

MODERN METHODS OF VACCINATION

AND THEIR

SCIENTIFIC BASIS

AN ADDRESS

BY

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I DESIRE in the first place to express my appreciation of the compliment you have paid me in asking me to open a discussion on modern methods of vaccination. The subject is one which cannot fail to be of special interest at the present moment, seeing that for the first time for a considerable number of years London is experiencing an epidemic of smallpox which, although thus far of insignificant extent relative to the total population, may not improbably, with the advent of winter, assume grave proportions unless energetic measures for its suppression are adopted. I desire to include under the title that has been chosen for the subject of discussion all methods that have tended to increase the amount and to improve the value and efficiency of vaccination, especially as carried out under official auspices at the present day; to include, therefore, all methods, experimental, legal, and

administrative, which have been and are being employed with the objects that I have mentioned. But, in order the better to appreciate the precise value of such modern methods, it is necessary, in the first instance, to digress a little, in order briefly to review, under these various headings, the history of vaccination from a period antecedent to the time when the operation first gained official recognition in this country.

As is, of course, well known, the introduction of vaccination dates from the publication in 1798 of Dr. Edward Jenner's historic pamphlet, the original draft of which had shortly before been rejected by the Royal Society. It is doubtless true that Dr. Jenner had been to some small extent anticipated by Jesty and others in the employment of the virus of cow-pox as a prophylactic against smallpox, but he it was who first realised the possibility of carrying on the disease through a series of human beings, by transferring the contents of the vaccine vesicles from arm to arm, and who, by his strenuous advocacy of the methods introduced by himself, first brought the matter prominently before the public. Early in the following year (1799) an extensive series of public vaccinations were initiated in London, mainly as the result of which Dr. Jenner was enabled to state, in 1801, that upwards of 6000 persons had been inoculated with the virus of cow-pox, and that the far greater part of them had since been inoculated with that of smallpox, and exposed to its infection in every rational way that could be devised, but without effect. For this rapid extension of the practice of vaccination Dr. Jenner was not a little indebted to the activity and enthusiasm of Dr. Pearson of St. George's Hospital, and Dr. Woodville of the Smallpox Hospital, who, when Jenner's stock of original lymph had come to an end, and opportunity for replenishing it did not immediately offer, were enabled, as the result of their discoveries of cow-pox outbreaks in various parts of London, to start independent series of vaccinations. In 1802 Dr. Jenner's discovery was brought to the notice of

the Legislature, with the result that a Committee of the House of Commons, after examining a number of witnesses eminent in the profession, issued a report entirely corroborative of Dr. Jenner's statements. In 1806, again, in consequence of an address to the King voted by the House of Commons, the Royal College of Physicians of London were instructed to inquire into the matter. Concerning the outcome of this inquiry, which extended over some nine months, it is stated, in the Appendix to the Report of the Select Committee on Vaccination of 1871, that "the College of Physicians feel it their duty strongly to recommend the practice of vaccination. They have been led to this conclusion by no preconceived opinion, but by the most unbiassed judgment, formed from an irresistible weight of evidence that has been laid before them." Sir John Simon has placed it on record that in consequence of this report, which was presented to the House of Commons in July, 1807, "the public mind was apparently quite satisfied on the subject, and from this period begins to date the almost universal vaccination of children of the educated classes in this country."

In 1809 the so-called National Vaccine Establishment was founded, of which Dr. Jenner was at first appointed Director, although he shortly after resigned the post. From this period onwards, in spite of a certain amount of opposition, the practice of vaccination became gradually more popular. But notwithstanding the fact that the value of the operation received ample recognition from Parliament, by whom its discoverer was substantially rewarded, it was not until the year 1840, in which the first Vaccination Act was passed, that the subject was dealt with by legislative enactment. By this Act, which was to some extent amended in the following year, every inhabitant of England and Wales was afforded the opportunity of obtaining vaccination at the public cost, although the question as to whether any person availed himself of its advantages or not was left entirely

to his own option. Another important provision of this Act was that the operation of smallpox inoculation, which prior to the introduction of vaccination had obtained a considerable hold on the populace, was now prohibited, the transference of smallpox virus from one person to another being made a penal offence.

Not until thirteen years later, in 1853, did vaccination become compulsory. The Act passed in this year made provision for the establishment of stations in each of the districts into which guardians and overseers were required to divide their unions and parishes in order to afford increased facilities for vaccination of the poorer classes. At these stations medical officers were to attend to perform the operation, and again for inspection of the result, and parents or others having charge of children, failing to cause them to be vaccinated, or, subsequently to vaccination, omitting to have them taken for inspection, rendered themselves liable to a penalty. Certain further enactments, to which specific reference is unnecessary, came into force in 1858 and 1861. Six years later, in consequence of certain difficulties having arisen, more particularly in regard to the enforcement of penalties, a Bill to consolidate and amend the law relating to vaccination was brought before the House of Commons. This, after reference to Select Committees of both Houses, was passed, and received the Royal assent on August 12th, 1867. Hardly, however, had it become law before strenuous opposition to its provisions was raised, Parliament being eventually petitioned to repeal it. Under these circumstances a Select Committee, to which reference has already been made, was appointed in the session of 1871 to inquire into the operation of the Act. As the result of careful consideration of the evidence brought before them, the Committee reported that in view of the great, though probably not absolute protection afforded by vaccination against attacks of smallpox, together with the almost absolute protection against death from that disease, it was the duty of the State to en-

deavour to secure the careful vaccination of the whole community. They were further of opinion, however, that multiple penalties should not be imposed in the case of the same child. These suggestions were embodied in a Bill which passed the House of Commons, and after amendment in the Upper House, involving some disagreement between the two legislative assemblies, became law in 1871. By this Act the Local Government Board were substituted for the Poor Law Board and the Lords of Her Majesty's Privy Council in the administration of the Vaccination Acts, and the powers of the Board were extended. Under the provisions of this Act and a further Act of 1874 the Local Government Board, in October of the latter year, issued an Order regulating the appointment, tenure of office, duties, and remuneration of vaccination officers, and also the institution and conduct of proceedings by them. In February, 1887, an Order dealing with the duties of public vaccinators was issued by the Board, and in February of the following year (1888) yet another Order altered the age limits at which re-vaccinations could be performed at the public expense.

Meanwhile, however, opposition to vaccination had been steadily increasing, and the administration of the Vaccination Acts became more and more difficult. Thus, although in the year 1872, the first year for which complete returns were made after the passing of the Act of 1871, the number of children in England and Wales whose vaccination was not finally accounted for amounted to 5·1 per cent. of the total number of births, and the same percentage was unaccounted for in 1883, subsequent to this date the percentage of cases not fully accounted for mounted gradually higher and higher.

It was under these circumstances that Mr. Ritchie, the then President of the Local Government Board, came to the conclusion that further investigation of the whole subject from every possible point of view was desirable, and accordingly in May, 1889, a Royal Commission was appointed, consisting of fifteen members,

under the presidency of the late Lord Herschell. The terms of reference were as follows:—To inquire and report as to (1) the effect of vaccination in reducing the prevalence of and mortality from smallpox; (2) what means, other than vaccination, can be used for diminishing the prevalence of smallpox, and how far such means could be relied on in place of vaccination; (3) objections made to vaccination on the ground of injurious effects alleged to result therefrom, and the nature and extent of any injurious effects which do, in fact, so result; (4) whether any, and if so what means should be adopted for preventing or lessening the ill effects, if any, resulting from vaccination; and whether, and if so by what means, vaccination with animal vaccine should be further facilitated as a part of public vaccination; (5) whether any alterations should be made in the arrangements and proceedings for securing the performance of vaccination, and in particular in the provisions of the Vaccination Acts with respect to prosecutions for non-compliance with the law.

After sittings extending over a period of six years the Royal Commission published their final Report in August, 1896. Once again the value of vaccination as a protection from smallpox was reaffirmed, the actual amount of such protection being declared to depend on the efficiency and thoroughness of the operation and its repetition after an interval of from seven to ten years. Injury following on the operation was declared to have been insignificant in the past, and under better precautions, which should be adopted in the future, likely to disappear completely. Certain suggestions also were put forward as to the best means of popularising vaccination, and as to alterations in regard to the infliction of penalties on defaulters, and the affording of a loophole to the “conscientious objector.”

