THE MILROY LECTURES.

ON

THE NATURAL HISTORY OF VACCINIA.

*Delivered at the Royal College of Physicians*By S. MONCKTON COPEMAN, M.A., M.D.CANTAB.,
M.R.C.P.,Medical Inspector to Her Majesty's Local Government Board; and
Lecturer on Public Health in the Medical School of
Westminster Hospital.

LECTURE I.

[AFTER expressing his acknowledgments for the honour done him by his selection for the office of Milroy Lecturer, Dr. Copeman observed that it was just a hundred years since the publication of Edward Jenner's epoch-making work, entitled *An Enquiry into the Causes and Effects of the Variolæ Vaccinæ: a Disease Discovered in some of the Western Counties of England, particularly Gloucestershire, and known by the name of the Cow-pox*. He then sketched the ravages produced by the disease in the past among populations unprotected by previous attacks of small-pox, and gave a short account of the introduction and use of inoculation. Passing on to the introduction of vaccination, he referred to Jenner's early labours, and next proceeded to consider the relationship between variola and vaccinia in the following terms:—]

THE RELATIONSHIP OF VARIOLA AND VACCINIA.

Although it is clear from Jenner's writings that he believed vaccinia to be nothing more nor less than "small-pox" of the cow, his theory appears not to have received general support even in his own day; and from that time onwards the value of the practice of vaccination has by some been impugned on the plea that inoculation of one disease—"cow-pox"—could not be expected to exert any really protective influence against the ravages of small-pox, a disease supposed by them to be of totally different origin. And if the thesis of essential difference between these maladies were capable of demonstration, no doubt the objection would be of considerable weight. For there exists but little well-authenticated evidence that the living virus of one disease is capable, when inoculated into an animal, of affording protection against the effects of inoculation of the virus of another and totally different disease; although, no doubt, when two different viruses are inoculated at nearly one and the same time the incubation period of one or other of them may be modified as to duration.

In his first paper Jenner, as has been said, advanced the thesis that small-pox and cow-pox are identical; but even at the present day controversy wages hotly around this question, and it still awaits a definite solution.

During the long period which has now elapsed since the introduction of vaccination, many observers have set themselves the task of attempting, by experimental methods, to solve the problem of the true relationship of variola to vaccinia.

These attempts have all been directed to the possibility of giving rise to cow-pox by the introduction in one or another manner of the virus of small-pox into the system of the bovine animal. In the great majority of such attempts, which are vastly more numerous than is generally supposed, the results have been entirely negative, although so numerous have been the experimenters who from time to time have attacked the problem, that the total number of instances in which an apparently successful result has been obtained is now considerable.

As far as I am aware, the first recorded experiments are those of Gassner, of Günzburg, in 1801, who succeeded, after no fewer than ten fruitless attempts, in directly inoculating a cow with small-pox virus. The lymph thus obtained was employed for the vaccination of four children from whom other seventeen were subsequently vaccinated. None of these exhibited any signs of small-pox.

Viborg, of Copenhagen, in 1807 is stated to have also been successful in variolating the cow.

Basil Thiele, of Kasan, twice, in 1836 and 1838 respectively, succeeding in inoculating the cow with small-pox matter, and in vaccinating children with the lymph thus obtained.

In the light of recent work on this subject, his conclusions are of much interest. As stated by himself, they are: "(1) The so-called vaccine disease is not an eruptive disease peculiar to the cow, but it is produced in it by the transmission of human small-pox to it; and the man, and not the cow, as has hitherto been thought, is the source of the disease; (2) the mild disease thus caused in the cow can, by direct transmission from the cow to man, produce in him as mild a disease, which gives protection against the natural small-pox."

Thiele also described a method by which he claimed to have brought about such modification of small-pox virus as to render benign its action on the human subject without the intermediate stage of implantation on the tissues of the cow. This altered potency of the material was brought about, according to his statement, by first keeping the small-pox lymph for a period of ten days between two slips of glass, after which milk was added to it, and the resulting mixture employed for the vaccination of children.

