for this table is the Holy Trinity Whitehaven Burial Register.

[19] Davenport et.al., 'Urban Inoculation', 194, fn. 24.

Table 5: Age Distribution of Smallpox Mortality (per cent) in Sweden, 1756-1810.[20]

Period	*Age Group*						
	0	1-2	3-4	5-9	10-24	25-49	50+
1756-60	30.3	31.0	18.5	13.9	5.5	0.6	0.2
1788-92	30.5	31.5	19.3	13.4	5.0	0.3	0.1
1806-10	27.3	32.4	18.3	16.0	5.3	0.5	0.3

This data indicates not only that age incidence was constant, but that there was a decline in the proportion of infants dying from smallpox under the age of one between 1788-92 and 1806-10. Table 5 therefore does not indicate an increasing endemicization of smallpox after the 1760s.

In one respect, burials are not a reliable way of measuring the infectiousness of the disease. There were marked variations in case fatality depending on age incidence, so that for example in Whitehaven smallpox mortality was about four times lower amongst children above five as it was in those under the age of two.[21] Fortunately, the Whitehaven Dispensary published figures of the number of smallpox cases as well as the number of deaths in the period 1783-1802, which indicates that smallpox became less frequent amongst infants under the age of two.

Table 6: Distribution by Age of Smallpox Cases (Per Cent) in the Whitehaven Dispensary,1783-1802.[22]

ge Group	*eriod*		
	783-1787	787-1795	795-1803
< 2	4.4	4.1	8.8
< 5	3.0	4.2	6.5
< 10	2.0	8.9	1.7
0+	.3	.8	.5
Total Number of Cases	63	86	5

Although the data in Table 6 is for a period after the 1760s, the marked fall in the incidence of the disease amongst the 0-2 age group in the period 1783-1802 is not consistent with an increase in the infectiousness of smallpox. There was also a major reduction of disease mortality in 1795-1803, which was almost certainly the result of the practice of inoculation – 1,079 inoculations were carried out in Whitehaven between 1783 and 1796.[23]

[20] The source of this table is from P. Skold, *The Two Faces of Smallpox* (Umea: The Demographic Data Base1996), 102, 106, 120

[21] Razzell, 'The Decline', 1317.

[22] Annual Reports of the Whitehaven Dispensary, 1783-1804 (Wellcome Trust Library).

[23] Creighton, *A History*, 508.

Davenport et.al. have produced important reconstitution data for the London parish of St. Martin's, which indicate an increasing concentration of smallpox in young children. There are however problems with this evidence, partly revealed by the number of adjustments required to estimate smallpox mortality levels. The overall adjustment to the data approximately doubled mortality in the different periods included in their Table 5, and the adjustments were made 'for missing causes of death and missing infants (presumed exported for burial).'[24] There is however extensive evidence that many of the missing deaths were in fact due to unregistered burials as a result of clerical negligence, with about 40 per cent absent from the London parish registers in the eighteenth century.[25] Additionally, the proportions of burials included in the study are only a minority of total burials – between seven and eighteen per cent – and such minorities are not likely to be entirely representative.[26]

Smallpox Mortality in London

The authors present evidence on smallpox mortality using the ratio of smallpox burials to all burials. A problem with this measure is that it does not take into account the marked decline in all-cause infant and child mortality in London and other cities during the second half of the eighteenth century. A reconstitution study of sixteen London parishes indicates that infant mortality fell from 409 per 1000 in 1700-49 to 141 per 1000 in 1800-49.[27]

Additionally, the number of children dying under the age of two as a proportion of the number of children baptised in the Bills of Mortality was as follows: 1740-49: 61%; 1750-59: 51%; 1760-69: 33%; 1770-79: 33%; 1780-89: 38%; 1790-99: 26%; 1800-09: 22%; 1810-19: 20%.[28] There is evidence that infant mortality nearly halved in the towns of Norwich, Ipswich, Canterbury and Northampton between the end of the seventeenth and middle of the nineteenth centuries, and this may also have been true of Manchester, which is a town included in Davenport et.al.'s analysis of smallpox mortality.[29]

A better measure of mortality is the expression of child burials as a proportion of the number of baptisms, as this includes all children potentially at risk of dying in the early years. It is possible to compare this measure with the results of the reconstitution study carried out by the authors.