Before this Royal Commission I had the honour of giving evidence, mainly in reference to the outcome of research work which I had been carrying on for several years previously. This work had dealt with methods of testing

the potency of various kinds of lymph, whether of human or bovine origin, and their relative protective powers against the virus of smallpox, and more particularly with the question of the purification and preservation of vaccine lymph derived from the calf.

Years before, the occurrence of certain fatal cases of erysipelas following on vaccination in the practice of the then public vaccinator at Norwich, concerning the origin of which an official inquiry was held at the time, had, boy though I then was, made a great impression on me. When commencing work on the subject of vaccination, the remembrance of this unfortunate event caused me to turn my attention to the possibility of avoiding the accidental transference of erysipelas and other diseases from one child to another, in the operation of vaccination, by the substitution of some preparation of animal lymph for the arm-to-arm method of vaccination with human lymph, which, prior to the passing of the Vaccination Act of 1898, was the only method officially recognised outside the metropolis.

On making inquiry into the matter, I found that there prevailed very commonly an idea that the use of crude calf lymph was undesirable, for the reason that it "took" more strongly than human lymph; that, in other words, more reaction and more generally "bad" arms were believed to be likely to result in cases vaccinated with lymph of bovine origin. In the course of a lengthy series of bacteriological inoculations of different culture media from various samples of vaccine lymph, carried out originally in the hope of isolating the specific contagium of vaccinia, I found that my culture tubes were apt to show abundant growth of micro-organisms which proved to be in no sense peculiar to vaccine lymph, consisting in part, indeed, of forms apparently identical with certain microbes commonly associated with suppurative processes. Moreover a further point was noted that in plate cultures inoculated from specimens of fresh calf lymph the number of

individual colonies which resulted was almost invariably much greater than in similar plate cultures, the nutrient medium of which had been inoculated with an equal quantity of fresh human lymph. And it appeared to me not improbable that this fact might have relation to the observed tendency of calf lymph to "take" strongly, to which I have already referred, and might be due, in turn, to the greater difficulty in keeping clean the skin of the calf, as compared with that of a child. The further fact was also noted that when vaccine lymph of either bovine or human origin was stored for any length of time in capillary glass tubes, the opacity which usually resulted after a longer or shorter period (an occurrence usually associated with deterioration of the efficiency of the lymph for purposes of vaccination) was due, in large part at any rate, to an enormous multiplication of extraneous micro-organisms, which found in the serum, of which the liquid portion of the lymph consisted, a favourable medium for their continued growth and multiplication.

With the object of obtaining, if possible, inhibition of these extraneous micro-organisms without injuriously affecting the specific contagium of vaccinia, and thus providing myself with material of more hopeful nature for the purposes of my research, I carried out, some twelve years ago, a series of experiments, which were first demonstrated to the International Congress of Hygiene in 1891, and subsequently to the Royal Commission. The results have since been set out fully in the Milroy Lectures for 1898. To these experiments, therefore, it is unnecessary for me on the present occasion to refer in detail. Suffice it to say that, eventually, the desired result was obtained by submitting the epithelial pulp of the vaccine vesicle, after careful trituration, to the continued action of a sterilised 50 per cent. watery solution of chemically pure glycerine for about four weeks; such treatment having the effect of at first inhibiting, and ultimately destroying altogether, the numerous extraneous micro-organisms originally present in the

lymph material.¹ Later, it became apparent that such an emulsion, if preserved and stored under favourable circumstances, of which a low temperature and protection from light are of special importance, was usually capable of retaining its efficiency as vaccine unimpaired for considerable periods. Still further investigations proved that not only was it possible to kill off all the bacteria ordinarily to be found in crude lymph material, but also the streptococcus of erysipelas and the bacillus of tubercle, even when for experimental purposes these micro-organisms had been added in relatively huge quantities to the lymph pulp prior to glycerination. Thus was gradually elaborated the method of ensuring the bacteriological purification of vaccine lymph to which the Royal Commissioners make reference in their final report, and which, as the result of further investigations carried out at their suggestion on behalf of the Government, has now been officially adopted in this country for the purposes of public vaccination.

In order to make adequate provision for the manufacture of glycerinated lymph on a sufficiently large scale it became necessary to revise and largely augment the arrangements previously in force under the auspices of the Government. Thus the Animal Vaccine Establishment in Lamb's Conduit Street, which had been founded in 1881 under the direction of the late Sir George Buchanan and Dr. Cory, mainly for the performance of vaccinations direct from calf to arm, was entirely renovated in order to comply with modern aseptic requirements, and provision was made for the accommodation of a largely increased number of calves. Also additional premises were leased of the British (now the Jenner) Institute of Preventive Medicine, and what are now known as the Government Lymph Laboratories were founded.

My late official chief, Sir Richard Thorne, and I had previously, at the instance of the Government, made a tour of inspection of the principal vaccine establishments

¹ See Plates I and II.

on the Continent, more especially those under Government control in Germany, where we found that the methods devised by myself had already been adopted. As the outcome of the practical experience thus acquired, supplemented by the results of a somewhat similar, although less extended series of visits made by Dr. F. R. Blaxall subsequent to his appointment as Bacteriologist to the Department, the laboratories were equipped so far as possible with everything in the way of apparatus and accessories that appeared likely to prove useful in commencing operations on a large scale. Exactly how large that scale was to prove, however, we hardly realised at the time, and very considerable augmentation of the modest staff with which the work was commenced, and large expenditure, for the installation of additional instruments, has been found necessary in order to ensure the enormous demand for lymph being met as promptly and efficiently as is now invariably the case.

The methods employed by the Government¹ in the production, preparation, and storage of vaccine lymph, and the work performed by the staff, may briefly be described as follows:

1. *Vaccination of the calf*.—Calves of suitable age (from three to six months), breed, and condition are placed in a quarantine stable for a week. Their health being ascertained to be satisfactory, they are transferred to the Animal Vaccine Establishment. Each calf, on admission, is examined as to its general health, is weighed, and its temperature taken, a record as to these points being kept. When required for vaccinating purposes the calf is strapped to a large tilting table, and the lower part of the abdomen, extending as far forward as the umbilicus and backwards into the flanks, is carefully shaved. This shaven area is first washed with a 5 per cent. solution of carbolic acid or lysol, then well syringed with tap water, and finally cleansed with sterilised water. The moisture from such washing is removed from this

¹ Report of the Medical Officer to the Local Government Board, 1899.

shaven area and from the adjacent skin by means of sterilised gauze sponges. By these means it is found that this area of skin can be freed from micro-organisms, as evidenced by absence of growth on surface agar-agar or gelatine culture media inoculated with scrapings. The calf is then vaccinated with glycerinated calf lymph, introduced into the skin in numerous parallel linear incisions by a sharp scalpel, previously sterilised, which is dipped from time to time in the vaccinating fluid. The incisions are designed to penetrate the epidermis and to open up the rete Malpighii, if possible, without drawing blood; and as they are made additional glycerinated lymph is run in along the whole length by the aid of a sterilised blunt instrument, such as an ivory or bone spatula. The inoculation of the incisions is effected immediately they are made, otherwise the lips of the wound are apt to swell and close the opening. After vaccination the calf is removed from the table, and is then so stalled in a stable as to prevent any injury to the vaccinated surface. The temperature of this stable is not allowed to fall below 60° F.

2. *Collection of the vaccine material.*—After five days (120 hours) the calf is again placed on the table and the vaccinated surface is thoroughly washed with soap and warm water, gently rubbed over it by the clean hands of the operator. It is again washed with tap-water and finally cleansed with sterilised water. Next, any crusts that may have formed upon the vesicular lines and any epidermal *débris* are removed by the careful use of a sterilised india-rubber pad. Superfluous moisture is absorbed by sterilised gauze sponges. At this stage the site of each incision should present a line of continuous vesiculation. The skin having been put firmly on the stretch, the vesicles and their contents are collected with a sterilised Volkmann's spoon, each line being treated in turn and scraped once only, care being taken that the edge of the spoon does not touch the neighbouring line of vesicles. In this way the vesicular pulp is removed

without admixture of blood. The pulp obtained by the above procedure is received into a previously sterilised stoppered bottle of known weight. The abraded skin surface of the calf is gently washed with warm water and dusted over with starch powder or boric acid powder. The animal is then removed from the table and is weighed. Nearly all calves show a considerable gain in weight during their stay at the station and during the vaccination process. Each calf is then transferred to the slaughterhouse attached to the Islington Cattle Market, and is there slaughtered. A complete examination is made, on behalf of the Board, of the carcass and all the viscera, by a veterinary surgeon especially appointed for the purpose. A report of this examination is received at the laboratories next morning. No lymph is used for any vaccination of the human subject until the animal in question is certified to have been healthy.