The same process was carried through with the lymph obtained from the first and following series of children vaccinated, until after ten generations addition of milk was found to be no longer necessary. Seeing that at this date (1836-38) true cow-pox was so much more widespread than at present, that at the commencement of the century Jenner confidently looked forward to its occurrence every year, and that in consequence the majority of milch cows were liable to become infected at one or another period of their existence, this empirical method of Thiele's bears a curious and noteworthy resemblance to one of the methods, proposed by Koch, for the treatment of rinderpest. This consists in the injection into susceptible animals of a mixture composed of a small proportion of virulent blood diluted with a much larger quantity of serum obtained from an immune animal. Milk, of course, is merely an emulsion due to suspension of fatty particles in a fluid which may be regarded as blood serum, so that it is conceivable that milk obtained from a cow which had suffered not long before from cow-pox, and so become, for the time at any rate, immune, might so far modify small-pox lymph added to it, as to produce some such effect as noted by Thiele when the milk was used for purposes of inoculation.

I have been unable to find any records dealing with a repetition of these experiments, but it would be interesting to make investigation of the possibility of producing a similar lessening in virulence of small-pox lymph, by admixture with the blood serum of a calf which had been vaccinated some few weeks beforehand.

Ceely, in February, 1839, inoculated three "sturks" with variolous lymph, with the result that in two of the three he obtained in due course what he considered to be vaccine vesicles. From these lymph stocks were established, which at once came into such extensive use that in the course of a few months at least a couple of thousand children had been vaccinated therefrom. In his paper recording these experiments he states that on former occasions, even though working purposely at different times of the year, he had altogether failed in attempts to variolate the cow.

In order to test the measure of protection afforded these children by his variola-descended lymph Ceely tried on a number of them the effect of subsequent variolous inoculation at varying intervals of time from their vaccination. In no case did he obtain any greater result locally than, on the authority of Willan, is known to have attended the test inoculations employed by Jenner and Woodville.

Unfortunately, owing to the particular methods used by Ceely in his variolous inoculations of cows, some doubt is thrown on the value of the results obtained by him. He was, according to his own account, working simultaneously with both variolous and vaccine lymph, so that it is difficult to exclude the possibility that his instruments may have unintentionally served to convey the infection of both diseases at one and the same time.

Several years before the commencement of his inoculation experiments Ceely had made trial of a method originally employed by Sonderland, of Barmen (1830), who claimed to have infected cows with the contagion of variola by way, presumably, of the respiratory tract. This he did by enveloping them in blankets taken from the bed in which a patient had

died of small-pox, and by hanging other blankets similarly infected around the head of each cow in order that the animal might breathe in the "effluvia" arising therefrom. It is stated that these cows subsequently manifested symptoms of cow-pox, and that from this source lymph was obtained and used on the human subject with the result that typical vaccine vesicles were produced. Ceely failed, however, in his attempt to bring about infection in similar fashion, as, indeed, have numerous observers in various parts of the world. Yet Ceely has himself recorded an occurrence observed by him in 1840, which, although apparently but little known, is of interest in this connection. He relates an instance in which five out of eight milch cows sickened with cow-pox within twelve to fourteen days of their having been seen to be licking over a quantity of flock from the mattress on which a patient had died of confluent small-pox, and which had been spread out in the field for purification. Careful inquiry at the time appears to leave no doubt that the animals, which had been on the same farm for a considerable period, were in good health at the time of their admission to the meadow in which the bedding was exposed, and also that there had not been any other case of cow-pox in the neighbourhood. The fact that all the animals became affected simultaneously, and after a period corresponding to the usual incubation period of variola, certainly affords some reason for the assumption that the outbreak owed its origin to the animals being exposed to the "effluvia" from the infected bedding. It is, of course, possible that infection by way of the digestive tract may have been a factor also in this case, since Chauveau and other observers have shown experimentally that such result may be possible, a number of cases having now been recorded in which vaccinia has been communicated both to the human subject and also to the lower animals by the ingestion of vaccine lymph or powdered vaccine crusts.

There surely has seldom been so indefatigable a repeater of experiments as Badcock, the Brighton chemist, who during a period of about twenty-five years performed more than 500 variolous inoculations. In December, 1840, Badcock, who had commenced his work without knowledge of Ceely's slightly earlier work, first succeeded in variolating a cow, from which he carried on a stock of what was indistinguishable from genuine vaccine lymph. Although he subsequently met with similar success on no fewer than thirty-seven separate occasions, the difficulty and uncertainty of the work will be appreciated on consideration of the fact that those experiments which eventuated in success represent but 7 per cent. of the total number. The lymph obtained by Badcock as the result of his variolation experiments has been largely employed; he supplied it to hundreds of medical practitioners, and many thousands of children are said to have been successfully vaccinated with it.

