Nestling cuckoos to vaccination—a commemoration of Edward Jenner

by David Bardell

The cuckoos comprise a large family of birds with worldwide distribution. Many of the more than 100 species inhabit the tropics, and those of the temperate regions migrate to the tropics for the winter. The cuckoo family takes its name from the song of the common or European cuckoo, *Cuculus canorus*.

The common cuckoo is found throughout Europe. In addition to its distinctive song, it is famous for another characteristic, brood parasitism. *C. canorus* lays its eggs in the nests of other species of birds, after which the nestling cuckoo is raised by the host birds. After the cuckoo hatches, the offspring of the host birds are ejected from the nest, resulting in destruction of unhatched eggs and death of nestlings. The ejection of host eggs and nestlings was a mystery. The mother cuckoo never returns to the nest after laying an egg therein. It was clear that a nestling cuckoo did not have the strength to throw objects as large as eggs and nestlings from the nest. Unlike cuckoos, most species of birds care for their young; therefore, the parents would not do such a horrific thing as murder their own young. Who then does commit the murderous act? The mystery was solved by Edward Jenner (Figure 1).

Of all the infectious diseases that have afflicted humankind, smallpox was one of the most devastating. The disease is highly contagious, and before preventive control it spread rapidly through the population. Death was often the outcome, and many of those who survived were hardly, if any, more fortunate than those who died, because they were often crippled or blinded as well as having hideous pockmark scarring of the face and body. Smallpox predates any known written records of the disease; some mummified bodies of ancient Egyptians show the typical scars of smallpox (Adams 1992). Throughout the centuries of recorded history smallpox smoldered in endemic form, with epidemics occurring frequently. During the eighteenth century the disease was not only widespread in the Old World, but was also prevalent in the New World (Mather 1722). Mercifully, in the closing years of the eighteenth century vaccination to prevent smallpox was discovered, the first immunization procedure against any disease. This discovery too was made by Jenner.

Biography of Jenner

Jenner was born in Berkeley, Gloucestershire, western England, on 17 May 1749 (Baron 1827). He was the sixth and youngest child of Stephen Jenner, vicar of Berkeley. His parents died when he was five years old, and thereafter he was brought up by a much older brother. Growing up in Berkeley, a small town in a dairy farming region, Jenner acquired a great love of nature. He collected fossils and other natural objects and was a keen observer of the local wildlife.

At the age of 13, in accordance with his own wishes, he was apprenticed to Daniel Ludlow, a surgeon in nearby Sodbury. On completion of his apprenticeship at 21, Jenner went to London for further training with John Hunter, a Scottish surgeon practicing there. Hunter was renowned as a surgeon. He was also noted for his research zeal into several areas of the natural and medical sciences. Hunter was a surgeon to the king, and elected to fellowship in the Royal Society, the premier scientific society in Britain. While in London, and on Hunter's recommendation, Jenner, in addition to his surgical studies, assisted in classifying and cataloging biological specimens brought back by Joseph Banks, naturalist aboard the *Endeavour* for Captain Cook's first voyage of discovery.

At the age of 24, Jenner returned to Berkeley to establish a practice in surgery. He was successful in his career and became a member of two societies for the advancement of medical knowledge. At that time surgery and medicine were separate professions. Nevertheless, surgeons frequently practiced medicine, and physicians often performed surgery, and in reality there was little difference between the professions. The major difference was in the education process—surgeons learned their profession by apprenticeship, whereas physicians were university educated. In addition to his medical interests, Jenner played the flute and violin, wrote poetry, and pursued activities in the natural sciences. In 1788 he married Catherine Kingscote. They had four children. In 1792 Jenner was awarded a medical degree by St. Andrews University, Scotland. Although he had previously practiced medicine as well as surgery, he thus officially became a physician as well as a surgeon.

The study of nestling cuckoos

Outside of his professional work, Jenner turned to his love of nature and employed some of his leisure hours studying the European cuckoo, with the hope of illustrating a subject not sufficiently investigated—the fate of the host birds' young after hatching of the cuckoo's egg (Jenner 1788).