3. *Glycerination of the vaccine material.*—The bottle containing the lymph pulp from each calf is taken to the laboratories, where the exact weight of the material is ascertained. The pulp is next transferred to a triturating machine; that employed being either one invented by Dr. Chalybäus of Dresden or a modified form of it. All the parts of the machine which come in contact with the lymph pulp are previously sterilised by prolonged steaming. The vaccine material, just as it is derived from the calf, is then passed through the machine, which is worked by an electric motor. When the pulp has been triturated in this way, the amount of subdivision it has undergone can be ascertained by suspending a loopful of the ground-up material in a watch-glass containing distilled water. If the trituration has been effectual such suspension should show only the minutest particles of pulp, causing the water to appear merely cloudy. The pulp is then passed through the machine a second time together with four times its weight of a sterilised mixture of 50 per cent. of pure glycerine in distilled water. The resulting mixture is then once more passed through the

machine, thus producing a fine and intimate emulsion. At this stage a loopful of the emulsion is withdrawn with a sterilised platinum needle, and agar-agar plates are established in order to estimate both the number and the quality of the micro-organisms present in the lymph.

4. *Storage of emulsion.*—The emulsion is next received into conical glass receptacles, previously sterilised. By means of a stopcock at the apex of the cone the glycerinated lymph is run into small sterilised test-tubes capable of holding from 4 to 10 c.c. Each tube is filled as completely as possible, so that very little air remains in contact with the emulsion. It is plugged with a sterilised cork, and sealed with melted paraffin, which has been rendered aseptic with carbolic acid, and is then placed in a dark, cool cupboard or ice-chest. Week by week agar-agar plates are established from the emulsion, with the result that the number of colonies is shown to diminish successively in the several plate cultures. At the end of a month the plates rarely show colonies of any sort.

5. *Use of the lymph at the Animal Vaccine Establishment prior to distribution.*—When the stage is reached at which agar plates show no growth after inoculation with the emulsion, samples of the lymph are drawn up into capillary tubes and despatched to the Animal Vaccine Establishment for the vaccination of children. The results of these vaccinations are recorded a week later, and, from the number and size of the vesicles obtained, an estimate is made as to the potency of the lymph.

6. *Transference of the glycerinated lymph to capillary tubes for distribution.*—When the lymph of a given calf has been shown to be satisfactory, the bulk of it is transferred to sterilised capillary tubes by means of special tube-filling machines worked by water-power. These tubes are next sealed in a small gas flame, every care being taken to prevent overheating of the lymph during the process. These sealed tubes are then stored in an ice-chest in boxes in such numbers that any quantity

demanded up to some 8000 tubes *per diem* can be at once despatched to the National Vaccine Establishment at Whitehall, from whence the lymph is distributed to public vaccinators.

7. *Recording the results of vaccinations by public vaccinators.*—Each public vaccinator receives, in response to application made to the National Vaccine Establishment, a consignment of lymph, together with a schedule in which to record the results of its use, and these schedules, after having been examined at the National Vaccine Establishment, are sent to the laboratories. The schedules indicate the series number of the lymph, the date of its despatch from the National Vaccine Establishment, the name of the public vaccinator to whom it was supplied, the number of tubes sent, the dates when the several tubes were used, the number of persons vaccinated, the number of scarifications made, and the number of vesicles obtained. All these details are recorded at the laboratories, and from the last two items information as to the success which has resulted, both as regards individuals vaccinated and insertions of lymph made, is obtained and set forth, both in full and in the form of a percentage. In addition to these records a register is kept stating the particulars of the calves employed, the details of the lymph obtained from each calf, including the results of the bacteriological examinations, the results of the use of the lymph at the Animal Vaccine Establishment, and also the number of tubes of each series despatched to the National Vaccine Establishment.

During the first year of operations nearly 500,000 tubes of glycerinated lymph were sent out from the Government Laboratories. Notwithstanding the difficulties that had naturally to be overcome in the inauguration of work of a character entirely new to practically all those engaged upon it, the success attending the use of the lymph at the hands of public vaccinators throughout the country was distinctly gratifying, the returns made by them to the National Vaccine Establishment showing that a case

success of 93 per cent. and an insertion success of 83 per cent. had been attained. With a recent lymph series concerning which it became necessary to make special inquiry, and which had been distributed to 160 public vaccinators, the case success and insertion success were found to be 98 per cent. and 93 per cent. respectively. And at the present time it is by no means an unusual experience at the laboratories for returns showing complete case success and insertion success to be received.

Under the provisions of the Vaccination Act, 1898, which came into force in January, 1899, for a period of five years, and of the Vaccination Order (1898) of the Local Government Board, numerous changes in connection with vaccination administration and with the performance of the operation were introduced, in addition to the supersession of arm-to-arm vaccination by the use of glycerinated calf lymph. Thus, whereas by the Vaccination Acts of 1867 and 1871 the parent or person having the custody of any child was required to procure its vaccination within three months of birth, this period, by the Act of 1898, has been extended to six months. Again, no parent is now liable to a penalty under the compulsory clauses of the Vaccination Act who affords proof that he has, within four months of the birth of a child, satisfied a stipendiary magistrate or two justices in petty sessions that he conscientiously believes that vaccination would be prejudicial to the health of the child. Moreover in no case can proceedings now be taken more than twice against a defaulting parent, namely, once under Section 29 of the Act of 1867, and once under Section 31 of the same Act, provided that the child has reached the age of four years. When first propounded, the so-called "Conscience Clause" was received with much hostile criticism, more particularly on the part of the medical journals; but it is now, I think, generally admitted that the clause has justified its existence, since its operation has practically done away with "martyrdom," and so has weakened to no slight extent

one of the principal weapons in the armoury of the anti-vaccinators.

The operative procedure in public vaccinations was formerly based on the necessity of carrying on a weekly series of transferences of vaccine lymph from arm to arm, this method having been originally introduced as the best means then attainable of insuring the activity and comparative purity of the lymph. In large urban districts, therefore, vaccinations were performed week by week throughout the year, while in small towns and rural districts quarterly or half-yearly periods, each comprising several weeks, usually sufficed. In the latter cases material for starting the series was generally obtained by vaccinating one or more infants a week previously; and if fresh lymph for this purpose could not be obtained from a private case or through the good offices of a neighbouring practitioner, a few doses of human or calf lymph, stored in tubes or on points respectively, was provided on application being made to the National Vaccine Establishment.

Again, for the purposes of arm-to-arm vaccination the provision of stations to which children were brought, first for the performance of the operation, and again after a week's interval for inspection of the results, was an essential. The occasional hardships to the mothers and a somewhat remote possibility of danger to the children involved in being taken long journeys to a vaccination station in bad weather, or arising from the collecting together in one room of a number of children and adults, one or more of whom might happen to be suffering at the time from some infectious disorder, are a few of the reasons which appeared to render a change in this regulation desirable; as a matter of fact, it would appear that nothing but good has arisen from the substitution of domiciliary for stational vaccination, coupled as it is with the use of glycerinated calf lymph, "or such other lymph as may be issued by the Local Government Board." It may here be mentioned, however, since the

fact appears to be comparatively unknown, that it is not essential for a public vaccinator to employ the lymph issued by the Government unless the parent or person in charge of the child exercises his right of insisting on its use. But the public vaccinator "must not employ lymph supplied by any person who does not keep an exact record of its source," and in any case he "must keep such record of the lymph he uses for vaccinating" as will enable him always to identify the origin of the lymph used in each operation. Further, the operator is enjoined never, when he has unsealed a tube of lymph, to attempt to keep any part of its contents for the purposes of vaccination on a future occasion. Moreover he is required to use an artificial blower for the purpose of expelling the lymph, instead of applying his mouth to the tube.

