COW-POX AND SMALL-POX :

JENNER, WOODVILLE, AND PEARSON.

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SOME EARLY VACCINATIONS AND THEIR RESULTS.

THE reproduction in the BRITISH MEDICAL JOURNAL of the beautiful and valuable series of plates by George Kirtland, so fortunately discovered at an old bookstall by Mr. G. W. Collins, affords a convenient opportunity of discussing, in connection with the Jenner centenary, one of the most interesting and curious episodes in the early history of vaccination.

In the year 1799 (the year following the publication of Jenner's *Inquiry*, in which work he first gave to the world the results of his investigations regarding the variolæ vaccinæ) the whole project of vaccinal prevention of small-pox ran serious risk of disaster. The risk was due, not to its enemies, but to one or two of its most active friends and promoters, and that utter collapse did not overtake the new prophylaxis was due partly to the shrewdness and sagacity of Jenner himself. At this time Dr. William Woodville was physician to the "Hospital for Small-pox and for Inoculation," which had been established in 1746 for the double purpose, as its name indicates, of treating small-pox cases and of carrying on the practice of variolous inoculation. It was only in 1796 that Woodville had published the first volume of his *History of Inoculation*, the second volume of which, though nearly ready for the press, was destined never to appear, owing not to Woodville's death, but to the introduction of the vaccine inoculation. Woodville was intensely interested in Jenner's work. Towards the end of January, 1799, he heard of an outbreak of cow-pox in a dairy in Gray's Inn Lane. The disease had infected the hands of several milkers. Armed with a copy of Jenner's plates he visited the dairy, accompanied by the President of the Royal Society and other well known men of the time. There being no doubt of the nature of the malady, and the vesicle on the arm of a milker, Sarah Price, being very perfect, Woodville at once started from this stock the practice of vaccination. In the middle of May he published the results of his operations under the title of Reports of a Series of Inoculations for the Variolæ Vaccinæ or Cow-pox. These inoculations had all been done at the Small-pox Hospital, and in a total of 500 cases about 300 had had a general eruption. As eruption had been the ordinary accompaniment of variolous inoculation, Woodville looked on these appearances following on his new procedure, not as of essential consequence, but yet as disappointing, and he certainly had not expected them after what Jenner had published. But the occurrences did not make him propose to discontinue vaccination and return to variolation, as, in spite of the eruptions, he found the new disease to be on the whole much milder than the old. Jenner, however, was greatly disturbed by these proceedings. He communicated with his friends regarding them, and he declared, axiomatically, that wherever variolous eruptions were produced, variolous matter must have produced them. A singular fact was that Jenner himself had received some matter from Woodville, taken from a patient, Ann Bumpus, who had 310 pustules on the body, and that that matter had been sent by Jenner to Dr. Marshall, who had done many inoculations with it indistinguishable in their results from those done from other sources and without eruption.

Dr. George Pearson, of St. George's Hospital, who was one of the first to take up the new inoculation, had obtained matter—also in January, 1799—from a dairy in Marylebone Fields as well as from the Gray's Inn Lane stock. No doubt he also was in the habit of visiting the small-pox hospital and of getting matter from the cases there. On March 12th of that year Pearson sent out to medical correspondents in the country and elsewhere 200 threads soaked in matter for vaccine inoculation.

WHAT WAS THE LYMPH USED?

In addition to the lymph from the two London dairies,

various other stocks were originated and distributed and interchanged by Jenner and Woodville and Pearson. Woodville states that he often went back to the cow for fresh inoculative material, and also that he got some from Jenner. It is now, however, impossible to disentangle all the records of all the strains of lymph that were brought into use and continued or discontinued, and I do not propose here to follow the details of the heated controversy which arose regarding Woodville's eruptions, and Jenner's criticism of the hospital results. My first object is to examine the question whether it is likely that much or any variolous matter was mistakenly distributed and used and propagated as vaccinal or whether it is probable or possible that, instead of cow-pox, the matter which survived the controversies and was ultimately brought into general use was really small-pox.

A careful examination of Woodville's Reports of his 500 cases reveals some interesting facts. These cases are in two series, of 200 and 300 respectively. Much more detail is given regarding the first or earlier series than regarding the second. As I have already mentioned, 300 cases of the total 500 had eruptions. Of the first series of 200 cases, 91 had eruptions, and in the second series of 300 cases the proportion of eruptive cases was even greater. In many of the cases, however, the pustules were few; in the 91 eruptive cases of the first series, 31 had only 5 pustules or less, 11 had from 6 to 10 pustules, and only 24 had over 100 pustules. In many of the slighter cases quite possibly the eruption may not have been variolous at all. Where, however, the eruption was of appreciable abundance and severity, it may be assumed to have been variolous.