Jenner studied the nests of several species of bird in which a cuckoo's egg had been deposited, with most

of his observations made on hedge-sparrows. Whatever species the host birds were, if there was a hatched cuckoo in the nest, the eggs and nestlings of the host birds were found in disarray outside the nest, the eggs usually broken and the nestlings dead. On replacing any living nestlings back in their nests, he later found them ejected again. However, if he removed the young cuckoo from the nest, the host birds' own eggs and nestlings remained in the nest and were cared for by their parents. Jenner then reported (1788, pp. 224–226):

> From these experiments, and supposing, from the feeble appearance of the young Cuckoo just disengaged from the shell, that it was utterly incapable of displacing either the egg or the young Sparrows, I was induced to believe, that the old Sparrows were the only agents in this seeming unnatural business; but I afterwards clearly perceived the cause of this strange phaenomenon, by discovering the young Cuckoo in the act of displacing its fellow-nestlings, as the following relation will fully evince.
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> June 18, 1787, I examined the nest of a Hedge-sparrow, which then contained a Cuckoo's and three Hedge-sparrow's eggs. On inspecting it the day following, I found the bird had hatched, but that the nest now contained only a young Cuckoo and one young Hedge-sparrow. The nest was placed so near the extremity of a hedge, that I could distinctly see what was going forward in it; and, to my astonishment, saw the young Cuckoo, though so newly hatched, in the act of turning out the young Hedge-sparrow.
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> The mode of accomplishing this was very curious. The little animal, with the assistance of its rump and wings, contrived to get the bird upon its back, and making a lodgement for the burden by elevating its elbows, clambered backward with it up the side of the nest till it reached the top, where resting for a moment, it threw off its load with a jerk, and quite disengaged it from the nest. It remained in this situation a short time, feeling about with the extremities of its wings, as if to be convinced whether the business was properly executed, and then dropped into the nest again. With these (the extremities of its wings) I have often seen it examine, as it were, an egg and nestling before it began its operations; and the nice sensibility which these parts appeared to possess seemed sufficiently to compensate the want of sight, which as yet it was destitute of. I afterwards put in an egg, and this, by a similar process, was conveyed to the edge of the nest, and thrown out. These experiments I have since repeated several times in different nests, and have always found the young Cuckoo disposed to act in the same manner. In climbing up the nest, it sometimes drops its burden, and thus is foiled in its endeavours; but, after a little respite, the work is resumed, and goes on almost incessantly till it is effected. It is wonderful to see the extraordinary exertions of the young Cuckoo, when it is two or three days old, if a bird be put into the nest with it that is too weighty for it to lift out. In this state it seems ever restless and uneasy.

Figure 1. Portrait of Edward Jenner painted in 1803 by James Northcote. By courtesy of the National Portrait Gallery, London.

As noted above, the nestling cuckoo sometimes drops its heavy burden and must then start the laborious task again. However, as Jenner discovered on physical examination of the nestling cuckoo, it does have an adaption to lessen the likelihood of its dropping the load (Jenner 1788, p. 226):

> The singularity of its shape is well adapted to these purposes; for, different from other newly-hatched birds, its back from the *scapulae* downwards is very broad, with a considerable depression in the middle. This depression seems formed by nature for the design of giving a more secure lodgement to the egg of the

> Hedge-sparrow, or of its young one, when the young Cuckoo is employed in removing either from the nest. When it is about twelve days old, this cavity is quite filled up, and then the back assumes the shape of nestling birds in general.

Comparing the size of adult birds, Jenner noted that the cuckoo is much larger than the hedge-sparrow. However, cuckoo's eggs are somewhat smaller than those of hedge-sparrows. Jenner gave an explanation of the necessity for a cuckoo placing its egg in the nest of a species producing small eggs (Jenner 1788, pp. 227–228):

> The smallness of the Cuckoo's egg in proportion to the size of the bird is a circumstance that hitherto, I believe, has escaped the notice of ornithologists. So great is the disproportion, that it is in general smaller than that of the Hedge-sparrow; whereas the difference in the size of the birds is nearly five to one.
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> The circumstance of the young Cuckoo's being destined by nature to throw out the young Hedge-sparrows, seems to account for the parent-cuckoo's dropping her egg in the nests of birds so small as those I have particularised. If it were to do this in the nest of a bird which produced a large egg, and consequently a large nestling, the young Cuckoo would probably find an insurmountable difficulty in solely possessing the nest, as its exertions would be unequal to the labour of turning out the young birds.