Two other sections of the "Instructions to Vaccinators under Contract" in the third schedule of the Vaccination Order of 1898 are of special importance. One of these refers to the aseptic precautions with which every stage of a vaccination should be carried out. "These should include (1) the cleansing of the surface of the skin before vaccination; (2) the use of sterilised instruments; and (3) the protection of the vaccinated surface against extraneous infection, both on the performance of the operation and on inspection of the results." The other section to which I would specially refer requires that, whenever possible, four separate good-sized vesicles, or groups of vesicles, not less than half an inch from one another, must be produced, and that in any case the total area of vesiculation resulting from the vaccination should not be less than half a square inch. As regards the standard thus set up and insisted on in the case of those vaccinators whose work comes under periodical inspection at the hands of the Medical Inspectors of the Local Government Board, it may at once be admitted that there is no special magic in the particular number "four." But an area of half a square inch having been

recognised in the Report of the Royal Commission as probably the least extent of vesiculation, absorption from which is capable of affording adequate protection to the individual against subsequent invasion by smallpox, the regulation requires that this area should be distributed over four insertions, mainly for the reason that experience has shown that less inflammatory reaction and permanent destruction of skin tissue is likely to ensue than if the attempt be made to secure the same area by means of a less number of insertions of lymph.

This leads us to the consideration of what constitutes "efficient" vaccination. The answer may be summarised as follows:—the clinical activity and bacteriological purity of the lymph employed for vaccination; the skilful performance of the operation itself; the making an adequate number of insertions of lymph over a sufficient area; the observance of precautions needful for ensuring strict asepsis, both at the time of vaccination and subsequently, until the vaccination wounds are soundly healed; all these are matters to be regarded as essential to "efficient vaccination." But, as has been well said by a writer in the 'Edinburgh Review,' "even after efficient vaccination a slow progress away from safety and towards danger is inevitable, and re-vaccination at least once after childhood is necessary if protection is to be maintained."

Much care has been exercised of late, not only by the Government but also in many of the trade establishments, especially on the Continent, in the preparation of the glycerinated calf lymph which, in public and private work alike, is now almost universally employed in this country. But this lymph, although under proper conditions usually capable of retaining its potency for many weeks or months, nevertheless under certain circumstances, at present imperfectly understood, is liable to become rapidly weakened, and even eventually to become altogether inert. Possibly the condition of the calves from which the lymph is obtained, especially as regards their general health and the suppleness or the reverse of their skin, or exposure of

the lymph to the action of light or to a high temperature, is of special importance. Consequently, in order to ensure the best results from its use, it is not only necessary that great care should be exercised in its manufacture, but it is also advisable that the lymph should be employed for vaccination as soon as possible after bacteriological examination has demonstrated its freedom from suppurative and other extraneous micro-organisms. We unfortunately at present possess no *test* of the efficiency of lymph other than the clinical one, and it is further of interest in this connection that samples of lymph capable of affording fair results on the calf may fail to cause equal response when employed for vaccination of the human subject. It is therefore of importance that, as is invariably done in the case of the lymph issued from the Government Laboratories, every batch should be tested on children before being distributed for general use.

As regards the carrying out of the operation itself, it is somewhat unfortunate that there exists no official definition of what constitutes a "successful vaccination," and in consequence it is open to any practitioner to give a certificate of successful vaccination in cases where but one minute vesicle may have been produced. It is to be feared that such certificates are too frequently given, and it cannot be too strongly urged that vaccination of this sort involves incomplete protection. The standard laid down by the Local Government Board, and to which reference has already been made, has for the most part proved easily attainable in practice, and it is much to be desired that in private as in public work the attainment of this standard should be aimed at in every instance. The suggestion has been made that, in the form employed in certifying to the success of a vaccination, the medical man performing the operation should be required to state the number of insertions of lymph made and the number of vesicles or groups of vesicles resulting therefrom. But it does not appear that the value of such a regulation would be very great in the absence of a further regulation requiring that

all vaccinators, public and private alike, shall conform to a definite standard. The further suggestion has been made that every medical man should become a public vaccinator, to the extent that he should have the right of claiming a fee from public funds for every vaccination performed by him, provided that he was willing that his work should be subject to inspection on behalf of the Government. But the originators of this idea can hardly have realised the magnitude of the inspectorial staff that would be required if such an arrangement were to be put in force.

The treatment of the arm, at the time of vaccination and subsequently during the progress of the case, is another subject which has aroused considerable controversy, and concerning which much divergence of opinion would appear to exist. Thus, in some quarters, the initial cleansing of the arm is said to be objected to by the parents as a reflection on the care, or want of care, on their part, as regards the condition of their children; but in general it is found that a little tactfulness in explaining the difference between ordinary and surgical cleanliness has sufficed to overcome the difficulty. In addition to this aspect of the case the friction employed in the process is of value in causing a slight capillary dilatation which undoubtedly contributes to the success of the operation. Water, soap and water, spirits of wine, or antiseptic solutions, of greater or less potency, containing boric or carbolic acid, lysol or perchloride of mercury, for instance, are employed by different operators for the purpose, of which, in all probability, a warm solution of boric acid is the most generally useful,—a stronger antiseptic, such as corrosive sublimate, unless removed by the subsequent use of sterilised water or alcohol, being liable to exert a somewhat deleterious effect upon the lymph.

The method to be employed at the operation and during the maturation of the vesicles for the protection of the vaccinated area from extraneous infection has not been defined by the regulations, for the reason that it

appeared probable that each man would best attain the desired end by the same methods that he would ordinarily employ in the treatment of any other case of minor surgical injury. As was to be expected, therefore, the means adopted for the protection of the vaccination wounds have been very various, and different trade firms have undoubtedly reaped an extensive harvest by the introduction and energetic advertisement of special dressings of one and another kind. In Paris, at the time of my official visit, a semi-transparent material, known as "taffetas Marinier," not unlike thin isinglass plaster, and which adheres to the skin when moistened with water, was, I found, invariably employed to protect the vaccinated area during the first few days following the operation; and a somewhat similar substance, advertised by an English firm, is, I believe, at present utilised to a considerable extent in this country. But during the second week of the process it is essential that some dressing of an absorbent nature should be employed, as it is during this period that oozing from the vesicles occasionally supervenes.

The means employed for retaining the dressings in position are almost as numerous as the latter themselves. At the Government Station in Lamb's Conduit Street a dressing composed of a couple of layers of boric lint, kept in place by means of pieces of rubber strapping which do not entirely encircle the arm, is applied at the time of vaccination, and this is replaced by another exactly similar dressing when, a week later, the case returns for inspection of the result. But, whatever be the nature of the dressing, the free use beneath it of a dusting powder of boric acid has a most beneficial effect in preventing any undue amount of inflammatory reaction.

Concerning the nature of the instrument best adapted for the purpose of vaccination I desire to offer a few remarks. Here, again, each operator will probably attain the greatest measure of success with that instrument to

the use of which he has been accustomed. But, speaking generally, the less complicated it be, the better. Again, it is desirable that it should be formed entirely of steel, so that it may be readily sterilised by boiling or by heating to redness in the flame of a spirit lamp, the first method being preferable as not tending to injure the temper of the metal. Possibly the best, and certainly the simplest form of instrument is the ordinary triangular-headed surgical needle, which possesses the advantage that on account of its small cost, a fresh one, if thought necessary, can be employed for every operation. It is curious to find, on turning to the old literature of small-pox inoculation, how all the processes of vaccination were originally copied from those which the inoculators had gradually elaborated. It was of course to these practitioners that Dr. Jenner was indebted for the model on which he framed his method of arm-to-arm vaccination, and, in connection with my choice of an instrument, I was specially interested to find that Dr. Emanuel Timoni, in a paper on the practice of inoculation among the Turks, presented to the Royal Society in 1716 by Dr. Woodward, makes the following statement:—"These punctures . . . succeed best in the muscles of the arm. . . . The needle is to be a three-edged surgeon's needle; it may likewise be performed with a lancet."

The manner of operating which affords the most generally successful results consists in blowing out the lymph from the capillary tube in which it is stored on the surface of the skin at different points, the number and situation of which must correspond with those of the vesicles it is desired to obtain. The skin, put slightly on the stretch, is then gently scarified, *through each droplet of lymph*, with the needle or other instrument, first in one direction and then in another more or less at right angles to the first, the drawing of blood being avoided as far as possible. In this way the corium or superficial layer of the skin is thoroughly opened up and in some measure removed, and thus the emulsion is brought into

intimate relation with the cells of the true skin beneath. Operating in this fashion, and employing lymph of normal potency, it is quite easy to obtain an area of vesiculation satisfying official requirements. Many operators, I find, reverse the procedure somewhat, first making their scarification and then rubbing on the lymph. But whether it be that some of the minute scratches are thus closed up as the lymph is applied, or whatever else the reason, certain it is that the results obtained are usually by no means comparable with those following on the method of scarification *through* the beads of lymph previously dropped upon the skin.