About twelve years (1852) after Badcock had obtained his first successful results, two American physicians (Drs. Adams and Putnam) were equally fortunate, and were able in consequence, as reported at the time in a Boston daily paper, to furnish all the vaccine matter requisite for use in the city and neighbourhood.

In 1865 a Commission appointed by the Society of Medical Sciences at Lyons, having Chauveau at its head, reported the results of a comprehensive series of experiments carried out by it during the two preceding years, the results of which were completely at variance with those obtained by previous investigators. These results have been admirably summarised in the report of the English Royal Commission on Vaccination.

"Inoculation of the cow or heifer with small-pox matter in any one of the thirty animals used did not give rise to a vaccine vesicle; nevertheless, a definite result was obtained, in the form however, not of a vesicle, but of a thickening and inflammation of the wound; when a puncture had been made this became a papule; lymph squeezed from such a papule, and inserted into a second animal, gave rise to a like papule; and this again might be used for a third animal, but often failed; and the effect could in no case be carried on through more than three or four removes. When the inoculation was repeated on an animal on which a previous inoculation had produced such a papule, no distinct papule was formed; and moreover, lymph squeezed from the seat of the latter inocu-

lation produced no effect at all when used for the subsequent inoculation of another animal.

"There is evidence that the development of the papule was the result of the specific action of the virus. This inference is strengthened by the fact that no such papule was produced by the Lyons Commission when the small-pox matter was inserted into an animal which had previously had cow-pox naturally or artificially; as well as by the fact that when an attempt was made to vaccinate, with vaccine lymph of proved efficacy, an animal on which a papule had been so developed by inoculation with small-pox matter, the vaccination failed, though the animal had never had natural cow-pox nor been vaccinated.

"The specific nature of the lymph of the 'Lyons' papule is held to be shown by the fact that such lymph, when used on the human subject, gave rise to small-pox. On the other hand, it has been urged that in this case the virus producing the effect was simply the original small-pox matter used in the inoculation producing the papule and still clinging to the wound. This, however, is considered to be disproved by the experience that lymph from a 'Lyons' papule of the second remove also gave rise in the human subject to small-pox. Thus, Chauveau and his Commission found that small-pox implanted in the bovine animal gave rise to a specific effect which was not cow-pox but was of the nature of small-pox, though its manifestations in the cow were different from those of small-pox in man."

A few years earlier—in 1860—Martin, of Boston, U.S.A., appears to have had a somewhat similar experience, as about 50 persons vaccinated by him from vesicles raised on a cow's udder by inoculation of variolous matter taken from a pock on the body of a man who had died of the disorder were nearly all attacked with small-pox, and 3 died.

Voigt, the Director of the Hamburg Vaccine Establishment, in 1881, brought into extensive use not only in Hamburg, but also in other parts of Germany, a strain of lymph of variolous origin. In the early summer of that year he inoculated three calves with lymph obtained from a case of small-pox. In two of these the operation was apparently unsuccessful, in view of which it is of interest to note the fact that all three calves were afterwards found to be insusceptible to vaccination. In the third calf a single vesicle appeared on the site of one out of five incisions made on the left side of the perineum. Voigt adds, however, that this same animal had been vaccinated in one small place in the right hypochondrium (for what reason is not obvious), and that at this point a normal vesicle developed. Voigt does not consider that this fact invalidates the apparent success of his experiment, for the reason that, as he says, the lymph derived from, as he considers, the variolous source, proved to be more potent as regards its observed effects on children and calves than the Beaugency vaccine lymph which he had in current use at the time his experiment was carried out. Both Chauveau and Berthel have, on the other hand, expressed the opinion that Voigt's variolo-vaccine is merely a continuation of the strain of animal vaccine previously employed in Hamburg.