[24] Davenport et.al., 'Urban inoculation', 202.
[25] Peter Razzell, 'Infant Mortality in London, 1550-1850: a Methodological Study', *Local Population Studies, 87 (2011)*; Peter Razzell, *Mortality Marriage and Population Growth in England, 1550-1850* (London: Caliban Books, 2016), 35.
[26] The exact proportions are: 1752-66: 16.3%; 1775-99: 18.2%; 1800-12: 7.3%.
[27] Razzell, *Mortality*, 35.
[28] *Ibid*, 38.
[29] *Ibid,* 34-36.

Table 7: Child Smallpox Burial Rates Measured by Reconstitution Research and the Ratio of Burials to Baptisms in St. Martin in the Fields.[30]

Period	*Reconstitution Research: Probability of Dying in Age Interval 0<23 Months, Adjusted Data*	*Period*	*Smallpox Burials <5 Years per 1000 Baptisms*
1752-66	59.9	1751-70	73
1775-99	79.9	1774-1800	101
1800-12	31.9	1801-12	56

The pattern is very similar in the two sets of data, in spite of slight period and methodological differences. The pattern of mortality of children under ten measured by burial/baptism ratios is also very similar to those for children under five: 1751-70: 86/1000, 1774-1800: 111/1000, 1801-12: 61/1000. As the majority of smallpox burials in London were children under the age of ten, it is appropriate to use the burial/baptism ratio for studying changes in mortality in this age group.

Table 8: Smallpox Mortality in St. John Wapping, 1763-1802.[31]

	Period			
	1763-72	1773-82	1783-92	1793-1802
Number of Smallpox Burials < 10 years	254	187	133	110
Number of Baptisms	1530	1657	1493	1316
Smallpox Burials <10 years per 1000 Baptisms	166	113	89	84

Smallpox mortality approximately halved between 1763-72 and 1793-1802 in Wapping, with most of the reduction occurring before 1792.

By bringing together existing data, we may summarize the history of smallpox mortality of children under of ten years in London as follows:

[30] Source: Davenport et.al.,'Urban Inoculation', 202; St. Martin in the Fields Sexton's Parish Register.
[31] Source: St. John Wapping Parish Register.

Table 9: Smallpox Mortality of Children under the Age of Ten Measured by the Burial/Baptism Ratio, London, 1760-1812.[32]

Period	*St. Martin's*	*Wapping*	*Stepney*	*Whitechapel*
1760-69	138/1000	166/1000	-	108/1000
1770-79	114/1000	113/1000	145/1000	62/1000
1780-89	108/1000	89/1000	77/1000	67/1000
1790-99	131/1000	84/1000	63/1000	58/1000
1800-12	64/1000	56/1000	46/1000	62/1000

Except for St. Martin's, there were significant falls in mortality in all areas in the late eighteenth century, consistent with what is known about the practice of inoculation in London. As we have previously seen, data from the London Bills of Mortality also indicates significant reductions in smallpox mortality during the second half of the eighteenth century – from 137 smallpox burials per 1000 baptisms in 1740-49 to 89 per 1000 in 1790-99.[33] Some of the smallpox burials were of course of adults and children over ten, but the decline of such burials according the parish studies reviewed was on average about 12% in the period between the middle and end of the eighteenth century, whereas the decline of mortality depicted above is of the order of 35%. Some of the reduction of smallpox in children over the age of ten and adults would have been due to inoculation in London, evidenced by the fact that the London Smallpox Hospital confined its in-patient inoculations to children aged over seven and to adults, who appear to have been the majority of in-patients.[34] The Bills of Mortality data therefore suggests, along with the evidence in Table 9, that there was a significant reduction in smallpox mortality in London during the late eighteenth century. It took many years before inoculation had been practised widely in London, but by the end of the eighteenth century it had become very popular in the metropolis.[35]