The operation having been completed, it is well to avoid too great haste in applying the protective-dressing, especially if this be of the nature of an absorbent pad, or if it be impregnated with some powerful germicide, as in the case of sal-alembroth wool. Some little time necessarily elapses before complete absorption of the vaccine emulsion and the exuded lymph has taken place, and, to ensure the best results, a little exercise of patience is essential. With the object of hastening this period of drying, I, some time ago, devised a method of removing the glycerine from the lymph emulsion, after such time as bacteriological tests showed that it had fulfilled its purpose of destroying extraneous micro-organisms, and replacing it with an equal amount of an inert fluid of similar specific gravity. But the more rapid drying of the vaccinated area thus obtained appeared hardly to compensate for the extra trouble involved in the special preparation of the lymph.

When every care has been taken to protect the arm during the progress of the vaccination, and to prevent the premature detachment of the crusts, the amount of permanent scarring of the skin which remains may be astonishingly slight. This is, I think, one of the results of modern methods of vaccination to which, as yet, attention has hardly been sufficiently directed, although in the future it is likely to prove a matter of considerable

importance. There can be little doubt but that the huge and deep scars which not infrequently resulted from the vaccinations of former years were due, to some extent, to excessive destruction of skin tissue by micro-organisms other than that specific to vaccinia. If this be so, then it becomes apparent that persistence of such large and deep scars, practically throughout life, does not necessarily afford evidence that any equivalent degree of immunity against the infection of smallpox is enjoyed by their possessor. To this fact attention has been called in a recent communication to the 'British Medical Journal,' although the writer propounds a somewhat different interpretation of the facts which he has observed.

The question naturally arises as to whether appreciable advantage to the community can be proved to have resulted from the adoption of our more modern methods of vaccination. It is for several reasons somewhat difficult to give, as yet, any very definite answer, although such statistics as are at present available are decidedly encouraging. There can be no doubt that the operation of the most recent Vaccination Act has been accompanied by a very considerable increase in the number of vaccinations performed, although it should be borne in mind that this increase is, in some degree at any rate, to be accounted for by the vaccination of cases previously in default, a source from which it is unlikely that the figures can be continuously augmented. None the less, however, it is matter for satisfaction that the vaccination of these outstanding cases should have been secured. From a return presented to the House of Commons on August 6th, 1900, which is the latest available source of information, we learn that in the year 1899, the first during which the Act of 1898 was in force, the number of certificates of successful primary vaccinations received showed an increase of 169,035, or no less than 33·8 per cent., over the figures for the previous year, the totals for the two years being 500,314 in 1898, and 669,349 in 1899 respectively.

But there is another source from which we may learn

something as to the value of modern methods of vaccination. I refer to the Annual Reports of the Registrar-General, under the heading "Deaths attributed to Cow-pox and other effects of Vaccination." For a series of years deaths thus registered averaged one every week for the whole of England and Wales, but whereas in 1889 and 1892 the actual number of deaths included under this heading was 58, and in 1893 it was 59, in 1900 the figures had sunk to 25. For England and Wales the statistics for the first three quarters of the present year are not as yet available, but, thanks to the courtesy of Dr. J. F. W. Tatham, I am able to state that in London during that period only two deaths occurred in which vaccination was referred to in the certificate. In this connection, also, it may be mentioned that, at the last dinner of the Public Vaccinators' Association, Dr. G. Danford Thomas was able to state that, contrary to his experience in former years, he had not had occasion, in the course of his duties as coroner, to hold an inquiry into a single case in which death was alleged to have been in any way due to vaccination since the date on which the Act of 1898 came into operation.

A couple of years hence the whole question of vaccination must again occupy the attention of the Legislature, by which time we may perhaps hope to have made further advance both in our methods and in the results obtained therefrom; for there is no finality in scientific work, and if in connection with the subject under consideration much has already been accomplished in the past, there are still undoubtedly many points awaiting elucidation in the future.

In conclusion, I desire briefly to call attention to a matter which has always aroused keen controversy, and which, just now, must needs be of special interest—the question, namely, as to *the relationship of vaccinia to smallpox*. For, not unfrequently, the difficulty experienced by myself and many other investigators in attempts to

transmit human smallpox to bovines, whether cows or calves, has been cited as a reason for regarding with distrust the theory, first expounded by Dr. Jenner, that cow-pox, whether carried through the horse as intermediary host or not, was originally derived from smallpox in the human being. But a great deal, at any rate, of the smallpox which was prevalent during the time that Dr. Jenner lived and wrote was of that comparatively mild variety which, under the name of "inoculated smallpox," was intentionally produced in healthy subjects, with the object of thereby conferring protection against subsequent attack by the disease in virulent form. So mild, indeed, at times were the results of inoculations in the hands of such operators as Adams and the brothers Sutton that no obvious effect was observed, with the exception of the local vesicle arising at the site of insertion of the smallpox virus, and the patients suffered but little inconvenience. Many of them doubtless, therefore, would be capable of following their ordinary avocations, which would hardly be possible in the case of persons contracting smallpox in the ordinary way, among whom the disease was apt to exhibit such virulence as to account for the death of perhaps 50 per cent. of those attacked.

Not only were the effects following on inoculation comparatively mild, but the disease in this form was intentionally brought into many country districts which otherwise might not have become invaded. In the light of these facts, it has for some years past been borne in upon my mind more and more convincingly that it was not improbably from the *inoculated form* of smallpox, rather than the ordinary variety, that much of the cow-pox in the pre-vaccination era was derived. It is not difficult to understand how that the cracks so often found on the udders of a cow might become infected by a milker with fingers contaminated by contact with the inoculated sore upon his arm.

I determined, therefore, if possible, to put the matter to the test, and learning that in Nubia and in certain

parts of India the inoculation of smallpox is still carried out, I made numerous endeavours to obtain the necessary material, but unfortunately, up to the present, without success.

In default of inoculated smallpox in the human subject I made trial of the monkey, which my previous work had shown to be readily susceptible to the disease, the various phases of which in this animal closely resemble those observed in man. The experiments were commenced in 1898, and the smallpox material has been obtained from cases coming under observation during outbreaks of this disease at Middlesbrough, Glasgow, and London. In each of three separate series of experiments the human smallpox lymph or pulp was first inoculated directly on calves, and in every instance, so far as could be observed, with altogether negative results. But with monkeys success was as invariably obtained; and when, after one or more passages through this animal, the contents of the local inoculation vesicles were employed for insertion on the calf, an effect was now produced which, after one or more removes in that animal, was indistinguishable from typical vaccinia. Moreover, from the contents of vesicles raised in this manner on the calf, children have in turn been vaccinated, a number of whom were afterwards kept under observation for about a couple of months. Every such vaccination "took" normally, and in no case was any bad result subsequently observed by myself or by the parents of the children, no "generalisation" of the eruption occurring in any instance. [A series of photographs of monkeys, calves, and children was shown on the screen.]

The point of interest in these experiments is found in the fact that whereas the human smallpox material employed could not be got to "take" directly on the calf, nevertheless results typical of ordinary vaccination were obtained when the strain of lymph, after inoculation with it of a series of monkeys, was again transferred from the inoculation vesicles on this animal to the epidermis of the

calf. Interesting corroboration of my results has recently come to my knowledge in which the use, on calves, of lymph from the vesicles of cases of human inoculated smallpox has afforded opportunity, in Burmah, of originating, on several different occasions, strains of excellent vaccine lymph.

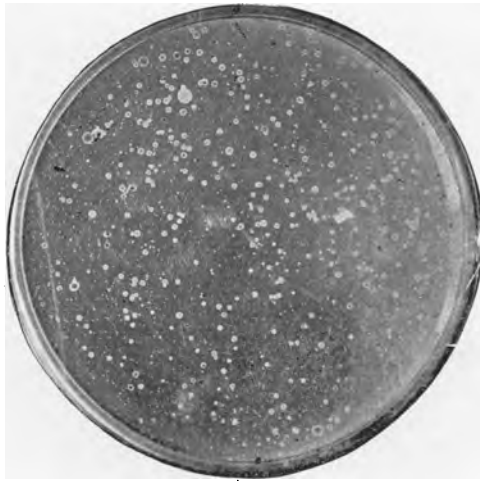


FIG. 1.