In 1885 Dr. Simpson succeeded in an attempt to inoculate a cow with small-pox lymph obtained from a young vaccinated girl; but, as far as I am aware, he did not publish the details of this experiment at the time. Dr. Cory, to whom Simpson sent points charged from the cow on the sixth day after inoculation, has given the following record of their use in his recent volume on *Vaccination*:

Three days after receiving the points, Dr. Cory employed them at the Animal Vaccine Establishment, Lamb's Conduit Street, for the vaccination of a young male calf. Three out of five insertions made with the lymph resulted in vesicles indistinguishable from those produced by the current lymph of the establishment. A second calf and also a child were therefore vaccinated from the first calf, with successful results in each instance, although in the calf only six vesicles resulted from seventeen insertions of the lymph. From this calf a continuous series of calf vaccinations were carried on during a period of six months. With the lymph obtained from these animals, 79 in number, no fewer than 1,247 children were vaccinated, 1,174 of whom afforded an insertion success of 98.4 per cent.

Some years later (in 1892) Dr. Simpson, then resident in Calcutta, was again successful in raising a stock of vaccine

lymph of variolous origin. Lymph was taken from a small-pox patient on the fifth, sixth, seventh, and eighth day of eruption, and each day a young calf was inoculated, the animal having been taken into the small-pox ward for the purpose.

The inoculations with the three later lymphs were unsuccessful, but the first calf showed on the sixth day of inoculation three papules on the abdomen and in the groin at points where no punctures or incisions had been made. These on the following day had developed into vesicles. Two of the incisions and one puncture also contained lymph. On the sixth day lymph was taken (whether from vesicles, incisions, or puncture, or all three is not clear from Dr. Simpson's paper) for the inoculation of another calf, from which again on the sixth day a child was vaccinated, the two insertions giving rise in due course to vesicles. From this child the strain of lymph was carried on successfully through nine generations; and Dr. Simpson remarks that each child showed splendid vaccine vesicles, much more typical in every respect than those obtained from the lymph which had been previously in use.

In 1886 and 1890 Fischer, the Director of the Institute for Vaccination at Carlsruhe, obtained two strains of variolous vaccine as the result of inoculation of calves with human small-pox lymph. In the first series Fischer inoculated a young female calf which he took into the small-pox ward of the Pforzheim Hospital for this purpose. Typical vaccine vesicles had developed on the sixth day, the lymph from which was carried on through twelve generations in the calf, after which it was successfully employed for the vaccination of children. Fischer states that the initial experiment of his second series was carried out in the Carlsruhe Institute, but that the animal was placed in a separate stable, and that every precaution was adopted to secure freedom from vaccine contamination. In this calf directly inoculated with small-pox lymph he again obtained, as in his experiments of four years previously, a vesicular eruption having the characteristic appearance of ordinary vaccinia. With lymph taken at the third remove from this calf he vaccinated his own grandson with complete success, and the strain, which has now been continued through a very large number of animals, has been brought by Fischer into general use.

Surgeon-Major King, in 1889, being then stationed at Madras, inoculated a young bull calf with fifth-day small-pox lymph obtained from a child suffering from the disease. On the eighth day after the inoculation a crop of vesicles made their appearance, not at points of insertion but some little distance away, from the lymph obtained from which another calf was then inoculated. In this calf again secondary vesicles appeared, but in addition vesicles also formed at each point of insertion of the lymph.

The lymph stock was carried on through three more generations in calves, the vesicular eruption being now in each instance strictly localised to the points of insertion. With lymph obtained from the fifth calf of the series a number of children were vaccinated successfully. Dr. Simpson reports that from the stock thus established by King 4,240 British and native soldiers have subsequently been vaccinated, and also a very large number of the native civil population, with most gratifying results, the percentages of success being much above that obtained from the lymph previously in use.

For reasons which are unknown to me, Surgeon-Major King's investigation appears to have been regarded with disfavour by the Government of Madras, by whom he was ordered back to his regiment and deprived of his special emoluments. Subsequently, however, this injustice was repaired by the reinstatement of Surgeon-Major King in his former position as Director of Vaccination in the Presidency.