Were these variolous eruptions due to the insertion of small-pox virus, or were they due to infection of the hospital atmosphere, or were these two separate agencies at work in different cases? No inherent impossibility attaches to any of the alternatives. There is abundant evidence that there may be a local development of vaccinia on the arm whilst small-pox is incubating in the blood. Looking to the close relationships of vaccinia and variola, this is exactly what one would expect. Cow small-pox and human small-pox are so nearly allied that the two may be cultivated on the same skin at the same time, and while the results of such experiments and observations are not always the same, and while the one virus may often modify the effects of the other, it seems to me a safe rule that vaccination should not be relied on as a certain preventive of small-pox by infection, until the vaccine vesicle has had time to develop.

As regards Woodville's cases, it appears that the great bulk of the eruptions which were really variolous in his first series of 200 cases must have been due to infection from the tainted atmosphere of the Small-pox Hospital. It is fortunate that in his notes Woodville clearly distinguishes between matter taken from the arm—from the vesicle of inoculation—and matter taken from pustules of the general eruption. The great majority of his 200 cases belong to the former category. There were, however, a few cases—about 14 or 15 in the 200—for which he used matter from a pustule on the body, and these we may take as variolous inoculations. All these cases had a general eruption, amounting in half a dozen of them to from 100 to 300 pustules. But when these cases are traced in the records, it is very important to note that they were not themselves used as sources of inoculation of future cases. In every one of them we come to a full stop, so that the strain of variolous matter was not continued.

WOODVILLE'S BLUNDER.

Towards the end of his 500 cases, however, Woodville's practice greatly degenerated, and he began to take matter much more freely from the pustules of the general eruption. It was on January 21st, 1799, that his first series of cases began. This series was completed shortly before the end of March. His Reports were published in the middle of May, but he does not state exactly when his second series of cases ended.

The next noteworthy point is that almost immediately after publication of his Reports—very likely as a result of publication—Woodville became alive to the fact that he had been blundering. On June 13th he wrote to the *Medical and Physical Journal* giving information which, he said, "I deem of con-

siderable importance, as it leads to a conclusion widely different from that published in the reports." This information was to the effect that "the results would probably have been more favourable if the matter used for communicating the infection had been taken from those only in whom the disease proved to be very mild." This statement as to great mildness is rather vague. Very likely Woodville did not care to go into too much detail as to his previous mistakes. Three weeks later, however, we learn indirectly exactly what it was that Woodville meant. On July 6th John Ring, a surgeon well known in early vaccination history, wrote to the same journal as follows: "Of those whom I have inoculated or seen inoculated with vaccinia matter, few have had any considerable eruption, and those few were inoculated with matter which there is reason to believe was not taken from the original pustule on the arm, *a circumstance which Dr. Woodville has proved to be of great consequence in this disease.*" (The italics are mine.) This letter of Ring's quite sufficiently indicates Woodville's meaning, and the change which had taken place in his practice immediately after the publication of his Reports.

It is not possible to ascertain quite accurately how long Woodville had been blundering; perhaps the time might extend to about a month, possibly a week or two longer; but even during that time he did not of course blunder with regard to all his cases, or with regard to anything like all of them. Through the medium of the medical periodicals of the time, and through the constant stream of correspondence that was passing between town and country regarding the new prophylaxis, it is not to be doubted that the profession as a whole quickly became aware of what had been going on, and that any practitioner who, during that month or six weeks, had received small-pox lymph in mistake for cow-pox, would be very unlikely to continue to propagate the infection.

PEARSON'S THREADS.

Coming now to Pearson's practice, I have already stated that on March 12th, 1799, he issued to medical correspondents 200 threads of material for inoculation. I cannot find the origin of this material stated in the publications of the time. Pearson had begun with two stocks of lymph—one from the Gray's Inn Lane outbreak and the other from Willan's dairy in Marylebone Fields. Very likely it was lymph from these sources that he sent out; but we cannot exclude the possibility of some of his material having come from cases operated on at the Small-pox Hospital. He states, however, at a later date that in March, 1799, he got another stock of lymph directly from the cow. If he received this lymph in time it is more than probable that it formed part of the material which he sent out on the 12th of that month. Supposing, however, that part of his stock came from the cases operated on at the hospital, is it likely that any of the matter was variolous? Almost certainly it was not so. Any hospital lymph which he sent out on March 12th must have had its immediate origin in operations performed at least eight days earlier. But Woodville's hospital practice had not then begun to deteriorate. He was at that time engaged on his first series of cases, and, as already noted, in the few instances in which he used matter from the general eruption, he did not take any matter from those who were thus operated on, so that these strains of small-pox lymph were at once discontinued.

