vaccine lymph which could be regarded as specific to vaccinia, several observers have sought to prove that organisms of a somewhat higher order than bacteria might be concerned in the production of this malady and also of variola. In this connection it may be mentioned that bodies believed to be of the nature of psorosperms or sporozoa have been described by Pfeiffer,²² Guarnieri,²³ Monti,²⁴ Van der Loeff, Doehle,²⁵ and Sicheer²⁶ on the Continent, and by Ruffer²⁷ and Jackson Clarke²⁸ in this country, as capable of demonstration in and among the epithelial cells of an inoculated area.

Ruffer and Plimmer describe the parasite in question as a small round body, which sometimes appears to have a more darkly-staining centre. It is, they say, about four times the size of an ordinary staphylococcus, and generally lies in a clear vacuole in the protoplasm of the epithelial cells of the stratum Malpighii, and occasionally indents the nucleus, though it has not been found enclosed in the latter structure. These observers state that they have found the same organisms in sections of skin from small-pox patients and in pustules of the larynx and trachea.

Pfeiffer describes similar bodies as to be found, not only in the epithelial cells of the vaccine vesicle, but equally in all other vesicular eruptions of man and the lower animals. Pfeiffer, Guarnieri, Ruffer, and Plimmer all assert that these parasites exhibit very slow amœboid movements.

There can, of course, be no doubt as to the occurrence of the appearances described, although one may not be prepared to accept the interpretation put upon them, and in this connection it is well to bear in mind, not only that the cell enclosures described by Guarnieri, Monti, and Ruffer are said by them to differ essentially in their staining reaction and in their appearance from those of Pfeiffer, Van der Loeff, and others, but also the fact that the most recent experimental work in this direction has been carried out on the cornea of the rabbit—an animal which there is reason for believing to be insusceptible to vaccinia. It may be added also that no such bodies have been satisfactorily demonstrated in vaccine lymph itself. It is therefore conceivable that the "parasites" in question may represent merely the result of epithelial irritation caused by the scarification, together with that—of a non-specific nature, however—set up by the vaccine lymph employed.

THE VIRUS OF SMALL-POX AND VACCINIA.

On the other hand there appears good reason for believing that the bacillus demonstrated by Klein and myself in reality constitutes the specific virus of small-pox and vaccinia respectively.

It is consequently of interest to note that the operation of vaccination is probably one of the earliest instances on record of the employment of a bacterial inoculation, although of course its true nature was not recognised at the time of its introduction.

A SMALL-POX ANTITOXIN.

Inspired by the investigations of Tizzoni and Cantani on tetanus, early in the course of my work on the pathology of vaccinia and variola, my attention was directed to the question of the production, if possible, of an antitoxic serum,²⁹ which might be of use in the treatment of small-pox, it being well known that vaccination is of practically no avail when once the disease has become developed.

The results of my first experiments in this direction, which were carried out on the monkey, were not very encouraging however, as owing to the fact that at that time I had not succeeded in isolating what I now believe to be the specific organisms of variola and vaccinia, I was only able to employ for my injections the blood serum of a monkey which had been vaccinated on several occasions.

Since my work was carried out a number of other observers have experimented in a similar direction, the results recorded by them being, however, of a somewhat conflicting nature. Thus Kramer and Boyce³⁰ were unable to produce any im-

munity even with large doses of serum from vaccinated calves, and recently Beumer and Peiper³¹ have arrived at a similar conclusion. On the other hand Kenyon,³² and also Hlava and Houl,³³ claim to have obtained successful results, but as far as can be judged from their publications, such claim would appear to rest on somewhat slender foundation, although Hlava and Houl state that in one instance the injection of their serum to the extent of 0.6 to 1.0 c.cm. per kilo of body-weight entirely prevented the action of vaccine lymph inoculated four days later. They have not put on record any experiment with variola as yet.

The fullest and most recent contribution to this subject is a long paper by Bèclère, Chambon, and Ménard.³⁴ The conclusion at which the authors arrive is that the serum of a vaccinated heifer, gathered after the drying of the pustules, immunised to a certain extent against the effects of subsequent vaccination, but the diagrams with which the paper is illustrated show that the antagonism is by no means complete.