Having cast its nestmates to their death, the nestling cuckoo receives the full attention of its foster parents and all the food brought back to the nest to satisfy its seemingly insatiable appetite. Although they do not live long, the host's nestlings do not die in vain, as Jenner commented (Jenner 1788, p. 228):

> Here it may be remarked, that though nature permits the young Cuckoo to make this great waste, yet the animals thus destroyed are not thrown away or rendered useless. At the season when this happens, great numbers of tender quadrupeds and reptiles are seeking provision; and if they find the callow nestlings which have fallen victims to the young Cuckoo, they are furnished with food well adapted to their peculiar state.

Some other studies of nature

To assist Hunter in his numerous research endeavors into natural and medical sciences, Jenner undertook several projects. These projects included a study of hibernating hedgehogs, in which he investigated body temperature, weight, and the amount of fat tissue throughout the hibernation period.

Jenner had a lifelong love of birds, and they were the subject of some of his poetic writings. His "Address to a Robin" (Baron 1827, p. 20) is a delightful piece of rhyming verse, the opening lines of which read:

> Come, sweetest of the feather'd throng!
> And soothe me with thy plaintive song

The robin addressed is the European robin, which is much smaller than the American robin.

Jenner's interest in birds also led to a lengthy study of bird migration. Although some species of birds were known at the time to migrate, there were other species not seen during winter that were thought by many to hibernate rather than migrate. Jenner provided strong evidence, based on the physical appearance of the birds, for migration and against hibernation. When the supposed hibernating birds make their first appearance after winter they are plump and fleshy, as well as strong on the wing and full of activity. However, when hibernating animals appear after winter they are languid and emaciated, their fat all gone.

Another avenue of inquiry concerned a common belief that some birds not seen during winter lacked flying strength for migration, and therefore hibernated. Although under normal circumstances such birds appear reluctant to take to flight, and then fly only a short distance before settling down again, Jenner noted that if they are forced on the wing by an extraordinary cause (i.e., a frightening experience) they exhibit strong flying ability. In other words, necessity begets exertion.

One of the birds studied, which Jenner contended was a migratory bird, was the landrail, also called a corncrake. It is now known that the European landrails migrate to Africa, but in Jenner's time many argued that it hibernated (Jenner 1824).

Despite his wide-ranging interests, due to the ever-increasing amount of time needed for the study into a preventive for smallpox Jenner had less and less time for natural science, and his studies on bird migration were not put together and published until after his death in 1823 (Jenner 1824). Nevertheless, it was Jenner's stature as a natural scientist that brought about his election to fellowship in the Royal Society seven years before he discovered vaccination (Royal Society 1789).

The discovery of vaccination

Centuries ago it was noticed that persons who recovered from smallpox rarely caught it again, and if they did it was never fatal. Therefore, it was better to have suffered a mild case of smallpox than never to have had the disease at all. A mild case removed the fear of having a severe, and perhaps fatal, case of smallpox. These observations led to the practice of smallpox inoculation, the deliberate introduction into the body of matter taken from a pustule of a person with a mild case of smallpox, with the intention of causing a mild disease in the inoculated person. The origin of smallpox inoculation is not known with certainty. It was practiced in Asia before being introduced into Europe by Timonius in 1714 from Turkey (Timonius 1714). The practice involved considerable risk to treated people and to the communities in which they lived because the inoculated disease was not always mild, and on occasion death was the outcome. Moreover, inoculated persons could be a source of natural infection to others, who often suffered a severe illness.

Twenty years of investigation by Jenner preceded the first vaccination in 1796, when Jenner inoculated cowpox matter to prevent smallpox (Jenner 1801). Cowpox, unlike smallpox, is a mild disease in human beings.