In May, 1892, Dr. Hime published the results obtained by him in a single experiment on variolation. The lymph employed for inoculation of the first calf was collected from a semi-confluent case of small-pox in a previously vaccinated woman aged 37 years. No details are given as to where the experiment was conducted, but presumably it was in the private establishment from which Dr. Hime supplies vaccine lymph, as he makes the statement that "the calf was placed on the ordinary vaccination table used for these animals." A number of skin incisions were made, into which the variolous lymph

was inserted. Of these incisions, all subsequently healed, being on the sixth day only "detectable to the touch by a slight roughness." Several "pocks," however, developed at points for the most part distinct from any of the incisions; and material taken from these on the ninth day of inoculation was employed for the direct inoculation of another calf. All the incisions made on this second calf had "taken" on the fifth day, when lymph was collected in tubes, and pulp removed by scraping. Some of the latter made into "conserve" with glycerine was sent to Fischer, of Carlsruhe, who obtained excellent results with it on a calf, from which children were in turn successfully vaccinated. Dr. Hime also himself vaccinated a child with a capillary tube of the lymph, in two insertions, at each of which points a typical vesicle presented itself on the eighth day.

The largest amount of research work in this direction during recent years is that of Haccius and Eternod (1892), of whom the former is the Director of the Swiss Vaccinal Institute at Lancy, Geneva, where the work was carried out.

Haccius gives an account of no fewer than seven successful series of experiments, in each of which a strain of variolous lymph, obtained in the first instance from the human being, was carried on from calf to calf through, in some instances, as many as six or seven removes. The general result was that by the second or at the most the third remove, the effect produced was altogether indistinguishable from that which we are accustomed to see in a calf that has been successfully vaccinated. With the lymph of the fifth or sixth remove, a number of previously-unprotected children were vaccinated with unfailing success. The resulting vesicles could in no way be distinguished from ordinary vaccination vesicles of equal age. The total number of animals employed in these experiments is not mentioned, but from certain statements in M. Haccius's publication, one gathers that it was very considerable. It is obvious, therefore, that the Lancy experience as to the small proportion of success to failures is similar to that of other observers. It is worthy of note also that in those animals in which inoculation of variolous matter appears to have been attended with success, no definite vesiculation was ever observed at the site of any of the punctures or incisions that were made. The usual result in the first remove from the human being was either a single vesicle or group of vesicular points on the site of a scarification or denudation of the skin.

It is particularly stated that every precaution was taken, as, for instance, by the sterilisation of the lancet before each operation, to prevent the accidental transmission of vaccinia.

Dr. Klein, who in 1879 had obtained in 31 trials what then appeared mere negative results, renewed his investigations in 1892, employing now calves for inoculation experiments instead of milch cows as in his earlier attempts. Having procured, at the hospital ships off Dartford, lymph from the vesicles of two cases of confluent small-pox, one at the sixth, the other at the seventh day after the appearance of the rash, this lymph was, on the same day, inoculated by linear cutaneous incisions on two calves at the Brown Institution. The inoculation of one of these calves afforded no indication of success, but on the other calf he obtained a local result in the groin, which, however, consisted not of a distinct vesicle, but merely a thickening and redness, together with a linear crust, at the site of certain of the incisions into which small-pox lymph had been introduced.

Lymph pressed from the thickened wounds, when inoculated into a second calf, produced also by the fifth day a like but rather more marked result, while the thickening and redness still further increased as the process was repeated in a third and fourth calf. In none of these animals was there any appearance of vesiculation.

At this stage the fourth calf of the series was removed to Lamb's Conduit Street, where Dr. Cory, with material obtained by clamping and scraping the thickened incisions on the seventh day, vaccinated an infant in five separate insertions with complete success. Each of these presented on the eighth day appearances characteristic of vaccinia. Moreover, Dr. Cory, who kept the child under observation from first to last, was unable to detect in the course of the disorder any deviation from the condition of affairs normal to vaccinia.

"Crusts" from the arm of this child were preserved and

utilised after being mashed up in sterile salt solution for the retrovaccination of another calf. In due course there resulted in about half of the total number of incisions vesiculation of a character not to be distinguished from that current in the calves vaccinated in the ordinary course at the Lamb's Conduit Street station.

Finally, after a lapse of six weeks, Klein submitted this retrovaccinated calf and other calves vaccinated from it to the test of a further and thorough vaccination with current calf lymph, with the result that all these animals entirely resisted vaccinia. I have learnt privately from Dr. Klein that in his former (1879) experiments on cows he in more than one instance obtained results somewhat similar to those witnessed in the calf on which his more recent successful inoculation was performed. He suggested at the time the advisability of attempting a transference to a second animal, but Ceely, who was superintending the experiments, insisted on the necessity of obtaining a vesicle in the first animal inoculated as the only criterion of success, and the suggestion was therefore overruled. For his own satisfaction, however, Klein endeavoured to vaccinate one of the cows which had shown some local reaction but entirely without result, the animal apparently being immune.