It would seem, therefore, that in default of having at command considerable quantities of a pure cultivation of the specific organism concerned, better results might probably be obtained by employing colts instead of calves for production of the serum, since, as Chauveau has shown, inoculation of colts not infrequently gives rise to a generalised eruption, the effect of which on the system is likely to be more potent than when the reaction, as is the case in calves, is limited to the area of inoculation. The writer hopes shortly to be in a position to publish the results of experiments carried out on the lines thus indicated.

If, as appears not improbable, further investigations should be attended by a greater measure of success than has at present been attained, we may hope before long to be in possession of an effectual method for the treatment of those cases in which the system has already become invaded by small-pox, which would form a fitting complement to the Jennerian process of preventive vaccination.

ANIMAL VACCINATION.¹

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INTRODUCTORY.

It is no uncommon error which leads people to suppose that the recent general recourse to the employment of vaccine taken direct from the calf (animal vaccine), as a

³¹ *Berl. klin. Woch.*, August 26th, 1895.

³² *Philadelphia Medical News*, February 2nd, 1895.

³³ *Wein klin. Rundschau*, October 6th and 13th, 1895.

³⁴ *Annales de l'Institut Pasteur*, January, 1896.

¹ By "animal vaccination" is meant in this paper the vaccination of human beings with animal (bovine) vaccine—that is, with vaccine from genuine cow-pox, and by "animal vaccine" is meant vaccine obtained from bovines (the calf). The nomenclature of vaccinia is very defective and misleading. Unfortunately, too, matters have been made still worse of late years by the employment of the terms "vaccine" and "vaccinate" to indicate the agent and the operation of protective inoculation against other diseases than small-pox. This was done by Pasteur with the generous and laudable object of keeping Jenner's great discovery for ever before men's minds. The result is none the less perplexing. Jenner employed the term "vaccine" as specifically referring to the cow (*Lat. vacca—a cow*). Nowadays it is high science to speak of the vaccine of diphtheria, or cholera, etc., when cow-pox and cows are in no ways concerned. The expression "pustule" as applied to the eruption of vaccinia is also entirely inaccurate and misleading, but no more so than the equally common term "vesicle." The specific Jennerian product of vaccination, from which vaccine is taken for vaccinating, is not a pustule nor does it contain pus, either in the human being or in animals. When it has ceased to be specific in character, and is undergoing some form of degeneration, it may or it may not become purulent. To call the "pock" a "pustule" suggests the untruth that pus is used for vaccinating. Neither is the Jennerian vaccine-pock a true "vesicle," though the vaccine may be partially contained in component vesicles; the pock of sheep-pox is a true unicellular vesicle. The term "lymph," too, is quite irrational as applied to the liquid exuded from the pock. It is not "lymph," and does not come from the lymphatics. It is serum mixed with a proportion—greater or less under varying circumstances—of the specific products of the morbid action going on in the successfully inoculated (or spontaneous?) pock. In the existing chaos of nomenclature "vaccination" is thoughtlessly used to signify both the operation of vaccinating and the disease which results from it. I would suggest that "pock" is the most suitable word for the local sore; that "vaccinia" (=cow-pox) should be employed to indicate the disease; and that "vaccine" should be used instead of the very inappropriate term "lymph" to indicate the specific virus of the Jennerian pock.

²² *Die Protozoen als Krankheitserreger*, Jena, 1890.

²³ *Centralb. f. Bakt.*, August 25th, 1894.

²⁴ *Loc. cit.*

²⁵ *Centralb. f. Bakt.*, Band xii, No. 25.

²⁶ *Münch. med. Woch.*, August 20th, 1895.

²⁷ *BRITISH MEDICAL JOURNAL*, June 30th, 1894.

²⁸ *Med. Press and Circular*, July 25th, 1894.

²⁹ *Trans. Epidemiological Society*, vol. xii, 1893.