Photograph of agar plate prepared with vaccine material *immediately*
after GLYCERINATION.

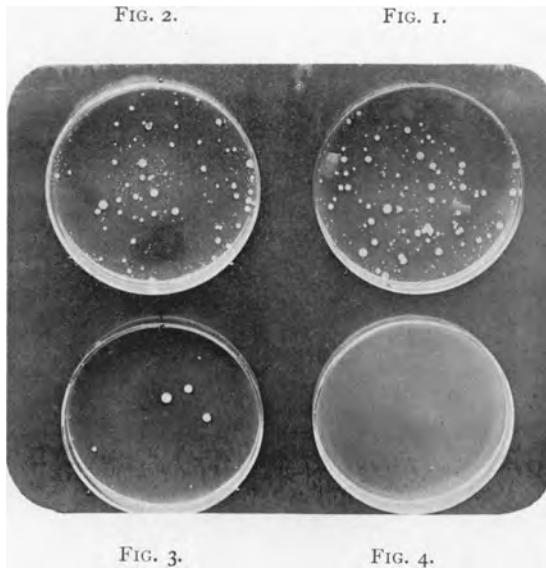
Numerous colonies have developed on incubation.



FIG. 2.

Photograph of similar agar plate prepared with vaccine material *four*
weeks after GLYCERINATION.

No colonies have developed on incubation.



Photograph of agar plates prepared with vaccine material *four weeks* after GLYCERINATION ; showing inhibitory effect of different percentages of glycerine.
 FIG. 1.—20 per cent. glycerine. FIG. 3.—40 per cent. glycerine.
 FIG. 2.—30 per cent. glycerine. FIG. 4.—50 per cent. glycerine.



FIG. 5.
 Photograph, by Dr. GORNALL, of a case of confluent Small-pox, in the vesicular stage. (Small-pox material for each series of experiments, illustrated in the following plates, was obtained from a similar case to that shown in this photograph.)



FIG. 1.

Photograph of monkey, showing result, on the eighth day, of inoculation with human small-pox lymph. Series I.



FIG. 2.

Photograph of calf, showing result, on the sixth day, of inoculation with variolo-vaccine lymph. Series I.
(Third remove from the monkey shown on Fig. 1.)

Copeman: Vaccination. Plate IV.



Photograph of child, taken on the eighth day of vaccination with lymph of variolous origin obtained from Calf No. 3, Series I. (Plate III.)



FIG. 1.

Photograph of Monkey, showing result, on the eighth day, of inoculation with glycerinated human small-pox lymph. Series III.



FIG. 2.

Photograph of calf, showing result, on the sixth day, of inoculation with variolo-vaccine lymph. Series III.
(Fourth remove from monkey shown above.)



Photograph of child, taken on the eighth day of vaccination with lymph of variolous origin, obtained from calf No. 4. Series III. (Plate V.)

DISCUSSION.

Dr. LEONARD DOBSON referred to the difficulties met with in the production of calf lymph. In his experience the best lymph was obtained from calves with light hair. The results, however, as tested by vaccination, varied greatly with the condition of the animal. In some instances, for example, good vesicles that had developed on the fourth day, on the fifth day dried up, leaving scabs alone. Lymph would become inert from many causes; if the glycerine were acid, sooner or later it would become inert; similarly it would do so if it were exposed to light or heat. It was unfortunate that there was no test for the activity of lymph except the result on the calf and on the child; and, moreover, lymph which produced a good result in the calf might be ineffective for the child. There was no test known at present by which the activity of lymph could be standardised. Recent complaints as to the efficiency of lymph were mostly in regard to the secondary vaccination of adults; the present epidemic gave the first general experience of this. In some cases it was possible to produce good vesiculation in the same person again and again within a short time from the use of different lymphs. He knew of the case of a child who in the space of four months had been vaccinated successfully no less than three times. In his own case, after having been successfully vaccinated with lymph from the Government laboratories, he shortly afterwards accidentally inoculated his finger with lymph from another source, with the result that a typical vesicle developed. What efficient re-vaccination really was was not yet established.

Professor SIMS WOODHEAD, in resuming the discussion introduced by Dr. Copeman, on December 10th, 1901,¹ said that he had done many experiments with the object of observing the effect of adding glycerine to calf lymph, and that he could corroborate Dr. Copeman's observations on the action of glycerine on vaccine lymph, and on micro-organisms. The non-sporing organisms, with a few exceptions, were almost entirely eliminated by a 50 per cent. solution of glycerine; even in such a resistant form as the *Streptococcus pyogenes aureus* a large number were eliminated, sometimes only about 5 per 1000 being left. The spore-bearing organisms were almost unaffected. Thus some indication as to the nature of the vaccine organisms, which might be so small as to be invisible with the highest powers of the microscope now available, was given. The organisms

¹ 'British Medical Journal,' December 14th, 1901, p. 1736.

present in lymph were chiefly skin organisms and non-sporing, and hence were amenable to glycerinisation. It had been pointed out by the Special Commission on Glycerinated Calf Vaccine Lymphs that when non-spore bearing organisms were present in large numbers this was due to imperfect glycerination, but that when spore-bearing organisms were in excess in any lymph it was an index that that lymph had not been sufficiently carefully collected. He alluded to the effect of glycerinisation on the activity of the lymph, and expressed the opinion that little or no weakening occurred within three or four weeks. After a longer time weakening probably did, to a slight extent, occur, but the deterioration was more likely to be due to under-glycerinisation than to over-glycerinisation. When organisms that grow best at the body temperature were in excess glycerinisation had a more active influence. The local inflammatory effect of vaccine had been considered of late by many to be greater than formerly, but this was probably due to imperfect glycerinisation, the greater part of the local effect being always due to extraneous organisms. He suggested that the Local Government Board might be able to prepare statistics from their returns to decide that point.

Dr. T. D. ACLAND said that whilst acting as medical officer to the Royal Commission on Vaccination he had had an unusual opportunity of seeing the methods of vaccination practised throughout the country, and of forming an opinion as to the manner in which the operation was carried out, and the cause and extent of vaccinal injuries. In the course of the same inquiry he had been brought intimately into relation with the Medical Department of the Local Government Board, and was able to appreciate the manner in which its officers carried out the difficult and often thankless task of maintaining efficient vaccination. There could be no question that the country owed much to Dr. Copeman for his researches into the origin and purity of vaccine lymph, and for his share in the establishment of an institute able to supply calf lymph on a scale quite impossible a few years ago. Dr. Acland hoped that the Government would take steps to establish a laboratory on a far larger scale than at present, so that all practitioners in the kingdom might be able to obtain lymph from a laboratory fitted with every requisite for perfect work, unfettered by economies necessary in an establishment run solely for trade purposes. He thought that it would be well also if all supplies of vaccine lymph were placed under Government control, and expressed regret that there should be two "Jenner Institutes" in this country—the one formerly known as the "British Institute of Preventive Medicine" in Chelsea, where the National Vaccine Establishment was temporarily situated, the other the Jenner Institute for calf lymph in Battersea, to which the name by priority

belonged. It was inevitable that confusion should arise between the two establishments, and it had arisen.

The Nature and Origin of Vaccine Lymph.

Vaccination, although it was the first protective inoculation practised on a large scale throughout the whole civilised world, had, in all things except the extent of its use, been outstripped in the scientific details of its technique by many of its successors in the department of protective inoculations as now carried out. The practical question now was whether a protective virus could be obtained from bovine animals by the inoculation of existing lymph, or of the virus of *inoculated* smallpox (which differs in many important particulars from the natural or exanthematous form). It would seem that Dr. Copeman, by transmitting smallpox through the monkey, and by inoculating bovines with the virus so obtained, had produced a lymph which was of a similar, and possibly of the same nature as that which would be obtained from cows who had accidentally contracted local pox from a milker suffering from inoculated smallpox. Lymph derived from such a source, and definitely derived from smallpox, seemed to be capable of producing "vaccinia" in man, whilst it had lost its power of transmitting smallpox. Whether this lymph was identical with what was called vaccine lymph could only be decided by further experiment. The lymph now in use in this country, whatever its origin, was not merely an attenuated smallpox virus, since, if this were the case, some amongst the many millions of vaccinated children would be likely to develop smallpox instead of vaccinia. Dr. Acland was not aware that any such case had been recorded. The generalised eruption, which in rare instances followed vaccination, was generalised vaccinia, not variola.