Moreover, Pearson himself, before he sent out his threads, had already been occupied with the question of the nature of the eruptive cases. On February 15th, 1799, he wrote to Jenner, stating that in the case of a child whom he had inoculated from one of Woodville's patients "the disorder proceeded exactly as the inoculated small-pox," and that, in consequence, he had suspected that Woodville might have used in mistake a variolating lancet; but Woodville had replied that the lancet had been newly ground, and was above suspicion. All the same, Pearson told Jenner that he intended to satisfy himself by making some experiments—"by inoculating patients with the matter of the eruptions." On March 12th, therefore, he was fully aware of the need there was for care as to the lymph he was about to send out to his medical brethren; and in the October number of the *Journal* he reports the results as follows: "From my correspondents I have not had a single case of eruption like the variolous

since that of Dr. Redfearn's, of Lynn; not one of this sort in Dr. Kelson's, of Sevenoaks, report of about 100 patients; not one in Dr. Mitchell's, of Chatham, of about 50 patients; not one in the report of near 100 patients from Dr. Harrison, of Horncastle, communicated to the Right Hon. Sir Joseph Banks; and, in short, not one case with these eruptions appear in the accounts from my other correspondents." De Carro, of Vienna, the principal vaccinator there, received his original supply of lymph from Pearson on March 20th, and very likely this was part of the 200 threads sent out on March 12th. This lymph was ultimately allowed to die out in Vienna, but the kind of material that Pearson was using and distributing at this time is indicated by the fact that in September, 1799, in writing to Pearson and Coleman for more lymph, de Carro stated that what he had already got from Pearson had given results like those depicted in Jenner's plates, as published in his *Inquiry*; and in October, 1800, he wrote that he had never seen eruptions. Pearson also sent matter to Paris, but the stock died out.

THE LYMPH GIVEN TO JENNER BY WOODVILLE.

Now we come to the interesting point as to the matter which Jenner received from Woodville, from the case of Ann Bumpus, who had 310 pustules. Is it possible that Jenner himself on this occasion mistook small-pox matter for cow-pox, and caused it to be distributed as such? Very fortunately there is sufficient evidence to indicate that this was not so, and that what Jenner got from Woodville was cow-pox, not small-pox. The date of the operation on Ann Bumpus herself was February 6th. It has already been noted that Woodville carefully recorded whether matter had been taken from the inoculated arm or from the pustules of the general eruption.

The exact pedigree of this lymph is as follows: On January 21st a girl, Collingridge, was inoculated on the left arm with matter taken from the teats of one of the cows affected at the Gray's Inn Lane Dairy. On the fifth day the vesicle had formed, and on that day Woodville inserted, no doubt as a test, variolous matter on the other arm. On the thirteenth day an eruption began to appear on the body. This was probably too early to be caused by the variolous inoculation, so that atmospheric infection again appears to have been the cause. But on the ninth day (January 30th) cow-pox matter had been taken from Collingridge's arm and inoculated on the arm of Sarah Butcher. No general eruption occurred in her case, and the test of variolous inoculation was applied on the sixteenth day (February 14th), when incrustation of the cow-pox vesicle had occurred. "The variolous inoculation produced a little redness, which disappeared in a few days." On the eighth day of this case (February 6th) cow-pox matter had been taken from Sarah Butcher's arm, and inserted in the arm of Ann Bumpus. I have already mentioned that it was at the Small-pox Hospital that these inoculations were being carried on by Woodville. On the eleventh day (February 17th) two or three pustules appeared on the face of Bumpus, and this was the beginning of an eruption which by the fifteenth day reached to a total of 310 pustules. It was from this case that Woodville gave lymph to Jenner. Jenner, however, received the lymph on February 15th (the ninth day), and it had been taken from the arm of Bumpus. At this date, indeed, there was nowhere else to take it from, as the general eruption had not begun. Variolation was not performed until the twenty-second day; and if Woodville had only recognised that the eruption was in all probability small-pox due to atmospheric infection in the hospital, he might have saved himself the trouble of so futile a test.

Woodville records five operations as done from Bumpus. Four of these had not a single pustule, and the other had 174 pustules. The strong contrast between these results—the total absence of pustules in four cases, and the large number present in the other—suggests that in the eruptive case another or additional agency had come into play—the agency of atmospheric infection. The suggestion further is that the matter which did not produce a single pustule in the four cases was vaccinal and not variolous. The lymph which Jenner got from Bumpus was obtained on February 15th. The general eruption appeared on Bumpus on the 17th, and on the 18th or 19th March, W. Walker was inoculated from

Bumpus. In Woodville's practice at this time he does not appear to have hesitated to go back to the same arm over and over again on different dates. He gives the date of Walker's inoculation as February 18th. It happens, however, that the father of Walker was an engraver, and took much interest in what was being done, and that he made sketches of the appearances on the arm at various dates during the progress of the case, and that these sketches were published in the first volume of the *Medical and Physical Journal*. Walker gives the date of the operation as Monday, February 19th, and states that it was done by Woodville in presence of Dr. Willan. No pustules resulted on the body. Close to and in contact with the two insertions made on the arm by Woodville, which developed in the ordinary way, there are four or five small vesicles which are noted as having appeared between the eleventh and the fourteenth day.

COW-POX OR SMALL-POX?

If we assume that Woodville, in the course of his second series of cases, or accidentally at any other time, or that Pearson, among some of his 200 threads, had actually sent out variolous matter under the name of cow-pox, the question remains whether there was any chance of this being largely propagated in the country, or whether the profession in the earliest years of vaccination had the means at hand to enable them to distinguish between inoculated variola and inoculated vaccinia. Of cow-pox on the cow very few of them knew anything, but with the phenomena of small-pox inoculation every medical man was well acquainted, the practice having been very extensively in vogue throughout the country for more than half a century.