³⁰ *BRITISH MEDICAL JOURNAL*, 1893, vol. ii, p. 989.

substitute for that taken from the arm (humanised vaccine), is a new and modern discovery, and that the discovery which has immortalised Jenner's name is diminished in value, or its true nature, as described by himself, is modified by the more recent practice. Nothing could be more erroneous. Jenner is not only the discoverer of the most pregnant and fruitful fact in pathology—namely, that the virus of a disease occurring in bovines and some other animals may be transmitted to man, and afterwards from man to man in uninterrupted series, without undergoing any essential change in character; he is also the originator of the modern systematised animal vaccination, now so largely used and often spoken of as if it were something quite novel. All Jenner's early experiments were made with virus taken direct from the animal—that is, with what to-day is called animal vaccine, employed by him in what to-day is commonly called animal vaccination—that is, the vaccination of human beings from bovines infected with vaccinia or cow-pox.² He had worked carefully and diligently at the nature and results of this direct vaccination from the animal before he attempted the epoch-making experiment³ of inoculating a human being with matter taken from a pock on the arm of another human being who had been successfully inoculated direct from the animal.

Jenner had abundant opportunity of making himself familiar with the characters of true cow-pox, and with his characteristic love for accurate knowledge, abundantly shown in his prolonged investigations concerning this disease, he fully availed himself of his advantages in this respect. Cow-pox was in his time of common occurrence in the country, and particularly so in Gloucestershire, where he carried on his medical practice, the district being largely devoted to dairy work. That there are various eruptions which affect the teats and udders of cows,⁴ the exact nature of many of which even to-day is not understood, he was well aware. In his *Inquiry* he drew attention to this important subject, and described one spurious form of "pustulous sores" which frequently appear spontaneously on the nipples of cows. Milkers sometimes, he says, become affected with sores on the hands, accompanied, it may be, with a feeling of indisposition. The symptoms, local and general, are however much less severe than those "which arise from that contagion which constitutes true cow-pox," and "specific effects on the human constitution" are not produced by it.

Jenner drew attention to the extreme importance of being able to distinguish true cow-pox from other similar diseases. Nothing could show more plainly the importance he attached to this point than the following words from the *Inquiry*:⁵ "It is," he writes, "of the utmost consequence to point it out here, lest the want of discrimination should occasion an idea of security⁶ from the infection of the small-pox which might prove delusive."

In a letter to a friend dated Cheltenham, September 29th,⁷ he recurs to this all-important subject: "I am fearful that before we thoroughly understand what is cow-pox matter and what is not, some confusion may arise, for which I shall unjustly be made answerable."

COW-POX AND SMALL-POX: JENNER'S VIEW.

The special and altogether remarkable characteristic of cow-pox in his eyes was that it protected against small-pox. "He always," writes Baron, "considered small-pox and cow-pox as modifications of the same distemper, and that in em-

ploying vaccine lymph, we only made use of means to impregnate the constitution with the disease in its mildest, instead of propagating it in its virulent and contagious form, as is done when small-pox is inoculated."⁸ As Sömmering expresses it, "Variola et vaccinia sunt morbi, non sua natura, sed gradu, diversi."

Baron, whose learning and painstaking industry are well illustrated by his researches as to epizootics, with a view to collecting information on the history of cow-pox, quotes, among many other authorities, a paper by Dr. Lazard,⁹ in which he describes an eruptive disease affecting black cattle in England:

"The disease among horned cattle is an eruptive fever of the variolous kind; it has all the characteristic symptoms, crisis, and event of the small-pox; and whether received by contagion, or by inoculation, has the same appearances, stages, and determination, except more favourable by inoculation, and with this distinctive and decisive property, that a beast having once had the sickness naturally or artificially, never has it a second time."

Many other quotations might be given showing that Jenner was not alone in regarding cow-pox as being variolous in its nature, and that the adoption of the name, variolæ vaccinae (= cow variola = cow-pox) was one which would seem in his own time, as in ours, appropriate.