The Preparation of Lymph.

Glycerine had long been used to dilute the lymph, and to serve as a medium for triturating the lymph products obtained from the calf, but no experiments were made previous to Dr. Copeman's to show that the treatment by glycerine was capable of producing a sterile lymph, that was a lymph freed from all extraneous organisms. Dr. Copeman's researches had at any rate shown that lymph freed from all organisms capable of cultivation on ordinary media did not lose its specific property. This answered the question which had been raised whether erysipelas was a stage in the evolution of inoculated cow-pox.

Standardising Lymph.

The standardisation of vaccine lymph had hitherto presented practically insuperable difficulties. It was possible that the

facts demonstrated by Drs. Calmette and Guérin¹ might enable this difficulty to be overcome. They had shown that the rabbit was susceptible to the vaccine virus, and consequently the potency of any particular batch of lymph might readily be tried before it was sent out. The method had been tested successfully for two years at Lille, with the great advantage that it was found possible to eliminate inert batches of lymph prepared for vaccination.

The Actual Methods of Vaccination.

Vaccination as practised was open to two main objections: (1) that the necessity for causing a local sore created a definite point of vulnerability in the individual vaccinated, and formed a possible starting-point for various inflammatory complications; (2) that it created a certain amount of opposition, since in the homes of the poor a vaccinated child imposed a burden on the often overworked mother which was hardly realised by those who had no practical acquaintance with the facts; the gain to the community was impersonal and remote, while the sick child was a present and very real source of anxiety and difficulty.

The necessity for producing a local pock seemed to depend upon the fact that so far all efforts to isolate and cultivate a "vaccinia" organism *in vitro* had failed, so that the only practicable method of administering vaccine lymph medicinally was to create a local pock of a certain area, arrived at by experience, and to leave the production of the immunising bodies to take place in the person of the individual vaccinated.

The Production of an Antitoxin in the Body by Local Inoculation (Vaccination).

Dr. Acland recognised two views as to the means whereby protection was attained by vaccination. (a) "That by the local inoculation a body, presumably an organism, is introduced into the tissues, which by its multiplication, after absorption, produces the desired antitoxins." According to this hypothesis, the number or extent of superficial vesications is immaterial, if only sufficient of the original virus was introduced at the point of inoculation to overcome the resistance of the individual. Dr. Acland knew of no evidence corroborative of this hypothesis; on the contrary, such evidence as there was went to show that (b) under ordinary circumstances a given area of vesication was necessary, and that the immunising effect of vaccination bore a more or less definite relation to the area of the vesicles. This would follow if it were a fact, as now generally supposed,

¹ 'Annales de l'Institut Pasteur,' 1901, vol. xv, p. 161.

that the area of vesiculation bore a direct relation to the amount of antitoxin produced. From these considerations several important questions—practical, therapeutical, and political—arose. 1. Why was it necessary to produce on the arm of a newly born infant the same number of vesicles as on a fully grown man? It might be urged as a matter of clinical experience that infants required a larger dose of vaccine lymph as of other remedial substances, such as arsenic and belladonna, because their tissues were more active, they were more susceptible to the infection of smallpox, and the changes (increase) in their body-weights had no parallel in the adult, all of which circumstances necessitated a proportionately larger reserve of the immunising material if the dose was to be effective. 2. How was it that different standards of efficient vaccination were permitted? Ought there not to be an irreducible minimum below which no certificate of successful vaccination should be given? If satisfactory immunity—a variable quantity for every individual—could only be procured by a certain standard of vaccination, it was surely desirable that there should be a uniform certificate of successful or efficient vaccination. At present it was mainly those vaccinated by the public vaccinator who were efficiently protected according to the official standard. Those vaccinated in private might have one, two, three, or four vesicles, according to the conscience of the operator or the insistence of the mother. The medical profession ought to endeavour to create a public opinion in favour of a really efficient standard of vaccination, and not give its tacit approval to its performance as a piece of therapeutic ritual which had to be got over as cheaply as possible. 3. Did the number or area of scars really give any indication as to the efficiency of protection? This was a most difficult question, but fortunately one to which a great deal of attention has been directed, notably by Dr. Coupland, whose work was a model of thoroughness, and by Dr. Barry, whose report on the smallpox epidemic at Sheffield was well known. It would appear from the figures given in the report of the Royal Commission on Vaccination, 1896, that in nearly 7000 cases the mortality was 6·2 amongst those with one mark, and 3·2 amongst those with four. These figures emphasised the fact that a minimal standard of efficient vaccination was much required if the community was to take full advantage of the protection of vaccination against smallpox. Vaccinia or immunity to subsequent vaccination had been produced by many experimenters without the formation of superficial vesicles both in man and animals. Burckhart vaccinated six children whose mothers had been successfully vaccinated whilst pregnant. The operation was unsuccessful in all of them. Kellock vaccinated 38 women in various stages of pregnancy, and found that the infants resisted vaccination directly as the stage of preg-

nancy at which the mother was vaccinated. In 21 cases the children of women who were vaccinated during the latter half of pregnancy proved insusceptible of vaccination; whilst in 14, whose mothers were vaccinated before the seventh month, vaccination was successfully performed. Smallpox contracted by a mother before her confinement might be transmitted to the fœtus, and a child whose mother had contracted smallpox during the third week before delivery might prove insusceptible to vaccination. Straus and Beclard, Chauveau and Ménard, had also made experiments which confirmed these clinical observations, since they had found that the serum of calves taken during the height of vaccinia produced a measure of immunity in other animals of the same species; when injected intra-venously the serum injections acted at once, whilst immunity was not secured in the calf by vaccination before the eleventh or twelfth day, or in the pig two days earlier. This date, according to Cory, was approximately the period after vaccination at which immunity began to be secured in man. The time varied very much in different individuals of the same species; in man probably the receptivity to successful vaccination diminished gradually during the second week, and became extinct before the fourth. Dr. Acland had recorded a case of vaccinia generalised by auto-inoculation, in which the pocks continued to develop for four weeks certainly. Such evidence tended to show (1) that the serum of a vaccinated animal was capable of modifying and possibly destroying the susceptibility of another animal of the same species to vaccination; (2) that it was not essential for the immune animal to have been actually vaccinated in order that it might be rendered refractive against further inoculations of the same virus; and (3) that whereas serum injections had a rapidly immunising power, vaccination was a comparatively slow process, a fact which had an important bearing on the question as to whether it served any useful purpose to vaccinate an individual who had already been exposed to the infection of smallpox. Dr. Acland then referred to the attempts which had been made to treat variola by the antitoxin of vaccinia. Kinyoun¹ had recorded two cases of variola treated with serum taken from a calf vaccinated four weeks previously. The observations were inconclusive. Each case received 15 c.c. of serum followed later by 20 c.c. more. One case died in seventy-two hours. In 1896 MM. Beclard, Chauveau, and Ménard had recorded² observations made on seventeen cases of variola of all ages treated by subcutaneous injections of serum taken from a vaccinated calf. In one case no less than a litre and a half was injected without causing any local or general disturbance, and

¹ 'Philadelphia Med. News,' February 2nd, 1895.

² 'Ann. de l'Institut Pasteur,' vol. x, 1896, p. 1.

the patient recovered. These cases had been alluded to by Dr. Copeman in his Milroy Lectures, but in a later communication the same observers had given an account of further experiments on the immunising power of the blood of man and animals, after vaccination, against the vaccinal or variolous infections, and they came to the definite conclusion that not only did the serum of a vaccinated calf taken on the fourteenth day after inoculation possess certain powers both in the direction of conferring immunity and assisting the cure in the body, but that it also acted on vaccine lymph in the test-tube, rendering it inert. They also concluded that the serum of convalescents from variola had the same destructive power over the vaccinal virus. All these experiments seemed to indicate the general truth of Jenner's hypothesis, and to supply the scientific basis which was lacking from his empirical practice—a practice which, although empirical, had stood the test of time and of rigid experimental test. They also served to indicate the direction in which the advance might be made. Dr. Copeman had made it possible to obtain from the calf a supply of antitoxin directly derived from variola; might it not be that this would afford a means of combating variola itself? It might well be asked that Dr. Copeman, should he be willing, should be granted the opportunity of testing the accuracy of the scientific facts by utilising them for the treatment of variola.