This decline in mortality is particularly impressive given that the virulence of smallpox was increasing at this time, as evidenced by the growth of case-fatality rates in the London Smallpox Hospital.[36] The long-term pattern of disease virulence was summarised by McVail, as follows:

[32] Source: The parish registers of St. Martin's, Wapping, Stepney and Whitechapel. For purposes of illustration, the figures in Table 9 have been presented by standardized decade. The exact decades are: St. Martin's: 1761-70, 1774-80, 1781-90, 1791-1800, 1801-12; Wapping: 1763-72, 1773-82, 1783-92. 1793-1802, 1803-12; Stepney 1774-79, 1780-89, 1790-99, 1800-08; Whitechapel: 1760-69,1770-79, 1780-89, 1790-99, 1800-12.
[33] Razzell, 'The decline',1332.
[34] *Ibid*, 1323,1324.
[35] For etailed evidence on the practice of inoculation in London in the late eighteenth and rearly nineteenth century see *Ibid*, 1320-1331.
[36] See Razzell, 'The decline', 1332.

> … natural smallpox gradually became throughout the eighteenth century, and up to the epidemic of 1870-73, a more virulent and fatal disease, its maximum fatality being on a large basis of facts 45 per cent …[37]

Smallpox had killed less than five per cent of children in London during the sixteenth century, and a number of sources indicate that its virulence grew steadily throughout the seventeenth, eighteenth and nineteenth centuries.[38] It is probable that the increases in smallpox mortality in St. Martin in the Fields and Manchester were the result of growing case fatality rates. It is possible that mortality also increased in northern areas where inoculation does not appear to have been so widely practised – although this was not the case in Whitehaven – and further clarification of this issue must depend on future research.

There is however an even more complex issue than the increasing virulence of smallpox, and that is the assumption made by Davenport et.al. that vaccination was introduced at the very beginning of the nineteenth century.

Inoculation and Vaccination in the Metropolis

There is no statistical data on the relative practice of inoculation and vaccination in London after the discovery of the latter in 1796. However, as has previously been seen, there is extensive anecdotal evidence that inoculation was widely supported and vaccination opposed by the general population in London during the first decade of the nineteenth century and beyond.[39] In a letter to Lettsom, dated July 1807, Jenner wrote: 'You will be sorry to hear the result of my interview with the Minister, Mr Perceval. I solicited ... whether it was the intention of government to give check to the licentious manner in which small-pox inoculation is at this time conducted in the metropolis ... [associated with] the capricious and prejudices of the misguided poor ... [40] Murray pointed out in 1808 that these inoculations were carried out 'in every street, court and alley, in the metropolis.'[41] This was partly because of the foreign nature of the new vaccination with its claimed origin in cowpox, but also because it failed to give the life-long protection provided by inoculation.[42]

In the London Smallpox Hospital, 'the number of vaccinations declined after 1805 from two thousand to sixteen hundred, while inoculations doubled from two to over four thousand five hundred. However … by 1808, vaccination and inoculation were again

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[37] Razzell, *The Conquest,*169. See also 170-71.
[38] *Ibid*, 169-179.
[39] Razzell, 'The decline', 1327, 1328.
[40] W.A. Barron, 'Gleanings from Sussex Archives: Brighton and the Smallpox', *The Sussex County Magazine,* 69, 70.
[41] C. Murray, *An Answer to Mr Highmore's Objections to the Bill before Parliament to Prevent the Spreading of Infection of the Smallpox* (London: 1808), 3.
[42] Peter Razzell, *Edward Jenner's Cowpox Vaccine: the History of a Medical Myth* (Firle: Caliban Books*,* 1980*),* 84.

equally popular.'[43] This suggests that the majority of cases carried out were inoculations, and that vaccination covered less than half of the population during the first decade of the nineteenth century.