The similarity of the appearances of the eruption in cow-pox and human variola has been dwelt on by innumerable writers of various dates, and no more eminent authority on the subject can be quoted than Chauveau. In explaining why he failed to test the nature of certain "lymph" by inoculating children with it, instead of limiting his experiments to animals, he says: "The first reason arises from the difficulty—let us say, rather, the impossibility—of distinguishing the primary eruption of variola from that produced by vaccinia."¹⁰ Though the likeness here insisted upon seems to be regarded as rather more confusing than is warranted, still it is interesting to note how one of the most acute observers and dialecticians of to-day agrees with Jenner and older writers as to the similarity of the diseases.

COW-POX AND "GREASE."

Jenner regarded cow-pox as being derived from "the grease," a disease affecting the hoofs of horses. "Thus," he says, "the disease makes its progress from the horse to the nipple of the cow, and from the cow to the human subject."¹¹ But though the equine disease, *after passage through the cow*, was in his opinion able to protect a person who had suffered from it against small-pox, so "that the person who had been thus affected is for ever after secure from the infection of the small-pox,"¹² he regarded the original equine disease which has not passed through the cow as not being equally protective. "Although," he says,¹³ "in the two former instances the system seemed to be secured, or nearly so, from variolous infection, by the absorption of matter from sores produced by the diseased heels of horses, yet the following case [that is No. xv in the *Inquiry*] decisively proves that this cannot be entirely relied upon, until a disease has been generated by the morbid matter from the horse on the nipple of the cow, and passed

⁸ *Life of Jenner*, vol. i, p. 162.

⁹ *Philosophical Transactions* for the year 1780, part 1, quoted in Baron, *loc. cit.*

¹⁰ "La première raison est tirée de la difficulté, disons plus, de l'impossibilité qu'il y a à distinguer l'éruption primitive de la variole de celle de la vaccine." Chauveau, Sur la Transformation des Virus, *Bulletin de l'Académie de Médecine*, Paris, October 20, 1891.

¹¹ *Inquiry*, introductory remarks, preceding Case i.

¹² *Inquiry*, *loc. cit.*

¹³ *Inquiry*, Case xv. One of the "two former instances" referred to above by Jenner (Case xiii) was that of a man who had never had cow-pox, but had suffered from sores on his fingers, with "pretty severe indisposition," due to accidental inoculation from the "sore heels" of infected horses. Six years afterwards Jenner inoculated him experimentally with variolous matter, without producing anything more than "slight inflammation" (presumably at the point of inoculation). Subsequent exposure to the contagion of small-pox had "as little effect." The second case (No. xiv) was that of a farmer, infected from the same source as No. xiii, and subsequently inoculated with variola. The result was merely "a little pain in the axilla," and "a slight indisposition" for three or four hours. "A few eruptions showed themselves on the forehead, but they very soon disappeared without advancing to maturation." The reader will, no doubt, recognise in these cases the history of persons "secured or nearly so," against variola as Jenner describes them. They probably had "varioid" or modified small-pox.

² This term is commonly employed in a vague manner to express the vaccination of the animal as well as of human beings with vaccine taken from the animal.

³ See *Inquiry* into the Causes and Effects of the Variolæ Vaccinae (1798), Case xvii.

⁴ Any reader of the Report on Eruptive Diseases of the Teats and Udders of Cows in Relation to Scarlet Fever in Man, by Professor Brown, C.B., of the Agricultural Department of the Privy Council, presented to Parliament in 1888, will be struck with the obscurity and complexity of this subject.

⁵ *Inquiry*, end of his introductory remarks preceding Case i.

⁶ That is, the person who had suffered from inoculation with the spurious disease might entertain the delusive idea that he was protected against small-pox, and learn to his cost that he was mistaken.

⁷ Baron's *Life of Edward Jenner*, vol. i, p. 155. There is no year assigned to the letter, but it is placed between one dated August 18th, 1798, and one dated November 20th, 1798, so one may assume Jenner's biographer regarded it as having been written in the interval. It would thus be later than the publication of the *Inquiry*, the dedicatory epistle to which is dated June 21st, 1798.

through that medium to the human subject." Again, he writes, "We have seen that the virus from the horse, when it proves infectious to the human subject, is not to be relied upon as rendering the system secure from variolous infection, but that the matter produced by it upon the nipple of the cow is perfectly so."¹⁴

JENNER'S VIEW AS TO THE PERMANENT EFFECT OF VACCINATION.