Dr. Acland then gave notice of the following resolution:

"That, in the opinion of this meeting of the Fellows of the Royal Medical and Chirurgical Society, it is desirable that the Government should without delay make such additions to the National Vaccine Establishment as shall enable it to supply glycerinated calf lymph to all medical practitioners who may desire to use it; and that, in view of the national importance of the subject, steps should be taken to test and regulate the sale of all imported lymph, and to inspect the manufacture of all that is made in this country."

Professor HACCIUS (Geneva) acknowledged the debt conferred on universal medical science by Jenner, and also later by Dr. Copeman. In 1892, when in Switzerland there was difficulty in procuring good calf lymph, he transmitted variola to a calf, from this to six other calves, and eventually with success to children, typical vaccine vesicles being formed. Professor Chauveau attacked these experiments on the ground of accidental inoculation with vaccinia in the laboratory, saying that the disease was vaccinia and not modified variola; but this source of fallacy was eliminated by transmitting the inoculated smallpox from calf to calf before inoculating it on children. Professor Chauveau had inoculated a cow with variola, and from the vesicle produced had inoculated a child who developed typical variola. This, however,

was to be explained by the direct transference of variola virus to the child, the cow being merely a stage in its transference. In Munich and Stettin smallpox had been transmitted to calves, the inoculations being performed apart from vaccine establishments. It was recognised that in many instances variola could not be thus transmitted to the calf, but he believed that the identity of variola and vaccinia would be established. His results on children were quite good, there being no generalised eruption. Allusion was made to glycerinated lymph and to powdered dry lymph—the one being successful, the other not. The collection of calf lymph was now conducted under better conditions than formerly, thus diminishing from the first the number of extraneous organisms. It was hoped that in a short time vaccination would become compulsory in Switzerland.

The discussion was adjourned.

ADJOURNED DISCUSSION, January 28th, 1902.

Dr. SIDNEY COUPLAND, in resuming this discussion, referred to the great improvement that had supervened in modern vaccination methods, mainly as a result of the introduction of glycerinated lymph, the use of which had been made obligatory by the Act of 1898. The objects of recent improvements had been to obviate the risks of the process, and there had been the even greater advance in having vaccination performed at home, and in raising the age of the children required to be vaccinated. The vaccinal injuries had been in the past, perhaps, too lightly considered by the profession. In the majority of cases with ill-effects it had not been the lymph which had been at fault, but some accidental complication. He quite agreed with Dr. Acland that full control of all the vaccine lymph used in this country should be in the hands of the Government. Large unsightly scars were unnecessary, and were often associated with inefficient vaccination. The scars from purified lymph were often small, and did not even present the size which was formerly supposed to be an essential index of good vaccination. Indeed, probably now the number of the scars was the best evidence of efficient protection. The question was probably one of dose, as in the use of antitoxin in cases of an infectious disease. The scars were numerically a permanent record of the dose, whilst the statistics of Marson, Gayton, Barry, and others prove that the efficiency of vaccination in mitigating an attack of smallpox is in direct relation to the number of insertions. Thus Barry found, at Sheffield, the proportion of mild attacks to be 20 per cent. in persons who had been vaccinated in *one* place only, and 52 per cent. in those who had *four* marks. It was admitted that vaccination was a good prophylactic against smallpox, but it had its limitations. When smallpox invaded

a house or other small community where all were equally exposed to infection, some escaped and others were attacked. Among those who had had smallpox previously, personally collected statistics showed that 1 in 20 were attacked a second time, and in the epidemic at Warrington, investigated by Dr. J. D. Savill, an even larger proportion, namely, 9 out of 41, had second attacks. But a single vaccination did not afford this degree of protection. Of those who had been only vaccinated once in childhood, about 25 per cent. were liable to contract the disease when living in a smallpox atmosphere. Recently vaccinated persons were much more powerfully protected than the more remote; about 1 in 7 of those who were vaccinated for the first time on their being exposed to smallpox infection contracted the disease. Revaccination properly performed conferred practically absolute immunity; even in a person who had had smallpox the immunity could be prolonged by revaccination. In children under ten vaccinated in infancy, liability to attack was about 1 in 11 or 12; but 2 out of 3 of unvaccinated children were likely to take the disease on being exposed to infection for the first time. These results, it was pointed out, were based on a relatively few cases—some three epidemics. It was probable that even recently vaccinated persons were not all absolutely immune, owing to their vaccination with various strains of lymph, some of which had become inert.

Dr. ALBERT E. COPE stated that he represented the body of public vaccinators, and that he wished to describe his own practice as an illustration of the way in which the actual work of vaccination was carried out. The arm in the case of infants, which had been washed by the mother, was first rubbed with a pledget of boric wool saturated in rectified spirit, and then dried with a pledget of dry wool. For revaccination a 20 per cent. carbolic soap was used with which to wash the arm. The water was boiled, a pledget of wood-wool was used to apply the soap, the excess was rapidly washed off with water or rectified spirit, and the arm was dried with a similar pledget. The instrument he had found most useful was a lancet made of platinum, hardened with iridium, so that it might be flame-sterilised. The best ejector of the lymph from the tube was a solid rubber bulb with a funnel-shaped perforation through which the tube was passed, and the outer aperture closed by the thumb before compression. Lymph was placed on the arm and the skin was lightly scratched through it, the faintest trace of blood being drawn. An interval was allowed until an erythematous reaction was visible, when a boric pad was applied and strapped on. This was allowed to remain for a week, then a powder of boric acid, zinc, and starch was applied under another boric pad. The most troublesome complication he had had was an eczema occurring under the strapping, which

subsided readily under the application of calamine lotion. Complications of any kind were very rare. Revaccination was obtainable at about fourteen after good vaccination in infancy ; it would be well to arrange for it to be done on children before leaving school, so that later it should not interfere with the daily work of adult life. This might well be made a Government regulation.

MR. WILLIAM F. BLAKE asked what constituted a successful revaccination. If two persons were vaccinated from the same tube, and one took but the other did not, could it be asserted that the person who did not take was protected against small-pox ? He also asked what was meant by the statement that had been made earlier in the discussion that successful vaccination might occur several times within a few months in the same person.

DR. F. CHURCHILL asked if there was any age beyond which vaccination might safely be discarded. It was probable that persons of all ages were liable to contract the disease. It was a question whether the present epidemics of smallpox were really so effectively controlled by improved methods of vaccination and isolation as in the earlier epidemics by rougher measures. It was possible that the more elaborate procedures acted as a deterrent against vaccination being universally had recourse to, because the poor have their infected children so amply provided for at the expense of the State.

DR. BERNARD O'CONNOR asked whether a second or third revaccination was necessary ; theoretically he had thought revaccination should be continued until it failed to produce any result.

DR. COPEMAN, in reply, stated that dilute glycerine had a gradual inhibitory effect on micro-organisms that were non-spore-bearing ; most of the pathogenic organisms were non-spore-bearing, and the spore-bearing organisms at all likely to be present were of no pathogenic importance. Even if such organisms as those of erysipelas and tubercle were intentionally added to the lymph in considerable quantity, the subsequent addition of glycerine gradually eliminated them, so that after an interval of about a month the lymph became entirely freed from infective qualities. The same dose or amount of vaccination was probably desirable in the child as in the adult. Probably a greater effect, however, relatively to the size of the individual was obtained in the adult. There was at present no efficient method of standardisation of lymph ; the only useful test was the clinical result. It was not possible as yet to afford the same degree of protection by injecting an antitoxic serum into the system. With the use of glycerinated lymph there was not the same destruction of skin tissue as even in what was considered perfect vaccination of years

ago. It was essential that all persons should be revaccinated at least once in later life. There was no doubt that a person might contract smallpox twice or even three times. In referring to the high degree of immunity that vaccination gave, he said that he had on two occasions accidentally inoculated himself with smallpox, with the result that no infection took place. If no effect was observed to follow the use of lymph which subsequently was suspected of being inert, an interval of at least a month should be allowed to elapse before revaccination, because a slight local immunity might be produced even by inadequate vaccination. In recent methods there was probably no weakening of the lymph by mixing with glycerine as compared with the old arm-to-arm method, for it was believed that the microbes of vaccinia were contained in the epithelial cells which were removed in the pulp from the calf, while in vaccination from the human arm only the fluid from the loculi was taken. Dr. Copeman, in conclusion, referred to the possibility of protection against smallpox by internal administration.