

21 September 2011

**The life and Legacy of Dr Edward Jenner FRS, pioneer of vaccination**

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This talk celebrates the life and legacy of Edward Jenner (1749 – 1823). Jenner was born and died in Berkeley, in the Severn vale, rich farming country then as it is now. He lived and worked there for most of his life as the local surgeon. His unique legacy is the formal discovery and promotion of vaccination; immunisation against smallpox through infection with cow pox. This is epitomised in the many pictures that are to be found of Jenner vaccinating an 8 year old, James Phipps, with matter taken from a pustule on the hand of a young woman also in the picture, Sarah Nelmes who had active cow pox. Six weeks later James proved resistant to infection with small pox proper. Central to Jenner’s life and legacy is the experiment these pictures depict and we will hear much more of his researches around cow pox later. I intend dividing this talk into four:-

Jenner’s beginnings from 1749 when he was born to 1773 when he returned to Berkeley having completed his surgical training.

His life in Berkeley from then up to the point of his seminal publication on vaccination, “the Inquiry” in 1798.

His life transformed by fame and the responsibility to nurture his discovery as “vaccine clerk” to the world up to his death in 1823

Celebrating Jenner and the achievements of vaccination.

Beginnings.

Jenner’s antecedents were bakers based around Slimbridge (now famous for the Wild Fowl Trust) in the Severn Vale. The Severn Vale is important to our story as it is cattle country; it is now and was then. The Jenners were successful business people and moved up the social scale. Edward’s father was born in 1702 and went to Oxford where he was educated as a churchman. He became vicar of Berkeley in 1729 (his living the gift of the Earl of Berkeley). He married in the same year and there were 9 children, 6 surviving to adulthood, Edward was number 8.

Edward was born in the vicarage in Berkeley in 1749 (not the current vicarage, the house concerned was demolished many years ago). Both of his parents died within two months of each other when he was just five. He was left in the care of his three sisters, the eldest nineteen. His brothers were at Oxford studying to join the church.

Aged eight he was sent to Wooton-under-Edge Grammar School . He was only at this school for one year but during that time he was variolated by the local surgeon, Mr Holbrow as there was an out break of smallpox in the town. Variolation is deliberate inoculation with smallpox, usually in childhood to avoid later natural infection. It was well known that recovery from smallpox gives life long immunity and variolation although it significant mortality of around 2% was a better bet than natural smallpox with a mortality of 12 – 20% and up to 40% in some outbreaks. However variolation did kill and it had another significant disadvantage if not properly handled, it spread smallpox. The story of the introduction of variolation to England holds lessons. Lady Mary Wortley is usually accredited with bringing this practice to the UK in 1721 but in 1714, Emanuele Timoni, reported on variolation, to the Royal Society in 1714. However Lady Mary was charismatic and well connected. She had come across variolation while in Constantinople with her husband who was ambassador and had one of her children variolated there. She was the friend of aristocrats including royalty and this was important to variolation becoming accepted in Britain. Princes Caroline of Wales, asked Hans Sloane in 1721 to conduct a trial of the procedure before accepting it for her children. This was conducted on prisoners from Newgate and confirmed its efficacy as well as relative safety. This was quite possibly the first formal clinical trial. Royal support later proved important to the take up of vaccination. However, back to the main story, young Edward’s experience of variolation at Wooton-under-Edge was his first brush with smallpox and may well have influenced his future thinking. Variolation began with a period of preparation, around two to four weeks. According to a contemporary account: “He was bled, to ascertain whether his blood was fine; was purged repeatedly, till he became emaciated and feeble; was kept on a very low diet; small in quantity, and dosed with a diet-drink to sweeten the blood. After this he was removed to one of the inoculation stables and isolated with other pupils while the inoculated smallpox ran its course over the next 10 to 14 days.” Fortunately for Jenner his disease was mild. It was still an experience that you would not forget.