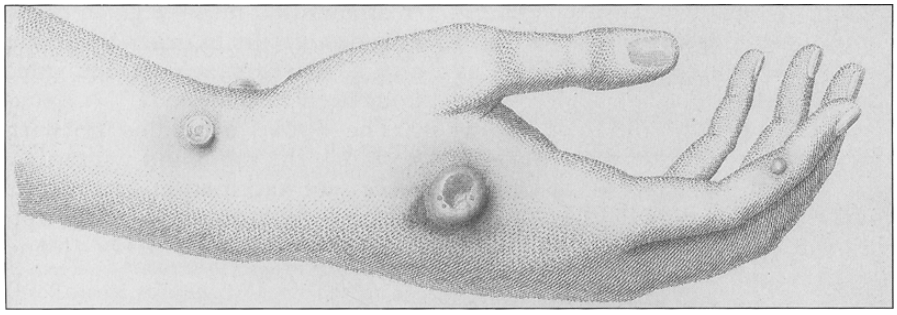

Figure 2. Jenner's illustration of cowpox lesions on the hand of Sarah Nelmes, a milkmaid. Matter taken from a lesion on this hand was used by Jenner to vaccinate James Phipps, an eight-year-old boy, giving him subsequent protection against smallpox. The lesion on the finger was not actually on the hand of Nelmes, but was on the hand of another milkmaid, and was placed there to show the appearance of an early lesion in comparison with the advanced lesion shown above the fingers. By permission of the British Library, London (British Library reference c112 f2).

> My inquiry into the nature of the Cow Pox commenced upwards of twenty-five years ago. My attention to this singular disease was first excited by observing, that among those in the country I was frequently called upon to inoculate, many resisted every effort to give them Small Pox. These patients I found had undergone a disease they called the Cow Pox, contracted by milking Cows. (Jenner 1801, pp. 1–2)

Cowpox was common at that time among persons having direct contact with cattle, but other than that the disease was generally unknown. The smallpox referred to in the above quotation was the disease condition that arose after inoculation with smallpox, hopefully a mild form of the disease.

In pursuing that exciting observation, a primary question to be addressed was whether resistance to inoculated smallpox was actually due to a previous case of cowpox or was rather a result of an earlier bout with smallpox, with protection coming as a result of that illness. Living in a rural area rather than an urban locale was of value in answering that question (Jenner 1798, p. 10):

> It is necessary to observe, that the utmost care was taken to ascertain, with the most scrupulous precision, that no one whose case is here adduced had gone through the Small Pox previous to these attempts to produce the disease. Had these experiments been conducted in a large city, or in a populous neighbourhood, some doubts might have been entertained; but here, where population is thin, and where such an event as a person's having had the Small Pox is always faithfully recorded, no risk of inaccuracy in this particular can arise.

Including in his study only persons who had been free from smallpox but who had a history of cowpox, Jenner proceeded with his investigation.

Smallpox occurred frequently in the local area over the period of the investigation (Jenner 1798). The threat of the disease led to a steady flow of people wanting smallpox inoculation. Thus in the course of his professional services Jenner was able to gather much evidence that people with a previous history of cowpox were protected from smallpox, because inoculated smallpox was mild in those people.

If infection with cowpox as a preventive treatment for smallpox was to be of value, it would need to confer a long period of protection. Jenner presented several cases to show longevity of protection following natural infection with cowpox (Jenner 1798, p. 11):

> I have purposely selected several cases in which the disease had appeared at a very distant period previous to the experiments made with variolous [smallpox] matter, to shew that the change produced in the constitution is not affected by time.

In one case, 27 years elapsed between natural infection with cowpox and inoculated smallpox, and the outcome was an extremely mild case of inoculated smallpox.

Evidence that previous natural infection with cowpox brought about protection against smallpox led to the question of whether or not artificially induced cowpox would have the same effect (Jenner 1801, p. 5):

> During the investigation of the casual Cow Pox, I was struck with the idea that it might be practicable to propagate the disease by inoculation, after the manner of the Small Pox.

By putting the idea to test, Jenner performed the first vaccination, because inoculated cowpox indeed gave the desired protection (Figure 2; Jenner 1798, pp. 32–34):

> I selected a healthy boy, about eight years old, for the purpose of inoculation for the Cow Pox. The matter was taken from a sore on the hand of a dairymaid, who was infected by her master's cows, and it was inserted, on the 14th of May, 1796, into the arm of the boy by means of two superficial incisions, barely penetrating the cutis, each about half an inch long.
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> On the seventh day he complained of uneasiness in the axilla, and on the ninth he became a little chilly, lost his appetite, and had a slight head-ach. 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.
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> In order to ascertain whether the boy, after feeling so slight an affection of the system from the Cow-pox virus, was secure from the contagion of the Small-pox, he was inoculated the 1st of July following with variolous matter, immediately taken from a pustule. Several slight punctures and incisions were made on both arms, and the matter was carefully inserted, but no disease followed.

Jenner subsequently inoculated several more people with cowpox matter, and on challenge with smallpox matter they were all resistant to it. In addition to matter taken from a pustule of a human with cowpox, Jenner also demonstrated the effectiveness of matter taken directly from

a cow (Jenner 1798).