That Jenner should expect that the protection against small-pox afforded by vaccination would be lifelong, as is usually (not always) the case with one attack of small-pox, was natural. It was common knowledge that one attack of small-pox is protective (as a rule but with exceptions) against a second. The general belief prevailed in Gloucestershire, confirmed by his own observations and experiments, that vaccination protected against small-pox; therefore, he would expect that vaccination would be as protective as an attack of small-pox, and in this he was not mistaken. But it must never be forgotten that a person may be thoroughly vaccinated or may be very imperfectly done. The protection afforded by one small ill-developed pock is very different from that given by several large, typical pocks. There can be little doubt that degree of protection provided by vaccination may vary in accordance with the mode in which it is done, from a very slight, fleeting protection to complete and permanent immunity.

VARIOLATION OF BOVINES.

It does not appear that Jenner, though he considered small-pox and cow-pox to be "modifications of the same distemper," ever attempted to inoculate bovines with variola. Baron is silent on the point. He does say, that at the time Lazard wrote, less importance was attached to the question of the connection between diseases of men and animals; "no trials, therefore, were made to ascertain whether the variola of man could be communicated to the brute, or *vice versa*. The discovery of the variolæ vaccinæ has fully established the latter point; and although attempts to demonstrate the former have failed in the hands of some, other investigators have been more successful."¹⁵

The identity of origin of variola and cow-pox may be regarded as established by the successful variolation of bovines (adults and calves by the following: ¹⁶ Guillon (London), 1827; Sonderland (Barmen), 1830; Thiele (Kasan), 1839; Ceely (Aylesbury), 1839; Reiter (Munich), 1839; Badcock (Brighton), 1840; Gassner, 1840; at the Berlin Veterinary College, 1840; Senfft (Bierstadt), 1872; Voigt (Hamburg), 1882; Haccius (Geneva), 1889; Fischer (Carlsruhe), 1890; Hime ¹⁷ (Bradford), 1892; Freyer, 1896.

Vaccine, resulting from the variolation of the calf (or beast) by the above experimenters, has been tested in every way, and its nature established beyond a doubt. The procedure of some of those mentioned, who simultaneously inoculated the animal with humanised vaccine on one side and with variola on the other (Ceely, Voigt) has been objected to as unscientific, and not convincing. But my own experiments are free from this defect, as I inoculated the calf with variola only.

I inoculated vaccine from this variolated calf (a) on a second calf, producing a superb eruption of cow-pox, and (b) on myself with only a trifling local effect (I have been very frequently revaccinated), and (c) on another medical man (revaccinated at the age of 32), on whom typical vaccine pocks were produced. Calves 1 and 2 proved refractory to a second inoculation with active calf vaccine. From calf 2 I vaccinated a child, producing typical Jennerian pocks, and a third calf, which had fine typical pocks. Both the child and calf 3 proved refractory to revaccination with active vaccine. Retrovaccination of a calf was performed from the child with similar positive results, and the vaccine was passed through several generations of children, always producing the same typical results. There is no possibility of doubt as to the fact that true cow-pox was produced by variolation of my first calf.

¹⁴ Inquiry, Case XVIII.

¹⁵ Baron's *Life of Jenner*, vol. 1, p. 216.

¹⁶ *Handbuch der sp. Therapie inn. Krankheiten*, Jena, 1894, B. 1, S. 249.

¹⁷ My experiments are described in the BRITISH MEDICAL JOURNAL for 1892; also in my evidence before the Royal Commission on Vaccination in the last (forthcoming) volume, of whose proceedings later details will appear than those given in the JOURNAL.

EFFICACY OF VARIOLA-VACCINE.

