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EDWARD JENNER: THE MAN AND HIS WORK

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The two-hundredth anniversary of the birth of Edward Jenner, "the discoverer of vaccination," was celebrated on Tuesday, May 17, and the time is opportune for a brief review of Jenner's life and the beginning of the new idea which he inaugurated, and which he was fortunate in seeing widely established in his lifetime. No man has suffered more from the excessive eulogy of well-meaning friends and later admirers, or from the invective of those who for some reason or other did not subscribe to his views.

Early Life

Edward Jenner was the son of the Rev. Stephen Jenner, rector of Rockhampton and vicar of Berkeley, in Gloucestershire. Born on May 17, 1749, he was educated at first at Wotton-under-Edge under a Mr. Clissold, and then went as a pupil of the Rev. Dr. Washbourn at Cirencester. When he was 5 his father died, and the boy was looked after by his elder brother, who was also in Holy Orders. It was decided that Edward was to practise medicine, and at the age of 13 he was apprenticed to Daniel Ludlow, a surgeon of Sodbury, near Bristol. In 1770 he became a student at St. George's Hospital, London, and was for two years a house pupil of John Hunter. During this period a warm friendship sprang up between master and pupil, and after Jenner left London he and Hunter corresponded regularly for 20 years—until Hunter's death in 1793. Jenner's letters to Hunter have all been lost or destroyed. But Jenner preserved carefully Hunter's letters to him. They are now in the Royal College of Surgeons, and were printed by Baron in his biography of Jenner. The correspondence was occasioned by the fact that Jenner was no longer in London. In 1772 Jenner left London and settled in his native town of Berkeley as a country practitioner.

It should be said that this translation appears to have been made because he wanted to be a country practitioner. He had many of the qualities which are essential to a successful physician or surgeon in town. He had had a long training in a practice which probably gave him plenty of experience, and he had been a favourite pupil of the great John Hunter. Statements are still being made that Jenner was not "a doctor." This is of course nonsense. If by "doctor" is meant a man who has qualified for a doctorate in medicine, then a considerable proportion of those who legally—and successfully—practise medicine to-day would not be entitled to this appellation. In Jenner's time this entry by apprenticeship was the normal course of training for all general practitioners—that is, "doctors." It is true that Jenner did become later on M.D. of St. Andrews University, and that he did not sit any examination or present any thesis for the degree. But this was also quite a usual practice, and many other famous men have obtained

their doctorate in the same way and at the same university. Jenner never became a Fellow of the Royal College of Physicians. He was asked to do so, but by the iron ruling of the statutes he could not be admitted without sitting an examination in Latin—and this trial he declined to undertake.

Jenner as a Country Practitioner

It was certainly his deep love of the county of his birth which induced Jenner to return to it and—with brief exceptions—to spend the remainder of his days there. He was by birth and breeding a countryman. He soon settled down in practice, and took an interest in what we would now term "current medical literature." He joined a medical society at Alveston, near Bristol, and was largely instrumental in the founding of a similar society at Rodborough. To the meetings of this latter society he contributed papers—especially one on ophthalmia and another on angina pectoris. There is every reason to believe that Jenner was a conscientious and successful practitioner. He also took an interest in music, played the flute and violin, and was a good fellow at social gatherings.

Jenner as a Naturalist

Love of nature was instilled into Jenner from his earliest years. We do not hear about it during his apprentice years, but when he was a pupil of John Hunter an event occurred which might have altered the course of his life. Captain Cook returned from his first voyage to the Pacific in 1771. A "Mr. Joseph Banks"—later Sir Joseph Banks, president of the Royal Society for 41 years—and a Swedish naturalist, Dr. Solander, had accompanied Cook on the voyage and had brought back a very large collection of botanical and zoological specimens. Edward Jenner was offered the job—no doubt a part-time one—of arranging the botanical specimens, and he did it well. According to one account he was even offered the post of naturalist to Cook's next expedition—but this could hardly have been the case.