There is however a more important problem with the introduction of vaccination, which is the nature and origins of the practice itself.

The Nature and Origins of Early Vaccination

In 1767 J.Z. Holwell published a book on variolation in India, stating that Indian inoculators always used 'matter from the inoculated pustules of the previous year', with the result that 'a few pustules generally appear round the edge of the wound … without a single eruption on any other part of the body.'[44] A number of English inoculators began subsequently to experiment with ways of attenuating the severity of inoculation, and one of the most successful experiments was described by Mudge in 1777:

> Messrs. Longworthy and Arscott, surgeons, in the spring of 1776, inoculated at Plympton … forty patients; of which number, thirty were injected with crude matter from the arm of a young woman [from the site of inoculation], five days after she had been inoculated … though the injection took place, so as to inflame them considerably, and to produce a very large prominent pustule, with matter on it, in each of them, yet not one of them had eruptive fever, or a single subsequent eruption, on any part of the body … it is to be remarked too that the matter which was in those pustules having been used to inoculate others produced on them exactly the same appearances, unattended also with either fever or smallpox.[45]

Mudge rejected the results of this experiment on the grounds that such attenuated inoculation would not guarantee protection against future attacks of smallpox given the mildness of symptoms, a problem that was later to be associated with vaccination. A number of other surgeons carried out similar experiments with mixed results, but not stating clearly what procedures they adopted in selecting the virus.[46] One of the most successful was Dr Adams, physician at the London Smallpox Hospital, who in 1808 attempted to transform smallpox through arm-to-arm inoculation into vaccine:

> By continuing with great caution to inoculate at the hospital from Pearl Small Pox and afterwards by selecting those arms which had the most appearance of CowPox, we had at last succeeded in procuring a succession of arms so nearly resembling the vaccine, that a universal suspicion prevailed amongst parents, that they were deceived by the substitution of one for the other.[47]

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[43] Razzell, 'The decline',1328.
[44] Razzell, *Edward Jenner's Cowpox Vaccine*, 85.
[45] *Ibid,* 87.
[46] *Ibid*, 88-90.
[47] *Ibid*, 89.

Adams was anxious to avoid the appearance of vaccination because of its unpopularity in London at this time, while at the same time creating a safer form of inoculation with less severe results. The essence of the technique was the use of virus from a previous site of inoculation, propagated through arm-to-arm inoculation. Jenner's biographer, John Baron, believed smallpox could be attenuated in this way, quoting Jenner in support of this view:

> After a series of inoculations with true variolous matter it has been often observed that the severity of the symptoms and the number of pustules gradually diminish till only one is to be seen, at the point of insertion … This fact did not escape the observation of Dr Jenner; in reference to which he has remarked in one of his memoranda, 'Here we see the cowpox and the smallpox acting similar parts: and that in either case the virus may steal, as it were, imperceptibly through the constitution, and give no signal of its presence.'[48]

This description of the attenuation of smallpox provides a background to a discussion of the origins of Jenner's own stocks of vaccine from 1796 onwards.[49] He himself had been inoculated as a boy in 1756 and went onto successfully to practice Suttonian inoculation for many years before his discovery of vaccination.[50] His initial claims for the value of vaccination were very modest:

> Should it be asked whether this investigation is a matter of mere curiosity, or whether it tends to any beneficial purpose? I should answer, that notwithstanding the happy effects of inoculation, with all the improvements which the practice has received since its first introduction into this country, it not very unfrequently produces deformity of the skin, and sometimes, under the best management, proves fatal.[51]