To complete the argument it may be as well to show, from the records of what was actually done, that the difference between local cow-pox and small-pox was recognised by the profession, and that the material in use was really cow-pox.

THE HOSPITAL ATMOSPHERE.

In the first place, it may be convenient to show that Woodville himself came to recognise the eruptions which occurred in his hospital cases as due to the hospital itself. In the latter part of the year 1800 he wrote thus to the *Medical and Physical Journal*:

"I had not long practised the vaccine inoculation at the hospital before I was requested to extend it into private families in the metropolis, where I soon discovered that the cow-pox uniformly appeared in its mildest form, and was never attended with eruptions. I also supplied several medical gentlemen with the vaccine matter, which was used by them with the like result. Hence I began to suspect that there existed some peculiar cause which rendered the patients under vaccine inoculation in the hospital more liable to pustules than others, and that this suspicion was well founded I have since, from daily experience, been fully convinced. At various times I procured the vaccine virus, as produced in different cows, and with it inoculated patients in the hospital, but the effects of all the matter I tried were perfectly similar, and pustules proved to be not less frequently the consequence of these trials than of those made with the matter formerly employed. The last matter of the vaccine poison which I introduced into the hospital was obtained from Dr. Jenner, and originally taken from Clark's cow before noticed; with this matter I inoculated at the hospital on the same day three patients, on one of whom about 100 variolous-like pustules were produced. This instance, and numerous others of the like kind which I could adduce, decidedly prove that where there can be no doubt entertained of the purity of the cow-pox matter with which the patients in the hospital are inoculated, pustules will frequently be the consequence."

It is curious, however, that he seems to have been slow in recognising the *modus operandi* of the hospital atmosphere, for in his *Observations on Cow-pox*, published in the middle of the same year, he writes regarding the eruptions: "I am disposed to attribute them to the adventitious co-operation of the variolous atmosphere to which the patients were exposed;" but "in what way the variolous myasms act in thus modifying the cow-pox, or why they co-operate in some and not in all cases of vaccine infection, I shall not even venture

a conjecture." But in the *Medical Journal* of December, 1800, he writes: "Respecting those to whom I have communicated the infection out of the hospital or among my private patients, I have not yet met with one instance in which variolous-like pustules took place." And in the same letter he says: "That the variolous effluvia, even after the vaccine inoculation has made a considerable progress, have in several instances occasioned an eruption resembling that of the small-pox;" and he begins to sum up thus: "From the preceding observations we may infer that in this metropolis and its vicinity, where the small-pox constantly more or less prevails, the vaccine inoculation must sometimes be attended with a pustular eruption of which it is not the cause."

WOODVILLE'S OWN DESCRIPTION.

In the course of his Reports on his 500 cases—published, it is to be borne in mind, in 1799, before his *Observations* and before his letter above quoted—Dr. Woodville writes thus regarding the local appearances of cow-pox and small-pox: "However, the local tumour excited from the inoculation of the cow-pox is commonly of a different appearance from that which is the consequence of inoculation with variolous matter; for if the inoculation be performed by a simple puncture the consequent tumour in the proportion of three times out of four, or more, assumes a form completely circular, and it continues circumscribed with its edges elevated and well defined, and its surface flat through every stage of the disease; while that which is produced from variolous matter either preserves a pustular form or spreads along the skin and becomes angulated and irregular, or disfigured by numerous vesiculae." This is a particularly interesting statement. The mention of the ratio "three times out of four" shows that Woodville had not always found what he called vaccinia to produce the typical vaccine appearance. The natural suggestion is that exceptions might well be expected, looking to the fact that towards the end of his 500 cases, on which he is here reporting, he had not infrequently been using matter from the general eruption. But in the first removes from the cow there may well have been some vaccine vesicles which showed their cousinship to small-pox by some modification in shape or course, and Collingridge's case, in which there were supernumerary vesicles, is an example of this. He is very clear, however, that the two diseases could proceed *pari passu* on the same subject and yet preserve their distinctive characters: "The general character of the tumour formed by the inoculation of the small-pox is very different from that of the cow-pox; and though on the same day a person be inoculated in one arm with the matter of the cow-pox and in the other with that of the small-pox, yet both tumours preserve their respective characteristic appearances throughout the whole course of the disease. This is certainly a strong proof that the two diseases, in respect of their local action, continue separate and distinct."

TESTIMONY OF OTHER PRACTITIONERS.

In the medical literature of the period there is abundant evidence that the profession generally was well acquainted with the difference between vaccination and variolation. Ring stated in his *Treatise on Cow-pox* that where matter from eruptive cases was used, that is, variolous matter, it never recovers the vaccine appearance by passing through different constitutions even when used from arm to arm. Fosbrooke, writing to the *Journal* in February, 1800, has no doubt that cow-pox is not accompanied by eruption. A pamphlet published in 1800 under the title of *A Comparative Statement of Facts and Observations relative to the Cow-pox* also distinguishes between the local appearances of the two diseases.