Aged nine he moved school to Cirencester. He was said to be keener on fossil collecting and natural history than the classics. Perhaps in recognition of his natural talents, but more likely because he was orphaned and there was not the parental drive, unlike his brothers he did not continue to prepare for Oxford. He was accepted as an apprentice surgeon by John Ludlow aged 12 in 1761. This was a turning point and very important for what followed. Ludlow had his practice based in Chipping Sodbury at Melbourne House, currently an Indian Restaurant. Jenner spent six years learning the knowledge and skills of a country surgeon. Here he will have first become aware that human cow pox which was caught from the udders of infected cows prevented infection with smallpox. He moved on at eighteen to St George’s Hospital, then at Hyde Park Corner in London to further his medical education where he studied under John Hunter for three years. His training was exceptionally long, but an important point for later, he was “gentry” and could afford it. He had inherited land from his father and had a private income from rents. Teaming up with Hunter was a very fortunate turn of events. They were kindred spirits and this not only extended Jenner’s education but started a life long friendship and collaboration with the greatest medical investigator of his era. Jenner called him “the dear man” and they were close friends and collaborators until Hunter’s death 25 years later.

An aside on John Hunter, he was the man who more than any other versed Jenner in the scientific to research. He taught Jenner to be a scientist and follow the principal of observation leading to hypothesis that can be tested by experiment. Hunter was a dynamo of a man, primarily involved in anatomical studies on human teeth, digestion particularly fat absorption and the role of lacteals, the lymphatic system, foetal development and placental circulation and with Jenner as we will see body temperature. He was also a forward thinking surgeon applying science to clinical problems such as inflammation; gun shot wounds, and most famously popliteal aneurysm and venereal disease.

During this time Jenner was also influenced by Joseph Banks and again they became long term friends and collaborators. Banks was a botanist and naturalist and most famous as the naturalist on Cook’s voyage on HM Bark Endeavour (1768 – 1771). Jenner was involved in cataloguing specimens after Bank’s return in 1771. Banks was President of Royal Society 1778 – 1820 and a help to Jenner in that role, Jenner became FRS in 1789, for “Observations on the Natural History of the Cuckoo”. Between 1780 – 82 Joseph Banks and Jenner collaborated in experiments on the use of human blood as a fertiliser. Studies were made on the growth of blackcurrants in Jenner’s garden.

Back in Berkeley, before fame (1773 – 1798)

In 1773 Jenner returned to Berkeley from London to live with his brother Stephen and practice as a surgeon in the county, indulge his “hobbies” and intellectual pursuits and find himself a wife. In setting up his practice he had many advantages. He was unusually well qualified and well connected. His status and steady income as a local landowner also gave him time to pursue interests other than his money earning job. His London contacts particularly John Hunter were a continuing influence and stimulus as well as his local colleagues. All these things contributed to the success story we have to tell. He was a bachelor for the next 15 years; he courted Catherine Kingscote for ten years. And they were married in 1788. The Cow Pox experiment was 23 years away. So what did Jenner get up to?

He practiced medicine across a large part of Gloucestershire bordered by Gloucester and Cheltenham in the North, the Severn, Wotton-under-Edge and the Cotswold escarpment and Thornbury to the South, an area of around 1600 square miles. This is remarkable in its own right considering transport was a horse. He met regularly with medical colleagues to socialise and advance one another’s practice through case presentation and discussion in medical societies that we will discuss. He was active in scientific research. He wrote, prose, poetry and endless letters as well as a few scientific papers. Eventually as we have learnt he got married (1788) and started a family. He was not always well, “melancholy” a problem and on at least one occasion very severe infection, probably Typhoid.

Jenner’s membership of medical societies must have been important in sustaining him professionally and intellectually and were certainly important to the cow pox story. The first was the Convivio-Medical Society. It met at the Ship Inn at Alveston which is about twelve miles from Berkeley. Its founder was John Fewster, a surgeon in Thornbury. He read a paper to the Medical Society of London in 1765 entitled, “Cow pox and its ability to prevent smallpox”. He never did the experiment but was an important friend of and influence on Jenner. Interestingly it was Jenner who put “Convivio” before Medical because it was more eating and drinking than medical case and science discussion. It was followed by the Medical Convivial Society which met at the Fleece Inn at Rodborough, about 15 miles from Berkeley and was much more disciplined and focussed on medical science. Notable Jenner papers were early and possibly the first description of coronary artery calcification based on post mortem studies at Wooton-under-Edge and studies of hydatid disease.

Jenner’s scientific interests were catholic. Serious concentration on cow pox came at the end of the period but his interests ranged from studies of hibernation in Hedgehogs to hydrogen balloons.