Of my own experiments, the most successful series may briefly be described as follows:

With variolous lymph (contained in two capillary tubes) taken on July 30th, 1892, from a vaccinated girl, aged 16, at the fifth to the sixth day of the eruption of discrete small-pox, I on August 11th inoculated a cow-calf A, about 6 weeks old, by thirty-two linear incisions and two superficial scarified patches made on the abdomen.

On August 13th (the third day) this calf presented nothing but a slight scab over the scarified patch.

On August 15th (the fifth day) some of the incisions were somewhat red and elevated, more particularly at several definite points which tended to be vesicular. At this date, on the inner aspect of each thigh, and distant in each instance from incisions or scarifications, was a crop of shotty and incipiently vesicular pimples.

On August 17th (the seventh day), having clamped three of the incisions, including those with the quasi-vesicular appearance, I removed the lymph with the crusts by scraping, and used the material for the inoculation on this date of Calf B. The accessory incipient vesicles I left untouched.

From first to last Calf A never exhibited any appreciable rise of temperature or indisposition of any sort.

On the ninth day the linear incisions, the cross scarifications, and the accessory vesicles of Calf A were in their decadence, and in a few days more the whole process was at an end.

More than a month later, namely, on September 22nd, I vaccinated this Calf A in 23 linear incisions with calf lymph obtained from the Government Animal Vaccine Establishment. The result was absolutely negative.

On August 17th, with the scrapings obtained the same day from Calf A, I inoculated a cow calf (B) 2 months old in 56 linear incisions on the abdomen. On the third day every one of these incisions was distinctly raised and bordered by a delicate pink flush.

On the fourth day (August 20th) all incisions had evidently taken, the areola about each being now well marked, and about one-eighth of an inch in width, but there was no definite vesiculation. At this date, after clamping, scrapings were taken from certain of the incisions for further experiment. No accessory vesicles appeared in this calf, which, along with Calf A, was vaccinated on September 22nd in 17 linear incisions with calf lymph obtained from the Animal Vaccine Establishment. The result, as in Calf A, was absolutely negative.

On August 20th, with scraping taken the same day from Calf B, I inoculated a small cow calf, C (seven weeks old) in twenty-seven linear incisions on the abdomen. On the fourth day (August 23rd) every incision had "taken," and in most of them there was evidence of commencing vesiculation. Two days later (August 25th) vesiculation was distinct in several of the incisions. At no time were there any accessory vesicles. This calf also was vaccinated (September 22nd) with calf lymph from the Animal Vaccine Establishment. Again the result was altogether negative.

Thus far I have obtained an undoubtedly successful result in one series only out of four attempts, but I have at any rate been able to satisfy myself that it is possible to variolate the calf, and further that the result obtained in the first instance may become greatly modified in the course of successive removes; and, again, that animals which have been thus treated are no longer susceptible to vaccination.

I may perhaps mention here that all my experiments were conducted at the Brown Institution, to avoid any possibility of contamination with vaccinia; that as a further precaution new scalpels were used, which were invariably first carefully sterilised in a flame; that before and after use the table was thoroughly washed with carbolic acid and hot water, and during the intervals of use kept exposed to the open air.

The Royal Commission on Vaccination, in the section of their report dealing with the question of the relationship of variola and vaccinia, show that the various series of inoculation experiments of which I have given a brief account fall into one or other of three categories.

The first category includes the experiments of Thiele, Ceely, Badcock, Voigt, Haccius and Eternod, King, Simpson, Hime, and others. In these experiments "inoculation of small-pox matter into the udder or adjoining parts of the bovine animal gave rise, at or near the site of inoculation, to a vesicle, either identical in visible characters with the ordinary vaccine vesicles produced by inoculation with the matter of cow-pox, or to a vesicle the features of which, while not corresponding wholly with those of a perfect vaccine vesicle, so closely resembles it as to justify the recognition of the vesicle as a vaccine vesicle."

"Also it includes experiments in which, though the local result had not the characters of a perfect vaccine vesicle, yet lymph from it, when carried through a second or third remove in the cow or calf, presented results fully manifesting those characters, and when again transferred to man gave results indistinguishable from the ordinary vaccine vesicles."