In January, 1801, Stokes, of Chesterfield, writing to the *Journal*, showed that he was similarly aware of the distinction, and two months later Hutchinson, of Manchester, wrote that "the absence of eruption is so striking that the public distrust cow-pox." They had been so used to the eruption of small-pox inoculation, that they doubted the virtue of any non-eruptive preventive. Writing in May, 1799, when Woodville's hospital practice was at its worst, the editor of the *Medical and Physical Journal* says that 97 per cent. of cow-pox cases were like Walker's, in which case there was no

eruption. In November, 1799, the *Medical Journal* gives the results of 300 cases inoculated at Finmere with matter which had been got from Woodville in the summer of that year, subsequent to the publication of his Reports, and only 4 of these had any eruption. From the same source over 700 cases were done at St. Helens, and they were practically without eruption. In February, 1800, Dr. Stewart recorded in the *Journal* 43 cases of which 1 only had a very trifling eruption, which disappeared quickly without suppuration. In October, 1800, Dr. Barry, of Cork, reported 250 cases, of which only 3 had eruptions, also disappearing without suppuration. In the *Medical Review* Mr. Taynton, of Bromley, wrote in April, 1800, that though he had vaccinated a great many cases, in no instance had there been anything like an eruption; and Dunning, of Plymouth, in his *Observation on Vaccination*, published in 1800, declared that cow-pox never gives rise to a general eruption. Even in the present day we are not unacquainted with occasional trifling eruptions of generalised vaccinia.

THE EFFECTS OF WOODVILLE'S BLUNDER NOT PERMANENT.

From such facts as these it appears to me that no other conclusion can be arrived at than that the errors committed by Woodville had no permanent or appreciable effect on the nature of the inoculative matter which came into use in this country and on the Continent. The nature of his mishaps was at once recognised by others, and was soon in effect admitted by himself. The profession as a whole all over Europe was well aware of the appearances and results of small-pox inoculation, and was in little danger of confusing the new disease with the old. The thousands of inoculative variolous tests which were performed after the early vaccinations in order to ascertain whether there still remained any remnant of susceptibility to small-pox were genuine tests, and cannot be set aside on any supposition that the original protective operation had been itself a variolation and not a vaccination, and the stocks of lymph which came into existence in these early times consisted not of small-pox attenuated by cultivation from arm to arm, but of cow-pox.

WHAT IS COW-POX?

In calling cow-pox "*variola vaccinae*" Jenner indicated his own opinion as to the nature of the disease. Some of his contemporaries who accepted vaccination as a preventive of variola denied altogether that it was small-pox of the cow. It was left to Robert Ceely, of Aylesbury, in the year 1839 to show that cows really can be inoculated with small-pox with the result of producing a result indistinguishable from that of cow-pox both locally and on its transference to the human skin. Badcock, of Brighton, got similar results in the following year, and much evidence has recently accumulated to the same effect. Surgeon-Major King of Madras, Hime of Bradford, Simpson of Calcutta, Haccius of the Swiss Vaccinal Institute, and Copeman and Klein for the Local Government Board have laboured in the same field, with the general result that in the course of a few removes the matter obtained has become suitable for using from arm to arm for purposes of ordinary vaccination. Occasionally, as in Chauveau's hands, small-pox and not cow-pox has resulted, so that it does appear as if small-pox matter may remain unchanged in the surface tissues of the cow, and may be again transferred to human beings. The age of the cow is perhaps of importance here, as calves appear to be more useful than older animals in effecting the desired transformation of the disease.

Cow-pox itself, then, is only attenuated small-pox, and its peculiarity is that the attenuation has left it, as an inoculable material, safe, convenient, and effective for the protection of the individual, while it is safe also in producing a disease which does not spread by atmospheric infection. The question remains, Could any other method of attenuation produce a like effect? There seems nothing inherently impossible in this. In the history of the subject, there are some interesting records of such attempts, and the more important of these are worthy of a little consideration. Here again, for the beginnings of this line of research we have to go back to Jenner. In the last century there was a practically unanimous belief in the medical profession that one attack of an

infectious disease was an absolute and lifelong protection against all future attack. True small-pox could not recur. When a person who was pitted with small-pox from a severe attack in infancy developed in later life a very mild attack, it was dubbed stone-pock, water-pock, horn-pock, etc., and was not small-pox.

"SWINE-POX."

Jenner, however, working away in his own fashion, slow yet persevering, had evidently concluded that these eruptions were variolous in their nature, and so early as 1789 he inoculated one of his own family with a modified variola which at that time and place was called "swine-pox." The inoculation was successful, and the test of variolation, afterwards applied, showed that the child had been protected against small-pox. But we hear no more of this line of inquiry on Jenner's part, his other investigations being confined to cow-pox.

"PEARL-POX."