The hedgehog studies were collaboration with Hunter who supplied the apparatus and in the process refined Jenner’s approach to science emphasising the importance of observation. His interest in natural history was extensive but his work with birds was seminal. What we know now to be migration was the issue, where do summer birds come from? Jenner’s interest in the cuckoo which is not around for long enough to fledge its young is central and by observation and experiment he was able to demonstrate that the job was handed on to third parties. With the help of nephews, nests containing cuckoos were kept under observation. Dissection of cuckoo chicks showed that they were equipped to remove others from the nest. Their ability to this could be countered by weighting them down with lead and the result of that experiment was conclusive. “Observations on the Natural History of the Cuckoo”, Philosophical Transactions of the Royal Society, London 1788 78:219-237 was the result and earned Jenner his FRS. But his interest in migration was much broader. “Some Observations on the Migration of Birds” Proceedings of the Royal Society, London, 1824 2:204, the published outcome of his work appeared after his death. Tartar emetic one of the key medicines in the pharmacopeia in Jenner’s time was of uncertain purity and as result efficacy. He devised a method for a purer preparation which he published but never profited from, “A Process for preparing pure Emetic Tartar by Re-crystallisation”, Transactions of the Society for the Improvement of Medical and Chirurgical Knowledge, vol I 1793. Hunter tried to make him more entrepreneurial and profit from it. The important thing here is the understanding of the importance of a standardised, science based approach so as to yield a product of reliable efficacy. We call this quality control these days. I t will be important later on to the vaccination story. Hydrogen balloons were fun and here the collaboration was with Earl Berkeley whose friendship towards and patronage of Jenner was important to vaccination. He was also the Berkeley family physician. Blood as a plant growth promoter has already been mentioned a collaboration with Joseph Banks.

A further word is needed on Jenner’s domestic arrangements before finally concentrating on vaccination and that is to mention the Chantry, Jenner’s main home from 1785, when he purchased it three years before he was married, until he died in 1823. It is where the cow pox work was done and the birthplace of vaccination. It must have been an ideal place to live and work and now it is home to the Jenner Trust’s efforts to keep his life and its legacy alive and remind all those who are interested of the massive achievements of vaccination across a broad range of infectious diseases. If you want to know and see more visit www.jennermuseum.com.

We have now reached the central issue, Jenner as the pioneer of vaccination. The main players in the 1796 experiment which we have already noted were Blossom, a “Gloucester” cow from a farm at Breadstone a hamlet that in effect is part of Berkeley. Her horns have mysteriously appeared in several medical history collections. Her hide is at St George’s Hospital Medical school. These days Gloucester cows are distinguished in that their milk is used to produce single Gloucester cheese, no other milk can be used. Blossom had cowpox which resulted in pustules on her teats. The virus, this was a general term for infectious agent in those days without knowing what that was, infected her milk maid, Sarah Nelmes, producing a pustule on her hand as well as in a mild way making her feel generally unwell. Jenner took material from Sarah’s pustule and inoculated it into the arms of James Phipps in the experiment we have described but what is really important to emphasise is that this was almost the end of Jenner’s research that led to the introduction of vaccination. Jenner had been following the scientific method. His objective; to answer a question of the natural world, is it true that a bout of cow pox means that you are immune to smallpox in the future? In his practice he observed cases of just that and these he published in the Inquiry as part of the process of making his scientific case for vaccination. Based on these observations he turned the question into an hypothesis, it is true that a bout of cow pox means that you are immune to smallpox in the future, extending it to say that deliberate rather than accidental infection with cow pox would have the same effect, similar to variolation but vastly mitigating the risks. Then he did the experiment. Astute observation has been the basis of many breakthroughs in medical science but perhaps the greatest were Jenner’s observations of cow pox and Alexander Fleming’s observations of the penicillin mould for which Fleming was awarded a Nobel prize. Having said that the intellectual climate was favourable and the knowledge that catching cow pox could protect against smallpox was certainly in the air in the eighteenth century. We have already acknowledged John Fewster’s, surgeon in Thornbury, paper to the Medical Society of London read in 1765, “Cow pox and its ability to prevent smallpox”. Also well known is that Benjamin Jesty a farmer living in Yetminster Dorset inoculated family members with cow pox in 1774 who proved resistant to natural smallpox when outbreaks occurred. But Jenner was the scientist and in addition to observation, hypothesis and experiment he published. His first attempt to publish his discovery was in 1796 but his paper to the Royal Society was rejected on the basis of insufficient evidence, more cases were required. This took Jenner a little time as cow pox temporarily disappeared from the Severn Vale but by 1798 he was ready and this time an independent publication, “An Inquiry into the Causes and Effects of the Variolae Vaccinae, known by the name of the Cow Pox”. London: Sampson Low, 1798 was the result. The first edition was dedicated to Jenner’s friend, Caleb Parry a physician at the Mineral Water Hospital in Bath and it is worth recording Jenner’s words here,