He was therefore anxious to discover a safer and less severe form of inoculation, and experimented on the 14th May 1796, when he injected James Phipps with cowpox taken from the hand of the milkmaid Sarah Nelmes.[52] After this first trial vaccination, Jenner did not achieve further success until the spring of 1798, when more than thirteen people were vaccinated again with cowpox discovered in the Berkeley area.[53] The clinical reactions at the site of injection were rather severe with 'an extensive erysipelatous inflammation … with some degree of pain', resulting in the application of 'a little mild caustic' to the sites of injection on two of the children vaccinated – the

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[48] *Ibid*, 91.
[49] Davenport et.al. mistakenly state that Jenner's first name was William, but it was in fact Edward. Davenport et.al., 'Urban inoculation',189.
[50] Razzell, *The Conquest,* 23, 93, 94
[51] *Ibid*, 93.
[52] It is possible that the cowpox in question was the result of a milkmaid accidentally inoculating the cow with smallpox, resulting from itching an arm which had previously been inoculated with smallpox. There had been a general inoculation in Berkeley in Gloucestershire in 1795. See Razzell, *The Conquest*, 114
[53] Razzell, *Edward Jenner's Cowpox Vaccine.*

prelude to a series of severe reactions which Jenner recommended should be treated with caustic.[54]

After these initial successes, Jenner lost his stock of vaccine and was unable to supply supporters with virus to carry out vaccinations. Towards the end of January 1799, an outbreak of cowpox was discovered at a London milk farm in Gray's Inn Lane, and William Woodville, physician to the London Smallpox Hospital, collected some cowpox and vaccinated fourteen people with the virus. However, anxious about the effectiveness of vaccination in protecting against smallpox in the London Smallpox Hospital, Woodville then variolated a number of them:

> Among the patients inoculated for the Cow Pox during the first week in which I obtained the matter of this disease, several were so circumstanced as to be afterwards constantly exposed to the Infection of Small Pox. Having no proof that the progress of the infection of the former would supersede that of the latter, I used the precaution to inoculate patients with variolous matter on the fifth day after that taken from the cow.[55]

Six of the ten cases had pustular eruptions strongly resembling smallpox, and of the next five hundred 'vaccinations' carried out by Woodville, nearly two-thirds had pustular eruptions other than at the site of injection, very similar to the results of the old inoculation.[56] These pustular eruptions diminished through subsequent arm-to-arm inoculation, particularly when taken from the site of a previous injection, until eventually these 'vaccinations' resulted in just a local vesicle at the site of injection, resembling classical vaccination.[57] This stock of 'vaccine' was sent out widely by Woodville and colleagues and eventually acquired the reputation of being the 'world's lymph'.[58]

Jenner had lost his own cowpox vaccine and was supplied on the 15th February 1799 with virus taken Woodville's stock of 'vaccine'. According to Woodville, 'the matter sent was taken from the arm of Ann Bumpus, who had three hundred and ten pustules, all of which suppurated.'[59] Jenner had received this virus on a dried thread from Pearson, and described the resulting inoculations as follows:

> Dr Pearson … was dispersing threads embued in the virus to various places in our own country, and to many parts of the Continent … in many places where the threads were sent a disease like mild smallpox frequently appeared; yet, curious to relate, the matter, after it had been used six or seven months, gave up the variolous character entirely and assumed the vaccine; the pustules declined more and more, and at length became extinct. I made a few experiments myself with this matter, and

[54] *Ibid*, 9-11.
[55] *Ibid*, 16.
[56] *Ibid,* 16,17.
[57] *Ibid,* 42-44.
[58] *Ibid*, 8, 32.
[59] *Ibid*, 22.

> I saw a few pustules on my first patients; but in my subsequent inoculations there were none.[60]

This process of attenuation of smallpox virus through arm-to-arm transmission – using sites of previous injections – is similar to that achieved by Longworthy and Arscott in their earlier trials with inoculation. However, in the earlier stages of attenuation, there were occasional severe reactions which in some cases led to minor smallpox epidemics.