When Jenner returned to Berkeley he carried on with his natural history pursuits; and from Hunter he received not only encouragement but repeated and insistent demands for specimens. We read of requests for the nests of various birds, a nest with a cuckoo's egg in it, for hedgehogs, and for all the many other animals or objects which John Hunter required in the course of his experiments. He even asked for a bustard—then becoming a rare bird—and got it. Jenner also carried out experiments under Hunter's directions. It was in a letter replying to comments or suggestions which Jenner had made that Hunter gave him the famous advice: "But why think? Why not try the experiment?"

In 1783 Hunter suggested to Jenner that he "must pursue the cuckoo this summer," and asked for "a true and particular account" of that bird. Jenner carried out his

FIG. 1.—The Old Vicarage at Berkeley, in which Jenner was born.

observations over a few years, and these resulted in a paper which was published in the *Philosophical Transactions of the Royal Society* in 1788 and for which Jenner was elected a Fellow in 1789. This paper contains many original observations of importance—especially those in which he describes how the young cuckoo actually throws its foster-brothers, or the eggs of its foster-parent, out of the nest. He described the extreme sensitivity of the wing tips of the young cuckoo during the performance of this operation, and also the fact that it has a depression between its scapulae which appeared to him to be designed to assist the performance. When the young cuckoo was 12 days old this depression had entirely disappeared. Accepted rather sceptically after their publication, these observations of Jenner's were supposed during the middle of the nineteenth century to have been quite discredited. In the last thirty years the acuteness and accuracy of Jenner's work have been vindicated—largely by the aid of photography.

In his later years Jenner took up the question of the migration of birds. He gave instances of various birds having been seen far out at sea, and showed that the same

birds will return to the same place one summer after another. This paper was published in the *Philosophical Transactions* in the year after his death.

Smallpox and Inoculation

The incidence of smallpox in this country reached its peak in the eighteenth century. Although there were outbreaks all over the country, it was in London that the disease showed such a constant prevalence. In the 80 years between 1721 and 1800 the annual deaths from smallpox in the Metropolis were less than 1,000 in only five individual years. In 1772 it caused 3,992 deaths in London. But the pock-marked faces of so many dwellers in the great city bore striking witness to the prevalence of the disease—in contradistinction to its mortality.

The practice of inoculation for preventive purposes was well recognized during the second half of the eighteenth century. The "prevention" desired was of course that from death, and not from the disease, which was transmitted during the operation to the individual to be inoculated. Inoculated smallpox was often fairly mild, and the theory was that it was better to obtain protection as a result of a mild attack at a convenient time than to risk a severe and possibly fatal attack when one wanted it least. Practised in the East from ancient times, inoculation was introduced into this country by Timoni (1714) and by Pylarini, and a renewed effort to popularize it was made by Lady Mary Wortley Montagu (1721), who had just returned from seeing it performed in Constantinople. After 1738 the practice increased, but nothing could get over the fact that the inoculated disease was often not mild and deaths were not infrequent. In 1840 the practice of inoculation became illegal.

The Beginnings of Vaccination

While he was an apprentice at Sodbury Jenner was struck by the fact that a young countrywoman had said that she could not take smallpox because she had had cowpox. He mentioned this curious statement to John Hunter, but the latter was apparently not interested. Years later Jenner began to collect examples of persons whom he could not inoculate successfully because they had had cowpox at some time during the course of their lives. Even at this early stage he seems to have been obsessed by the feeling that cowpox ought to give complete and permanent immunity to smallpox. This is indeed strange, since every practitioner knew that smallpox did not always give complete and permanent protection against itself. By this time John Hunter was dead, and there was no one of his experience and acuteness with whom Jenner could discuss the matter.

Jenner therefore set out to show that cowpox protected against smallpox, and also that cowpox could be transmitted from one human being to another just as smallpox could.

There should be no misconception of what was in Jenner's mind. Though his arguments and deductions are possibly not too well expressed, his line of thought clearly was constructive and of considerable originality. It was one thing to show that a person who had had a natural attack of cowpox was thereafter possessed of considerable immunity to smallpox.