Chauveau insists that variola-vaccine speedily becomes inert, and ceases to produce active virus when inoculated. This assertion is, however, contrary to facts established by myself, Voigt, and others. Voigt¹⁸ has used no other vaccine at Hamburg from January 1st, 1882, up to the present. In 1895, he had the opportunity of testing the efficacy of the primary vaccinations done with his variola-vaccine in 1882, by the regular compulsory revaccination of the children done that year, which fell due in 1895. The result showed that the success of the revaccinations was extraordinarily low, only 69.2 being successful, evidently in consequence of the excellent effect of the primary vaccination with Voigt's variola-vaccine. In no other town in Germany were such good results obtained.

Crookshank¹⁹ maintains that the matter taken from the animals variolated by Ceely produced small-pox and not vaccinia in the person inoculated by him with it. But this objection will hardly be regarded as worthy of consideration when we consider that those who witnessed the experiments were competent to judge, and were more familiar with small-pox than most people are nowadays. Besides, not one case is recorded of the disease spreading by infection from the persons inoculated from these animals, and there was certainly nothing which suggested to those who watched the cases at the time that the patients had small-pox, and not vaccinia.

Chauveau²⁰ failed to variolate adult bovines, and did undoubtedly inoculate small-pox on a child by means of matter taken from an animal which he had experimentally inoculated with variola. But his failure cannot invalidate my experiments and those of others. I and several others have used the calf in preference to the adult animal. Chauveau, though professing to repeat our experiments, has persistently refused to use the calf, or to inoculate in the same way we did. Had he really repeated our experiments, instead of omitting important conditions, he might, and no doubt would, have got the same results we did. He protests that variola inoculated in bovines produces a disease which is genuine, though attenuated, variola, and not cow-pox; and he asserts, in the face of indisputable facts, that the virus of variola, after a few passages through bovines, dies out. There are some who will not be convinced, even though one should rise from the grave. The variola-vaccine of Ceely, Badcock, Voigt, Fisher, and others has been employed to vaccinate hundreds of thousands of persons with the best results, and has never yet caused small-pox, though Chauveau says the vaccine used is variolous and not bovine pox at all.

NATURE OF "GREASE."

The intimate connection between "the grease" of the horse and the cow-pox of bovines was deeply impressed on Jenner's mind, and, as we have seen, he regarded the latter as the result of the passage of the virus of "the grease" through the system of a bovine animal. To-day the conviction exists in the minds of most authorities that cow-pox is not primarily a disease of bovines.

The true nature of the grease has been definitely established, mainly through the masterly analysis of the eminent veterinarian, Professor H. Bouley,²¹ of Alfort. He established, beyond any room for doubt, the fact that the grease is a specific disease of the horse, strictly analogous to cow-pox, interchangeable with it, in the sense that the grease inoculated on bovines produces cow-pox, and cow-pox inoculated in equines produces all the symptoms of the grease, and each disease protects the animal which has suffered from it against the other. Both are communicable to man by inoculation, and protect him against a second attack and against variola. Further, each disease can be produced in the respective animals by inoculation with the virus of small-pox. Both diseases, therefore, have a common nature and common origin, and therefore Bouley was justified in giving to the grease the name now by common assent assigned to it, of horse-pox.

¹⁸ *Deutsch. Vierteljahrsschrift f. öf. Gesundheitspflege*, 1896.

¹⁹ *History and Pathology of Vaccination*, 2 vols, London, 1889.

²⁰ *Bulletin de l'Académie de Médecine*, Paris, No. 41, 1891.

²¹ De l'origine de la Vaccine sur le Cheval, Discours à l'Académie de Médecine, in the *Recueil de Médecine Vétérinaire*, 1862. See also *Leçons de Pathologie Comparée: Le Progrès en Médecine par l'Experimentation*, Paris, 1882, by the same author.

COW-POX IN NON-BOVINE ANIMALS.

Cow-pox is also transmissible to the goat, the dog, the ass, the camel, the rabbit, the guinea-pig, the monkey, and the sheep. The last-named animal, however, offers a less favourable soil for the culture of the disease than some of the others. The horse is particularly susceptible. While human beings and bovines may be regarded as possessing about equal receptivity to the virus, the horse must be recognised as being more susceptible than either.