In the year 1807, Dr. Adams, Woodville's successor at the Small-pox Hospital, tried an exactly similar method. He took matter from an outbreak of what, owing to the whitish appearance and small size of the vesicles, was called "pearl-pox," and he declares that "at last" he had got the vaccine appearance. But the singular fact is that an examination of his records shows that he got the vaccine appearance not merely at last but at first. The very first case that he did with the matter of pearl-pox had on the tenth day a "vaccine appearance." Along with this local result there was an eruption of 150 pustules. In the first remove from this case, the local result was "perfectly vaccine in all its stages," and in the second remove the remarks are similar. In some there was more or less of a pustular eruption, and in others there was no eruption. Owing, however, as Adams states, to prejudice against vaccination, the operations were not continued. It is very unfortunate that no plates or diagrams illustrate the register of these cases, and that we have nothing to guide us in the way of description beyond such terms as "vaccine" or "perfectly vaccine." It is unfortunate also that these experiments with pearl-pox appear never to have been repeated, and indeed, so far as I am aware, there is no further mention of pearl-pox itself.

"VARIOLOID."

In another series of experiments in the direction of variolous attenuation, vaccination itself played a prominent part. In the *Journal Général de Médecine* for 1827 there is an account of a discussion which took place in the Academy of Medicine regarding certain inoculations which had been performed by a surgeon named Guillou. In the course of a small-pox epidemic, the disease when it attacked the vaccinated manifested itself as varioloid. Guillou's stock of vaccine lymph had become exhausted. In the emergency he took matter from the varioloid eruption. The matter was taken on the fifth day of the eruption from a girl, aged 15, and with it a baby was inoculated in 10 places. The result, he says, consisted of 10 fine vaccine vesicles. From these he inoculated 40 infants, and from these again another 100. Satisfied with his success, he began a new series of operations, choosing two *écoliers* suffering from varioloid, who had been vaccinated a long time previously, but whose age is not stated. Here, also, he declares that the result was excellent, but he mentions that there was not wanting in some cases an accompaniment of general eruption with fever. These operations of Guillou's, however, were brought to an end through the interference of the Minister of the Interior, who was advised by the Committee of the Academy that the experiments were dangerous and that the local result was variolous, not vaccinal. Curiously enough, in Ireland, a good many years ago the authorities of that time similarly objected to the use of vaccine matter which had been produced in the cow by the insertion of variola. Guillou's own thesis appears to have been that a vaccinated human subject, a considerable time after his vaccination, occupies the same position, with regard to attenuation of variola, as we now believe, and as Jenner from the very beginning suspected or believed, that the bovine animal occupies. Just

as small-pox inserted in the calf may be modified into cow-pox, so small-pox inserted in a vaccinated subject may be similarly modified.

THIELE'S EXPERIMENTS.

In his *Papers on Vaccination* (published 1857) Sir John Simon gives an extract from a paper by Dr. Thiele, of Kasan, recording certain experiments made towards attenuation of small-pox. Thiele held that cow-pox as manifested in the cow has its source in human small-pox, and that small-pox could, without the interference of the cow, be artificially modified, so as to give it all the properties of vaccinia. To accomplish this attenuation he said that it was essential that the lymph from human small-pox should lie for ten days between glasses sealed with wax, and should then be diluted with warm cow's milk and inoculated like common vaccine. At first he said such an inoculation causes large pustules at the points of insertion, and is accompanied by a preliminary fever about the third or fourth day, and by a secondary and more violent fever between the eleventh and fourteenth day. Locally there is a considerable areola, and small pustules surround the inoculated places. The cicatrix is larger and deeper than usual, and the edges are sometimes sharp. He lays it down that this procedure must be observed during ten generations. By that time the pustule will have gradually become equal to a vaccine vesicle. When the secondary fever ceases to appear, the vaccinator can safely proceed to arm-to-arm inoculation without further attenuation of the lymph by cow's milk. The reader of these extracts is apt to feel curious as to the particular reasons which made Thiele resort to cow's milk in his experiments. Had he any half-formed theory that as cow-pox was in his opinion derived from human small-pox, and was itself developed on the cow's teats, the secretion of the cow's udder might have some peculiar virtue in the direction of dilution or attenuation of small-pox? The extracts given by Simon, however, throw no light on this side question.

EXPERIMENTS OF TROUSSEAU AND DELPECH.

In the second volume of his *Clinical Medicine* Trousseau records a series of experiments made by himself and Dr. Delpech for the attenuation of small-pox. He used modified small-pox, which he defines as "simply small-pox modified either by antecedent small-pox or antecedent vaccination." If, as is most likely, the cases he chose as sources of inoculative material had their modification due to vaccination, then his experiments were similar to those of Guillou. His results, however, are not similarly described. "In spite of that precaution (the selection of mild cases) I always communicated natural small-pox, of the distinct form, it is true, but still unmistakable, natural small-pox."¹ Further on² he reports the results a little more favourably. "We obtained the desired result in some children, to the extent that the mother pustule (*le maître bouton*), the pustule of inoculation was alone developed, and that around it there were little pustules, its satellites.....In some cases I attained the complete success of having only the pustule of inoculation; but in others, in which the very tame virus had been employed, there were general eruptions, and, worse still, communication of small-pox to non-inoculated persons. In one case.....the small-pox resumed all its original violence, after having passed through a succession of individuals in a series of inoculations." For such reasons he found it his duty "to renounce inoculation." It will be observed in Trousseau's description of the local result that he does not assert that he got the typical vaccine appearance—"around it there were little pustules, its satellites." Such pustules are shown in Kirtland's plates of inoculated small-pox. In one of Woodville's earliest cases, the case of Collingridge already mentioned, and vaccinated directly from the cow, it is noted that on the eleventh day the inoculated part was "beset with minute confluent pustules," so that here also we have not the typical vaccine appearance.