In the second category are placed the experiments of Klein and myself. In no instance did either of us obtain any appearance of vesiculation in the animals directly inoculated with small-pox virus, although the appearance of the eruption tended to resemble more and more that typical of vaccinia, the further the remove, through a series of calves, from the original strain.

In the third category are included the practically negative result of the Lyons Commission, obtained by Chauveau and his fellow-workers. A brief account of these has already been set out.

With the exception, then, of Martin and of Chauveau and his colleagues of the Lyons Commission, all the observers mentioned claim to have obtained positive results—in a certain number of their experiments at any rate—as regards the production of typical vaccinia, after one or more removes, as the result of variolation of the cow or calf.

By no one, apparently, has success been attained invariably, but it is among the experiments of the earlier observers especially, who made use for the most part of heifers and milch cows, that the largest proportion of abortive attempts are to be met with. Subsequent experience has shown that success is much more likely to be attained if calves be used instead of heifers or cows. In this way, perhaps, Chauveau's somewhat anomalous results may be in part explained.

With reference to recent experiments on variolation of the calf, it is worthy of note that, as previously mentioned, different observers have obtained local effects in that animal, which in different calves of a series have varied considerably. The final result has, however, after a greater or less number of removes from calf to calf, been invariably the same—namely, a local vesicle is produced, which by no means at our command, such as the appearance and course thereof, or the protective power of the lymph derived therefrom, is distinguishable from true vaccinia.

Although practically there is unanimity of opinion among those who have worked at this subject, it must be confessed that, seeing the conditions under which they were carried out, many, particularly of the earlier experiments, are of little worth.

Some of the main objections are based on the fact that experiments on this subject have almost without exception been performed in establishments devoted to the continuous

cultivation of vaccinia; on the use concomitantly of vaccine and of variolous lymph on the same animal; and on the want of care as to the cleanliness and freedom from vaccine contamination of lancets and "points" used in the experiments.

Objection of similar sort against the variolations of the calf which have been achieved in recent years is hardly valid. In some of the more recent cases, at least, special precautions have been taken to ensure that the instruments and table were sterilised, and to render the environment of the animal such as to afford no likelihood of the communication of vaccinia. Most especially was this so as regards Klein's investigations and my own.

The number of successful cases which have been recorded is now so large that it is difficult to believe that sources of fallacy of the above sort should have been present in every instance, and it is therefore well-nigh impossible to resist the conclusion that a change of small-pox into vaccinia must really have come about. Nevertheless, there are found even at the present day those who, like Juhel and Dupuy (1894) and Layet (1895), maintain the essential duality of variola and vaccinia. It is, however, difficult to understand how the results obtained by the last-mentioned especially can bear the interpretation he would place upon them, seeing that he obtained, as the result of inoculating heifers with small-pox lymph, a vesicular eruption, the lymph derived from which reproduced the disease on other heifers. Moreover, subsequent vaccination of all his series of animals was either abortive or wholly without result.

Hervieux (1895), the Director of the Vaccine Institute attached to the Académie de Médecine, takes up a similar position to that of Layet and his collaborators, Le Dantec and Benech. He asserts that the only point of similarity between variola and vaccinia which has been brought forward by those who believe in the relationship of these disorders is the likeness between the vesicles which are found in either case, and denies that this point forms any argument in favour of their identity. He also considers that the use of lymph of variolous origin is fraught with danger; and so, doubtless, it may be when that employed is derived—as in Chauveau's and Martin's cases, for instance—directly from the animal first inoculated.

If, as I believe, it can be conclusively proved that small-pox lymph, by passing through the system of the calf, can be so altered in character as to become deprived of its power of causing a generalised eruption, while inducing at the site of inoculation a vesicle indistinguishable from a typical vaccine vesicle; and more important still, if it be shown that when transferred again to man, it has by such treatment completely lost its former power to produce an infectious disease, it may fairly be asserted that cow-pox—or rather, that artificially-inoculated form of the disease which we term vaccinia—is nothing more or less than variola modified by transmission through the bovine animal. Perhaps the most reasonable interpretation of such results may be that small-pox and vaccinia are both of them descended from a common stock—from an ancestor, for instance—which resembled vaccinia far more than it resembled small-pox. It is conceivable, indeed, that the seeming vaccinia, obtained in the calf by inoculation of small-pox matter into that animal, may after all be but a reversion to an antecedent type; and in this connection we may call to mind a fact of universal experience, namely, that vaccinia, however it may have arisen in the past, or is made to appear in the present, exhibits little tendency to "sport" (as, for instance, by manifesting a "generalised eruption") in the direction of small-pox.