FIG. 2.—Chantry Cottage, Berkeley, in which Jenner lived most of his life and died.

EDWARD JENNER (1749 - 1823)

This is a photograph of the original pastel portrait (now in the Wellcome Historical Museum) made by J. R. Smith in 1800 and exhibited in the Royal Academy in that year. It is now reproduced for the first time by the courtesy of the Museum.

Cowpox was a disease of cows, and only a fraction of the population ever has any direct contact with these animals. Furthermore, cowpox was present only in certain counties of England, and only at intervals. It was quite another thing to set out deliberately with the intention of showing that cowpox, naturally acquired, could be transmitted artificially *from person to person* so that there would result an increasing reservoir of persons who had been given the opportunity of becoming invulnerable—or “immune,” as we would say—to smallpox. There is no doubt that this was what was in Jenner’s mind. At a later date opponents of his views put forward counter-claims to priority. For example, there was the case of Benjamin Jesty, a farmer who twenty years before had inoculated his wife and children with cowpox to prevent them from contracting smallpox. But Jesty had no notion of perpetuating the cowpox from one individual to another. This was the cardinal factor in Jenner’s doctrine, and it was an idea which had probably not occurred seriously to anyone before; at least, no one had ever attempted to put it into practice.

Once this point is clearly grasped certain interesting questions arise. To show the pitfalls in Jenner’s path it is sufficient to take one example. Only a few months after the publication of his famous book Jenner sent to a friend in London some lymph from the cowpox vesicle on a child’s arm. The lymph was dried and preserved in a quill. Before long people were discussing the methods of transmitting lymph to a distance—dried on lancets, and in other ways. If lymph from the human pock could be stored and transmitted in this way, why could not lymph from the pock on the cow? After all, this is essentially the method which we use to-day. The answer appears to be that Jenner was impressed early in his investigations by the fact that there are two types of cowpox in the cow—the true disease, and another form which he called “spurious cowpox.” We now know that this view is wrong; but Jenner believed it, and he also believed that the spurious type does not give immunity to smallpox. On the other hand, true cowpox in the human bred true. He was therefore afraid that if the practice of using dried lymph from cows was widely adopted numerous failures might result. There was also the possibility that septic diseases might be transmitted or that the lymph might be taken at the wrong time. Difficulties of this type must have caused Jenner much reflection—and are ignored by many who are wise 150 years after the event.

The Inquiry

In May, 1796, Jenner found that the dairymaid Sarah Nelmes had a “typical” cowpox lesion on her finger, and on the 14th of the month he inoculated the boy James Phipps with matter from this lesion. The local result was similar to that following variolous inoculation. On July 1 Jenner inoculated the boy with matter from a case of smallpox. The inoculation was unsuccessful. Jenner drew up in 1797 a short treatise embodying his results, and it was presented unofficially to the President of the Royal Society (Sir Joseph Banks). Two manuscripts of this first draft are in existence—one in the Royal College of Surgeons and the other in the Wellcome Historical Museum. The paper was refused, and Jenner in the following spring added further material and published the work privately in July, 1798. The book bears the title: *An Inquiry into the Causes and Effects of the Variolae Vaccinae, a disease discovered in some of the Western Counties of England particularly Gloucestershire, and known by the name of the Cow Pox*. A second edition was published in 1800 and a third in 1801. The work was also translated into many languages.

After the publication of this work Jenner spent three months in London (1798) looking for volunteers for vaccination. In this he was quite unsuccessful. But he left in the hands of Henry Cline, the surgeon, the quill of dried lymph referred to above. Cline used it as a measure of counter-irritation in a case of hip disease, and found that the patient had become immune to inoculated smallpox. From this case the practice of vaccination began to spread. Very soon a difficulty arose, since Dr. Woodville had been distributing lymph derived from vaccinations carried out at the smallpox hospital, and not unnaturally it produced mild smallpox eruptions. Dr. Pearson, a fashionable physician, had taken up vaccination enthusiastically, and in 1800 he proposed to establish an institution for gratuitous vaccination. Jenner was offered the post of “Extra Consulting Physician.” From this and other incidents it was apparent that Pearson was trying to filch from Jenner the credit for the discovery. But events such as these could not rob him of the many honours which soon came to him, and which he received modestly but with due appreciation. Jenner spent some time in London in 1800, and he was then requested to vaccinate the 85th regiment, which he did personally.