In the present age of scientific investigation it is remarkable that a disease of so peculiar nature as the cow-pox, which has appeared in this and some of the neighbouring counties for such a series of years, should so long have escaped particular attention. Finding the prevailing notions on the subject, both among men of our profession and others, extremely vague and indeterminate, and conceiving the facts might appear at once both curious and useful, I have instituted as strict an inquiry into the causes and effects of this singular malady as local circumstances would admit.

The following pages are the result, which from motives of most affectionate regard, are dedicated to you, by

Your sincere friend,

Edward Jenner

Berkeley, Gloucestershire, June 21st, 1978

Exploring the Inquiry demonstrates just how careful Jenner’s work was. It presents 23 case reports recording immunity to smallpox either due to natural infection with cow pox or inoculation with material from a cow pox pustule. Case 1 Joseph Merret, is an example of the former, he had cow pox in 1770. In 1795 he was variolated in Berkeley along with his family because smallpox was active. Jenner could not make the smallpox material “take” although he made several attempts. Case 16 is Sarah Nelmes and to quote Jenner’s words, “a dairymaid at a farmer’s near this place, was infected with the cow-pox from her master’s cows in May, 1796. She received the infection on a part of her hand which had previously in a slight degree injured by a scratch from a thorn, a large pustulous sore and the usual symptoms accompanying the disease were produced in consequence. The pustule was so expressive of the true character of the cow-pox, as it commonly appears upon the hand, that I have given representation to it in the annexed plate”. The plate is crucially important, effective vaccination was dependent on the proper identification of cow pox and transferring the correct material from pustules. Jenner was at pains in the Inquiry and subsequent publications to labour this point. A standardised approach was needed to maximise the effectiveness of vaccination.

Case 17 was James Phipps and again Jenner’s own words tell the story best.

“The more accurately to observe the progress of the infection I selected a healthy boy, about eight years old, for the purpose of the inoculation of the cow-pox. The matter was taken from a sore on the hand of a dairymaid, who was infected by her master’s cows, on 14th May, 1796, into the arm of the boy by means of two superficial incisions, barely penetrating the cutis, each about half an inch long.

On the seventh day he complained of uneasiness in the axilla, and on the ninth became a little chilly, lost his appetite and had a slight headache. During the whole of this day he was perceptibly indisposed, and spent the night with some degree of restlessness, but on the following day he was perfectly well. The appearances of the incisions in their progress to a state of maturation were much the same as when produced in a similar manner by variolous matter.

In order to ascertain whether the boy, after feeling so slight an affection of the system from the cow-pox virus, was secure from contagion of the smallpox, he was inoculated on the 1st of July following with various matter immediately taken from a pustule. Several slight punctures and incisions were made on both his arms, and the matter was carefully inserted, but no disease followed. Several months afterwards he was again inoculated with variolous matter, but no sensible effect was produced on the constitution”

The rest of the cases were similar. The Inquiry was an immediate “hit” and was in its third edition by 1800. Important to the adoption of vaccination it had royal support. From the second it was dedicated to George III. Jenner was received by the king on 7th March 1799 and subsequently by the Prince of Wales at Carlton House emphasising the regard in which he was held at the highest level. That is not surprising as smallpox was a scourge in all classes of society. It deserved Jenner’s nickname for it “the speckled monster” and a further quote “there is no disease which presents a more melancholy scene than the natural smallpox as it frequently occurs”. Where it was endemic up to 40% of the population caught it, usually in childhood. Victims were extremely ill for around three weeks. Around 1 in 6 died of the acute illness. Many who survived were blinded by scarring of their eyes. The pocks heal with scarring so are disfiguring. Smallpox has often changed the course of history. The first two queens of England reigned as a result of Edward VI’s death from it at the age of 16. Queen Elizabeth 1st had it in 1562 and survived but with a pocked face hence the heavy makeup which is so famous. One of George III’s sons, Octavius died of inoculated smallpox at the age of four when he was variolated.