On December 11th 1799, Dr. Andre of Petworth in Sussex, wrote the following account of the 'vaccine' which had been sent to him by Pearson for his practice of vaccination:

> The matter sent from Brighton to Petworth produced a disease in every shape resembling smallpox: the time of sickening, the symptoms, the eruptions and their maturation were the same. The number inoculated was fourteen. Three of these were children at the breast; the number of eruptions was from three to twelve. The ages of the remaining eleven were from three to fourteen, and the number of eruptions from fifty to a thousand.[61]

An elderly woman visiting the house in which the children were isolated caught smallpox, infected her husband, and died soon afterwards of the disease.[62] This was not the only case of an epidemic being caused by the use of the new 'vaccine'. At the beginning of July 1800, Dr Waterhouse of Marblehead near Boston in the United States, received vaccine from Haygarth of Bath, which had been 'procured from Dr Jenner's stock by Mr. Creaser.'[63] Waterhouse gave the following description of two of the first cases he 'vaccinated' with this virus:

> They both went through the disease with … symptoms … very similar to those of the lighter kind from the inoculation for the smallpox … The striking similarity of symptoms has induced some practitioners in this country … to conclude, that the kine-pox [cowpox] was only a variety of the smallpox.[64]

The result of these inoculations was an outbreak of epidemic smallpox in Marblehead.[65] Waterhouse attempted to justify his practice of vaccination by writing that 'the like occurrences took place in Geneva, and at several places in England, especially at Petworth, where the virus gave a spurious disease … the effects formed a counterpart to the disasters at Marblehead.'[66] He further noted that 'if we are to judge the force of the disease by the number of pustules, it certainly becomes milder as it recedes from the cow', confirming the progressive attenuation of inoculation by arm to arm transfer.

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[60] *Ibid*, 7, 8.
[61] *Ibid*, 7.
[62] *Ibid.*
[63] *Ibid,* 65.
[64] *Ibid,* 65.
[65] Razzell, *The Conquest,* 47; Razzell, *Edward Jenner's Cowpox Vaccine*, 68, 69.
[66] Razzell, *Edwards Jenner's Cowpox Vaccine*, 73.

There is some evidence that Jenner found other stocks of cowpox for the creation of vaccines,[67] but it is unclear whether these were used widely in England. It appears that Woodville's 'vaccine' continued to be used in London and elsewhere until the middle of the nineteenth century, and it was replaced because it became less effective due to its progressive attenuation.[68]

The Nature of Vaccines

The nature of the vaccinia virus has been clarified by laboratory tests, including DNA analysis. Derek Baxby, the leading authority on the microbiology of poxviruses, has concluded that vaccinia 'could not have been derived from cowpox or smallpox viruses during the last 200 years.'[69] He has further concluded that 'in the case of cowpox, bovine infection is very rare and the domestic cat is the most commonly detected victim. The likely reservoir hosts are rodents, and include … bank voles and woodmice in Britain.'[70]

It is for this reason that Jenner and others probably found it very difficult to locate cowpox. In the nineteenth century in order to create stocks of vaccine a number surgeons resorted to the inoculation of cows with smallpox.[71] It has been argued that some of these stocks of "variola-vaccine" resulted from cross-contamination from residual strains of vaccines still present in the vaccine institutes.[72] However, the inoculation of cows with smallpox was widely practised in India, often in places and depots new to the production of vaccines.