About the same time the practice spread to the United States, where Professor Benjamin Waterhouse was largely instrumental in obtaining results. France, Spain, and the Mediterranean countries soon followed.

Jenner’s Later Life

Vaccination was now becoming an established practice throughout the world, and Jenner was kept busy with a very voluminous correspondence. There is no doubt that his practice and his affairs had suffered as a result of his devotion to the cause which he had made. His friends advised him to petition Parliament for a grant, and in 1802, after a thorough inquiry, he was voted a sum of £10,000. In the following year he presided at the annual meeting of the Royal Jennerian Society, but a few years later its affairs were found unsatisfactory, and it was replaced by the National Vaccine Establishment. For a brief period he took a house in London and carried on a London practice. In 1806 Parliament again considered his case, voting him a sum of £20,000. Between that date and 1815, when his wife died, he resided at Berkeley and at Cheltenham. He now settled finally at Chantry Cottage, Berkeley—in which so much of his work had been done—and there he died on Jan. 26, 1823.

Epilogue

Jenner was indisputably the “discoverer of vaccination”—the promoter of the deliberate practice which he had been the first to envisage and to carry out. It is true that his *Inquiry* is a record of a very small number of cases and even fewer deliberate experiments. But an investigation must be judged by its results. The *Inquiry* led almost immediately to far more experiments in many countries than a regiment of individual investigators could have undertaken. When once the practice had been launched Jenner helped it forward in every possible way. He personally vaccinated individuals almost daily; in the early stages he attended meetings, and helped by interviews with all those in authority who could further his end—the abolition of smallpox. From 1798 until his death he carried on an extensive correspondence with scientists and physicians in many lands.

It may be considered a tragedy that Jenner in his first book maintained that cowpoxing—if properly carried out

—was an absolute and permanent preventive of smallpox, and he continued to maintain this view until the end. But it is possible that this indomitable assurance acted as a sheet-anchor to steady the bark in seas which were sometimes rough.

Of Jenner the man any country could be proud. To him fame came, at the age of 49, almost overnight, and he preserved a calmness and an equanimity which are much to be praised. Even in a country at war with Britain his name acted as a charm. At the end of the Treaty of Amiens two Englishmen were held in France, and were suffering from the effects of confinement. It was suggested that Jenner should write a letter to Napoleon asking for their release. This petition was read by Napoleon, who was about to refuse the request, when the name of the sender was pointed out to him. "Jenner!" said Napoleon. "We can refuse nothing to that man."

Certain celebrations were held on May 17 in connexion with this centenary. In the afternoon Sir Edward Mellanby gave an address at the Royal College of Surgeons on Jenner and his influence on research. In the late afternoon Sir Henry Dale opened an exhibition of manuscripts and relics of Jenner at the Wellcome Historical Medical Museum at 28, Portman Square; and in the evening a reception was held at the Royal College of Physicians.

EHRlich's ALDEHYDE TEST FOR UROBILINOGEN

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Since Neubauer discovered in 1903 that the "mysterious substance" in urine described by Ehrlich as reacting with his aldehyde reagent was urobilinogen, the aldehyde test has come into routine use as an aid to diagnosis and prognosis in haemolytic anaemias and liver disease.

One of us (L. S. P. D.) has used this test for 25 years and has repeatedly stressed its value in lectures to undergraduate and postgraduate students. The investigation described below and a detailed study of the literature on tests for urobilinogen were undertaken as a direct result of a recent experience which gravely shook his confidence in the value of Ehrlich's aldehyde test.