Two fearsome aspects of smallpox inoculation had been fatalities that sometimes occurred as a consequence of the treatment and transmission of smallpox from inoculated persons to others. Jenner took these dangers into consideration with respect to cowpox inoculation before attempting this treatment. Concerning fatalities, based on his experience of treating many patients with cowpox over many years Jenner had the security of never having come across a fatality from cowpox. With regard to the possibility of an inoculated person transmitting cowpox to someone else, by purposefully observing patients with cowpox and the people they lived with and associated with Jenner determined that cowpox was not transmissible between human beings.

At no time did Jenner act in an improper or imprudent manner during his studies leading to the discovery of vaccination. His patients wanted smallpox inoculation for themselves or their children. In performing that service he noted the outcome of inoculation in relation to whether or not his patients had a past history of natural infection with cowpox. Those patients inoculated with cowpox matter, and then inoculated with smallpox matter to ascertain if they were protected from smallpox, had asked to receive smallpox inoculation anyway.

The success of smallpox vaccination

Such was the prevalence and fear of smallpox, and the advantages of vaccination over smallpox inoculation, that vaccination was enthusiastically received and quickly spread far from Gloucestershire. Because the first immunizing material came from cowpox, the term *vaccination* came to be used (from the Latin *vacca*, or cow). John Clinch, a longtime friend of Jenner, gave the first vaccinations in the New World in 1798 in Newfoundland. He used cowpox matter sent to him by Jenner. The first vaccinations in the United States were given in 1800 by Benjamin Waterhouse, a physician and professor at Harvard College, with cowpox matter obtained from England (Waterhouse 1800). Waterhouse vaccinated his five-year-old son. After the success of that, as determined by vaccination sequelae (redness, swelling, and the development of a characteristic pustule at the site of vaccination), he subsequently vaccinated his three-year-old son, his year-old infant daughter, the nurserymaid, and other servants. Again, after noting success without any problems, he moved out of the family circle into the population at large and became a strong advocate of vaccination.

It should not be construed that smallpox vaccination became established without any problems or controversy. However, many of the problems could have been avoided if Jenner's procedure had been followed in accordance with his report. Although Jenner gave descriptions of cowpox pustules on cows and on human skin (Jenner 1798), some medical practitioners used exudate from any kind of skin eruptions on cows as vaccine; if the material came from a disease other than cowpox, the result was a lack of protection from smallpox. Jenner had forewarned of this risk in his 1798 treatise, and in a later publication he reiterated the need to be able to distinguish between cowpox and other eruptive diseases of the skin of cattle (Jenner 1799). Jenner drew attention to the fact that most practitioners of human medicine are not familiar with animal diseases such as cowpox. Therefore, it was incumbent on surgeons and physicians obtaining vaccine material from local animals to be sure that it was indeed cowpox matter.

Among the controversies was one that arose after some people vaccinated at the London Smallpox Hospital developed smallpox pustules. Was it because the cowpox matter had become contaminated with smallpox matter? That was ruled out because the physician administering the treatment had successfully used the same vaccine elsewhere on other people without any of the recipients developing smallpox. Apparently, the smallpox sufferers had naturally caught smallpox while waiting to be vaccinated at the hospital (Jenner and Woodville 1800). Vaccination is a preventive treatment that must be given before infection occurs in order for immunity to develop against the infectious agent.

The above problems notwithstanding, the rapid and widespread success of vaccination gave Jenner reason to be more than a little optimistic about his discovery (Jenner 1801, pp. 7–8):

> The numbers who have partaken of its benefits throughout Europe and other parts of the Globe are incalculable; and now it becomes too manifest to admit of controversy, that the annihilation of the Small Pox, the most dreadful scourge of the human species, must be the final result of this practice.

After a well-planned global campaign in which vaccination played the major role, the World Health Organization in 1977 declared smallpox eradicated from the world.

Conclusion

Although Jenner recognized the significance of his discovery for human welfare and received international acclaim for it, he never sought financial gain from the discovery. Indeed, quite the opposite—he freely gave of his own time in promoting vaccination, giving advice, and assisting others worldwide to establish the treatment. The demands on Jenner from around the world concerning matters related to smallpox vaccination, and his obligations to his medical practice, left him virtually no time for his other major interest, the study of birds.

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