Bhattachrya has described how vaccines were produced in India as follows:

> The most common form of vaccine is use during the nineteenth century was humanised lymph, initially produced by the vaccinators themselves and later in designated depots. This vaccine was generally collected and used locally. The production process involved the collection of pustular material from a cow or buffalo that had been inoculated with smallpox matter. Human beings were operated on with this artificially induced cowpox and then used as sources of vaccine.[73]

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[67] *Ibid*, 33, 38
[68] *Ibid*, 40, 84.
[69] D. Baxby, 'Poxviruses' in L. Collier et.al. (eds.), *Topley and Wilson's Microbiology and Microbial Infections, Volume 1 Virology, Chapter 21 (1998),* 369; D. Baxby, *Jenner's Smallpox Vaccine: the Riddle of Vaccinia Virus and Its Origins* (London: Heinemann,1981).
[70] Baxby, 'Poxviruses', 377.
[71] Razzell, *Edward Jenner's Cowpox Vaccine*, 98, 99.
[72] A. Herlich et.al., 'Experimental Studies in Transforming Variola Virus into Vaccinia Virus, *Archiv fur die Gesamte Virusforschung*' 12 (1963).
[73] S. Bhattacharya et.al., *Fractured States: Smallpox, Public Health and Vaccination Policy in British India, 1800-1947,* (Hyderabad, India: Orient Longman, 2005), 37.

Some of these vaccines were produced in new depots where no vaccination had been practised previously:

> An animal-vaccine depot was started at Shillong on 13 January 1890, and the lymph from calves inoculated here was subsequently distributed to all civil stations in Bengal. Indeed, the trials were considered so successful that this lymph was preferred to that received from depots in England and Darjeeling.[74]

Bhattachrya has summarized the practice of vaccination in India as follows: 'Cowpox was rare in India – vaccine was often produced by using smallpox scabs to infect animals (not just cows) and the resultant pox pustules were then widely used as a source of vaccine.'[75]

However, modern laboratory research has established that it is impossible to transform smallpox into cowpox,[76] and as Crookshank observed in 1889, 'those who have been have been inoculated with … "variola-vaccine" lymph have not, in the true sense of the word, been vaccinated, they have not been Cow Poxed, but they have been variolated.'[77]

The origin of the Lister Institute stock of vaccine in England is unknown, but there is some evidence that it was sent from Cologne sometime after 1871, and is reported to have been taken from the arm of a Prussian soldier suffering from smallpox.[78]

Conclusion.

Davenport , Boulton and Schwarz have raised some fundamental issues about the history of smallpox in the late eighteenth and early nineteenth century. The present commentary has ranged widely in order to examine some of the implications of their arguments, but the balance the evidence does not point to the increasing infectiousness of the disease. The data reviewed suggests that inoculation in all its forms reduced disease mortality both before and after the end of the eighteenth century. Vaccination – whether derived from smallpox or not – had a significant influence on the popularity of the practice, particularly in areas where the smallpox was endemic, affecting mainly young children.

Parents had feared the disease, and although not entirely fatalistic, had often been unwilling to expose their children to a known risk associated with the old inoculation, but were willing to embrace the new more attenuated 'vaccination' because of its very safe outcome. However, the latter did not give the life-long protection associated with

[74] *Ibid,* 40.
[75] Personal communication from Sanjoy Bhattacharya. See also Bhattacharya, *Expunging Variola: the Control and Eradication of Smallpox in India* (Hyderabad, India: Orient Longman, 2006).
[76] Herlich et.al., 'Experimental Studies'.
[77] E.M. Crookshank, *History and Pathology of Vaccination,* 1 (London: H.K. Lewis, 1889), 301.
[78] Baxby, *Jenner's Smallpox Vaccine,* 181.

variolation, and there were instances of subsequent attacks after vaccination which sometimes resulted in death.

Inoculation had been practised particularly widely in the south of England, where both adults and children were vulnerable to smallpox. When the disease arrived in a parish it created a panic response, which created the conditions for general inoculations. However, as the population became familiar with the benefits of Suttonian inoculation, urban areas like London and Whitehaven did resort widely to the practice, which began to diminish mortality.

Without inoculation and the more attenuated vaccination, England and many other countries would have been decimated by smallpox, with perhaps up to forty-five per cent of the population dying from the disease by the late nineteenth century, equivalent to a new bubonic plague. Whatever the exact relationship between variolation and vaccination, this stands out as a major achievement of preventative medicine.