Mr. Picton and Dr. Collins, in their addendum to the report of the Royal Commission on Vaccination, lay much stress on the want of "evidence to show that inoculation of the pox of the cow on the human skin has ever produced small-pox."

Variola and vaccinia may, nevertheless, have a common ancestry, since it is not unlikely that variola may have departed widely from the original type, and have gained an exalted virulence by repeated passage through man under conditions favourable to its propagation and activity. If this evolution of the disease has in fact taken place, variola may have suddenly reverted, under greatly changed conditions—as, for instance, implantation on the bovine animal—to an ancestral type. But the reverse process—that is, sudden "sport" of vaccinia in the direction of small-pox—is not to be expected.

It is most unlikely that a less differentiated form (cow-pox), also emanating from the common ancestral stock, should attain to the most exalted virulence in a single individual, and, *per saltum*, declare itself as small-pox, as the dissentient Commissioners insist that it ought to do.

CLINICAL LECTURE

ON

A CASE OF LOCALISED MYELITIS,

AFFECTING THE FIFTH LUMBAR AND THE SACRAL SEGMENTS OF THE SPINAL CORD, THE RESULT OF A SLIGHT TRAUMATIC INJURY;

AND

A CASE OF PARALYSIS OF ALL FOUR LIMBS,

DUE TO A SPINAL INJURY.

Delivered at the Edinburgh Royal Infirmary

By BYROM BRAMWELL, M.D., F.R.C.P.Ed., F.R.S.Ed.,

Physician to the Royal Infirmary, Edinburgh; Lecturer on the Principles and Practice of Medicine and on Clinical Medicine in the School of Medicine, Edinburgh.

(Concluded from page 1174.)

ALTHOUGH we have arrived at the conclusion that the lesion is situated within the spinal cord, we have by no means exhausted the anatomical diagnosis. We have next to endeavour to determine the exact part of the spinal cord (in its vertical and transverse diameters) which is involved. This point of diagnosis is decided by observing the exact distribution of the symptoms (the motor paralysis, sensory derangements, disturbances of reflex action, the vasomotor and trophic derangements).

The spinal cord consists of a series of segments placed one above the other; each segment consists of two symmetrical lateral halves to which a pair of spinal nerve roots is attached, and each segment of the spinal cord may be regarded as a separate spinal cord for the portions or areas of the body to which the spinal nerves connected with it are distributed. Now, as I pointed out in the first edition of my book on the spinal cord, published now a good many years ago, the essence of the clinical examination of the spinal cord consists in the examination of the motor, sensory, reflex, vasomotor, and trophic functions of each of the individual segments in detail.

In this case there is no difficulty in coming to a conclusion as to the exact part of the spinal cord which is affected, for the symptoms are very remarkably localised to the areas of distribution of certain spinal segments. This case may in fact be regarded as a physiological experiment made by disease in the animal man. It is rare to meet with cases of cord disease. I refer, of course, to indiscriminate lesions in which the symptoms are so accurately localised and limited in their distribution, and it is for this reason that cases such as this are of so much scientific interest and importance.

It is by the careful observation of cases such as this that we are enabled to increase and advance our knowledge of the functions of the spinal cord. The case is an excellent illustration of the importance of clinical observation, and confirms the view that I am never weary of expressing—that the observation of the effects of disease in man is, for the purposes of human physiology (and that, be it remembered, is the physiology which chiefly concerns the practical physician and the practical surgeon), quite as important—in fact when we are fortunate enough to meet with cases in which the lesion is so localised and the symptoms are so sharply defined as they are in this case I would say much more important—than experimental observations on the lower animals. But I must not allow myself to be diverted into a discussion on this point—the value of accurate clinical observations as a means of elucidating the physiology of the nervous system of man.

In dealing with such a case as this, the first point is to get the facts accurately. This necessitates care, time, much patient clinical observation, and above all the most scrupulous exactness and truthfulness. Dr. Colman and I have given