I am not going to attempt to appraise the total value of these various experiments of Adams, Guillou, Trousseau, and Thiele. The weight to be attached to them, as a whole, must be matter of opinion. We know nothing of pearl-pox

nowadays; the local results got by Adams are not delineated, and are not sufficiently described, and Trousseau had not the same experience as Guillou. Under the law prohibiting variolation, the experiments cannot be repeated in this country, and so it almost seems as if we must remain in the dark regarding the possibilities of small-pox attenuation without the intervention of the cow. Even, however, if the small-pox could be cultivated down to the mother pustule, with or without its satellites, and could then be established permanently as a local and non-infectious disease, we would still have to pursue the inquiry as to the thoroughness and duration of protection acquired in this way. In the last century there was a small percentage of variolous inoculations—perhaps 6 or 7 per cent.—in which there was no eruption, and opinions differed greatly as to whether such a result gave much protection against natural small-pox.

THE JENNERIAN ATTENUATION.

With regard to cow-pox the case is different. Jenner formed the opinion that it gave life-long safety. Among milkers there are many instances on record which would go to support this view, were it not for one important difficulty. Obviously, the accidental inoculation of a milker's hands was a vaccination, not of an infant or child, but of an adolescent or adult. It was like a primary vaccination done in adult life in the present day, and was, as regards the age at which it was performed, equal to an ordinary revaccination. There was no subsequent growth and development and increase in bulk of the individual such as occurs after the primary vaccination of a baby, and renders necessary a repetition of the protective procedure. Needless to say, the excessive inflammation which often accompanied casual cow-pox inoculation had nothing in it protective against future small-pox. Extraneous filth inoculated along with cow-pox had no virtue, and the fact that the inoculation usually took place not on a carefully protected spot on the upper arm, but on parts of such mobility as the fingers or hands, constantly in use and constantly exposed to dirt and injury, would make the inflammation and general disturbance all the worse, without adding one whit to the protection. In our own day we have got fairly rid of these extraneous complications, and we have fairly gauged and measured the powers of vaccination, both as to the amount and duration of its protective influence, and as to the amount of local inoculation necessary to produce a satisfactory result. We have concluded that infantile vaccination, properly and sufficiently performed, gives a protection which during juvenility leaves little or nothing to be feared from small-pox. As adolescence advances this protection diminishes in value, though it by no means disappears. On account of this diminution it is an essential precaution in the interests of the maximum amount of safety that vaccination should be repeated, and this second operation is fairly sufficient for the rest of life, as no such subsequent change takes place in the tissues of the protected individual as had taken place after the infantile vaccination. In the presence of a small-pox epidemic even a third vaccination might be desirable, especially in circumstances of exceptional exposure, and after a very long interval from the second vaccination. There is no evidence that other systems of small-pox attenuation would give equal, or nearly equal, protection. While, therefore, the whole subject of disease attenuation is of the greatest possible interest, there is, after all, little practical reason to concern ourselves with the possibilities and powers of variola attenuated by other methods, and there is no reason for departing from that particular method of attenuation which we owe to the genius of Jenner.

EARLY ILLUSTRATIONS.

An examination of the facts shows that there was abundant opportunity to learn the exact appearances of vaccinia. In his *Inquiry* in 1798, these had been delineated by Jenner in coloured plates. In April, 1799, or just after Pearson had sent out his threads, and while Woodville's practice was at its worst, the *Medical and Physical Journal* published a plate giving on a hand and arm several examples of the typical rounded form of vaccine vesicles. In the following year a little work was published by C. R. Aikin, in which he depicted the successive stages of local vaccinia. The *Medical and Physical*

¹ *Sydenham Society's Transactions*, pp. 79-80.

² Page 92 et seq.

Journal states that this book was sold in thousands. Its second edition was published in 1801, and the plate to that edition is dated October 10th, 1800. There could be no possibility of any medical man who chose to look at any of these plates failing to note the differences between vaccination as shown by Aikin and others and inoculated small-pox as known from everyday experience. In 1802, as a frontispiece to a work published by Pearson, entitled *An Examination of the Report to the House of Commons*, there is a plate giving side by side at successive dates the course both of vaccination and small-pox inoculation. In 1801 the Society of Medicine in Paris published a plate showing the local results of the matter that had been taken to Paris by Woodville himself, after that which had been originally supplied by Pearson had died out. This visit of Woodville's to Paris was made in July, 1800, after he had become aware of the faultiness of his proceedings in April, 1799. This French plate of 1801 was reproduced in 1840 in a *Memoir on Revaccination* published in Paris. The vesicles shown are typical of vaccinia and give no suggestion of variolation.