A colleague in London, who was under his care for severe and prolonged infective hepatitis, had been instructed to test his urine with Ehrlich's aldehyde reagent at regular intervals and to keep a record of the findings. This record, together with other information, was sent to Edinburgh to enable progress to be assessed between consultations in London. The reaction for urobilinogen was strongly positive during the early stages of the disease, becoming weaker as the severity of the hepatitis steadily increased, and later becoming strongly positive when improvement began after three months' illness. Coincident with clinical recovery, the reaction again became weaker and finally negative. After a further three months, when the patient appeared to have made a complete clinical and biochemical return to normal, he reported that his urine again showed a red colour when tested with Ehrlich's aldehyde reagent. This made him doubt the

value of the test, so he proceeded to repeat it on samples of urine from various members of his household. In each case a positive reaction was obtained, the colour appearing rapidly and being indistinguishable from that obtained for urobilinogen. One of us (L. S. P. D.), having personally checked these findings, decided to investigate the matter further. The firm from which the patient had obtained his bottle of reagent was Savory and Moore, who have co-operated with us in every way by supplying information and samples of reagent.

It is right to point out at this stage that the reagent supplied by Savory and Moore to us and subsequently tested repeatedly was entirely satisfactory. The false positive reactions obtained by our patient were undoubtedly due to the presence of some oxidizing agent which had developed spontaneously or had been introduced accidentally into the bottle of reagent. The fact that this could occur was in itself an indication of the need for investigation into Ehrlich's aldehyde test.

Ehrlich's aldehyde reagent, which consists of a solution of paradimethylaminobenzaldehyde in hydrochloric acid, has been used by many workers, but, as may be seen from Table I, there have been considerable differences in the

TABLE I.—The Composition of Various Aldehyde Reagents and the Quantities of Reagent and Urine Employed

Origin or Type of Reagent	Quantity of Benzaldehyde in Reagent (%)	Quantity of HCl in Reagent (%)	Volume of Reagent Used (ml.)	Volume of Urine Used (ml.)	Final Concentration of Benzaldehyde (%)	Final Concentration of HCl (%)
(a) Reagents used by other workers:						
Watson (1944)	0.28	22	2.5	2.5	0.14	11*
Naumann (1936)	1.0	36	0.15	2.0	0.07	2.5
Wallace and Diamond (1925)	2.0	20	1.0	10.0	0.18	1.8
Farmer (1937)	2.0	18	1.0	10.0	0.18	1.6
Sparkman (1939)	6.6	18	1.0	10.0	0.60	1.6
Hutchison and Hunter (1940)	2.0	5	1.0†	3.0†	0.50†	1.1†
Chamberlain (1947)	3.0	18	0.1†	5.0	0.06†	0.35†
(b) Reagents tested in present investigation:						
Savory and Moore	2.0	18	0.5	5.0	0.18	1.6
Ehrlich's rosindole	0.87	0.6	1.0	5.0	0.14	1.1

* Immediately neutralized by sodium acetate.

† Approximate figures only, as authors stated quantity in "drops."

composition of the reagents used and in the relative quantities of reagent and urine employed. With the various reagents in current use the final concentration of hydrochloric acid varies between 0.35 and 2.5% (excluding Watson's reagent, in which the hydrochloric acid is immediately neutralized by sodium acetate).^{*} The final concentration of paradimethylaminobenzaldehyde varies between 0.06 and 0.6%. Terwen (1925) in his studies of urobilinogen used an ethereal solution of benzaldehyde. In the Royal Infirmary, Edinburgh, Ehrlich's rosindole reagent was issued many years ago for the urobilinogen test, and the wards have continued to use it with apparent satisfaction. This reagent was originally designed for testing indole formation by *Bacterium coli* and other organisms, and its composition is as follows: paradimethylaminobenzaldehyde, 4 g.; absolute alcohol, 380 ml.; and concentrated hydrochloric acid, 80 ml.

^{*}The percentages for hydrochloric acid concentration in Table I refer to the concentrations of hydrogen chloride calculated on the basis that concentrated hydrochloric acid represents a saturated aqueous solution (approximately 36% w/w) of hydrogen chloride.