Before moving on to the next phase of our story, the ethics of Jenner’s work are often questioned particularly the inoculation experiments. His defence is that they were based on carefully documented observation. Nature had if you like performed the experiment. Jenner appreciated James Phipps role and left him a cottage in his will which is close to the Chantry in Berkeley and where a museum to Jenner was first established.

“Vaccine Clerk to the World” (1798 – 1823)

The efficacy of vaccination was quickly demonstrated by others. Jenner quickly became world famous. The method was being used across Europe and North America by 1799. It was adopted by the Navy in 1800. It had reached India by 1802. The organisation of vaccination was complicated as until the 1860s it was dependent on collecting material from human pustules. Various institutions were established. In June 1799, the London Vaccine-Pock Institution was founded by George Pearson. In January 1802, the Royal Jennerian Society of which Jenner became president of its Medical Council. Both offered free vaccination. Jenner did not always see eye to eye with the conduct of these organisations and in particular fell out badly with Pearson who as a result promoted Benjamin Jesty’s claim to the discovery. In 1809 the National Vaccine Establishment of which Jenner was made Director but he was never active, effectively moving to retirement in 1809. This was the main source of vaccine lymph in Britain until a vaccines produced in calf’s skin became available in 1861. During this time Jenner’s main role was to make sure that his discovery was understood and used to maximum benefit. Jenner published four further pamphlets attempting to standardise vaccination by 1806 and was involved in correspondence across the globe with vaccinators until his death. Hence the title “Vaccine Clerk to the World”

Jenner lived relatively quietly in Berkeley and Cheltenham from 1809. He died at the Chantry on 25th January 1823 of a stroke. He is buried in the church next door to his home. Westminster Abbey was offered but could not be afforded and it is fitting that his remains are resting close to the place of his discovery.

Celebrating Jenner and the achievements of vaccination.

Thomas Jefferson writing as President of the United States said it best in a letter to Jenner, 1806 “It is owing to your discovery that in the future the peoples of the World will learn about this disgusting smallpox disease only from ancient traditions.” It took 171 years but the last case of naturally transmitted smallpox occurred in Somalia in 1977 and the World Health Organisation declared the World free from smallpox on 5th August 1980. That is Jenner’s legacy and countless millions of lives have been saved in the process. However it is broader than that. Jenner demonstrated that inoculation with one disease –cow pox- could protect against another smallpox. Cow pox produced only mild illness and recovery was full in otherwise healthy individuals. Individuals were protected from a life threatening disease through recovery from a mild one. We now know that this worked because both viruses are part of the same family, the Orthopox viruses with enough in common in surface structure for the immune system to see them as the same.

Louis Pasteur was the next great scientist to take up the baton, through his research developing three new vaccines, to chicken cholera in 1880, to anthrax in 1881 and in 1884 rabies vaccine. He discovered a different approach; the responsible pathogen could be attenuated to reduce its virulence so that it produced little or no illness but still established immunity. Pasteur called the overall approach “Vaccination” in honour of Edward Jenner. There are now twenty four vaccines in world wide use in human medicine saving millions of lives and preventing debilitating infectious disease, for more see, http://www.historyofvaccines.org/ and http://www.gavialliance.org.

Jenner was honoured worldwide. For some time his London statue was in Trafalgar Square now in the Italian garden in Kensington Gardens. He was one of just six scientists used on stamps in 2110 to celebrate 350 years of the Royal Society.

A favourite monument is the Temple of Vaccinia which is located at the bottom of the Chantry garden in Berkeley. It was the gift of Robert Ferryman a long term friend and admirer of Jenner. It was designed and constructed at some time between 1796 and 1804 and named by Jenner. He used it once a week as a vaccination station for the local poor. To visit the Temple and pay personal homage to the great man but more importantly learn more of his life and legacy you can do no better than visit Jenner’s House, the place where it all actually happened, online at www.jennermuseum.com or preferably in person.

This has been I hope a very positive story but opposition to vaccination was present right from 1798 and is still very prevalent. See Gareth Williams’ lecture in this short series on matters related to Jenner, “From Jenner to Wakefield: The long shadow of the anti-vaccination movement” for more.

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Edward Jenner’s House

Berkeley, Gloucestershire

www.jennermuseum.com