Indeed, I have met with no evidence in the history of inoculation that any such vesicles as were portrayed by Jenner, Aikin, and others, had ever before been seen or heard of as a result of any inoculative process. The appearances shown in the plates in question were those of vaccinia as we still know it. No such plates had ever before been published, because no such disease had ever before been known, and the very existence of the plates is proof of the nature of the inoculative material that was being used.

We thus have on record not merely the written description but a delineation of the actual appearance of vaccinia as known to Jenner and Pearson and Woodville. A plate by Ballhorn and Stromeyer, published in Germany, also shows, though not so explicitly as the others, the contrast between vaccinia and variola. Ring's *Treatise on Cow-pox*, in 1803, contained a series of similar illustrations.

KIRTLAND'S COLOURED DRAWINGS.

None of these plates, however, are at all equal in detail and elaboration to those which are published in the *BRITISH MEDICAL JOURNAL* to-day. These drawings of Kirtland's do not seem ever to have been reproduced, and no doubt the cost would make it almost impossible to publish them at the time.

Kirtland's plates are themselves so eloquent that it is almost an act of supererogation to attempt to describe what is so well depicted. They show vaccination and variolation day by day from the second to the sixteenth day, both inclusive. Up till the fifth day the difference appears to be merely in degree of size and inflammation. Both are circular and both are growing, but on the fifth day there is just an indication of the nature of the difference which is about to develop itself. At the variolated spot there is an appreciable beginning of an areola, and close to the vesicle two very small vesicles or satellites have just made their appearance. On the following day (the sixth) there are two or three more supernumerary vesicles. On the seventh day all have coalesced so as to make a single irregularly-shaped figure, and the surrounding redness is much increased. By this time also the vesicle has become a pustule, yellowish at and near the margin, and bluish in the centre. On the eighth day this sore has extended its borders, and a new group of satellites has appeared around it. On the ninth day there is an addition to the satellites, but the striking feature is the deepening of the areola. In the centre the colour is becoming darker. On these last two days two little vesicles, becoming pustular, have established themselves outside the general areola. All this time the vaccine vesicle has been pursuing its course as we know it to do in the present day. The circular form is retained throughout; there are no satellites, and on the ninth day the areola somewhat resembles that of the

variola inoculation of the sixth day. On the tenth day there is shown a decided change on the variolated arm. Instead of scattered satellites there is a broad circle of confluent vesicles surrounding the original spot. On the eleventh day these have become yellower in hue, the areola has again extended, and round the confluent circle there are new satellites; but in addition the general eruption has begun to show itself on the arm and forearm, the eruption at this time consisting of red papules, which on the twelfth day are vesicular at the apex, and have become pustular by the fourteenth day. By the fifteenth day the areola surrounding each of these pustules of the general eruption has disappeared. Umbilication is not so clearly indicated by Kirtland in these eruptive pustules as might have been expected. With regard to the congeries of supernumerary pustules surrounding the inoculated spot, on the eleventh and twelfth day they are shown with a central punctated depression, but by the thirteenth day the "bridle" has given way underneath, the umbilication has gone, and we have instead a globular appearance. On the fourteenth day the globules are much enlarged and distended, and their yellow colour has at one part of the circle a tendency to darkening into brown, and here also the pustules are contracting rather than distended. The centre of the original inoculation is also getting darker, and in the heart of it there is just an indication of a crust. The surrounding inflammation has certainly not extended since the twelfth day, but is rather moving towards diminution. By the fifteenth day there is obvious decadence of the whole process; the areola is rapidly disappearing, the pustules are much darker, there is considerable incrustation, especially at the part which had shown this tendency on the previous day, and the centre also is darker. The series of plates closes with the sixteenth day. The pustules have lost their separate existence, the surrounding areola has disappeared excepting for a narrow line just at the edge of the circle, and there is a general contraction of the affected area. One could almost have wished that the plates had been continued for a day or two longer so as to show whether the red line at the base of the crusts on one side is merely a remainder of the areola, or whether there is here a tendency to a separation of the crust and the leaving of an ulcer to heal by granulation from the base and margins. It is unnecessary to follow in detail the course of the vaccine inoculation. The same appearances can be seen at the present time by any medical man who watches the course of one of his own cases. The vaccination of 1802 is identical with the vaccination of 1896, and there is cultivation neither upwards nor downwards.

The appearances of small-pox inoculation being such as are recorded by Kirtland and Pearson and others, it is simply impossible to suppose that medical men, knowing what small-pox inoculation was like—knowing it to be as we have it depicted by Kirtland and others—and knowing, further, from Jenner and Aikin and the *Medical and Physical Journal*, etc., what vaccinia was like, could readily blunder between the two. It is impossible to account for the capacity for error of particular individuals, and here and there a mistake no doubt occurred; but such exceptions weigh nothing with regard to the general question as to whether the material used for vaccination in the early years was cow-pox or small-pox.

[The Chromographic reproductions of George Kirtland's coloured drawings of vaccinia and inoculated variola will be found facing this page.]