"SPONTANEOUS" COW-POX.

Although the occurrence of so-called "spontaneous" cow-pox (meaning thereby cases of the disease the source of which cannot be satisfactorily traced) has become very rare, as compared with what it was in Jenner's time, still cases are met with from time to time, and have been seen within quite recent years in England, France, Belgium, and other countries.

A few years ago vaccine from such a "spontaneous" case occurring at Bouge, near Namur, was adopted at the Government calf vaccine-station in Brussels, from which to maintain the regular vaccinations instead of the old Beaugency stock, which had previously been in use.

IDENTITY OF COW-POX AND HORSE-POX.

The two animal diseases, cow-pox and horse-pox, therefore, are in essence but one. They are characterised by a specific eruption on the integument, at the same time being constitutional diseases, one attack of which protects against a second for a period the exact length of which is not determined. In bovines the eruption is almost exclusively observed on the udder or teats. The number of pocks is always small, not exceeding some 20 to 30, even in severe cases.

The integument is the seat of election of the vaccine virus. The special seat of the vaccine pock is the upper and middle layers of the stratum lucidum. The pock of variola occupies the same site, but extends to the "prickle cells." It is exclusively in the mucous or cutaneous surfaces that the virus of vaccinia is cultivated. This may be demonstrated in various ways, for example:

1. Inoculation of vaccine in the anterior chamber of the eye produces immunity without any eruption.
2. Intravenous injection of vaccine produces immunity without eruption.
3. Transfusion of the blood of an animal during the stage of active eruption into the calf²² and the horse produces immunity without eruption. The quantity of blood to be transfused must be very considerable, 4 to 6 kilos. (= 8.8 to 13.2 lbs.)
4. Blood or serum of an animal suffering from cow-pox used for a surface inoculation does not produce an eruption of vaccine-pocks.

Hence it is evident that the virus is not cultivated in the blood. The unknown organism which produces the disease can only be present in the blood in extremely small quantity, although experiment proves that other soluble substances exist in the blood of the infected animal which render it both immunising and curative against cow-pox, and there is some reason to hope, against small-pox also.²³

IMMUNITY PRODUCED BY VACCINATION.

The immunity resulting from successful vaccination is the result of the local culture during the evolution of the pock, of an organism (unknown), which causes the production of an immunising substance. The absorption of this substance causes the subsequent immunity. A different explanation has been suggested, founded on the fact that pocks only occur at the site of the dermal inoculation, and that such inoculation does not produce a generalised eruption. It has been suggested that this is due to the absorption of a portion of the inoculated vaccine into the general circulation, this absorbed portion being subsequently conveyed to the cutaneous tissues, and producing immunity there, too early to allow of a generalised eruption being caused. The skin of the calf has certainly not been rendered immune to inoculation with vaccine before the fifth

or sixth day, as a rule. A calf may be inoculated daily for five days, and the pocks of each day will mature in succession at the proper time, and not simultaneously. In fact, this method is sometimes employed when there is a desire to utilise fully the vaccinogenic ability of one calf, and when, owing to the heat of the weather, a cause, it is desired to produce a small quantity of vaccine on several successive days rather than the whole quantity on one day. The human subject is affected in a strictly analogous manner. Vaccinations made daily after the primary inoculation succeed up to the fifth or sixth day, as a rule; after the seventh day failures become more frequent, and they are the rule after the ninth day, so that complete immunity against the action of the vaccine virus (so far as failure to produce a typical vaccine pock) is not attained in the human being until about the tenth day succeeding vaccination. This is true whether animal or human vaccine be employed.

ANIMAL VACCINATION.

As vaccinia is the same disease as cow-pox in the cow and horse-pox in the horse, the course of human vaccinia is uniform, whether it be developed from humanised vaccine (that is, animal vaccine which has passed through one or more human beings) or from bovine or equine pock.²⁴

As stated by Mr. Shirley Murphy:²⁵ "Judged by the experience gained during the first year's operation at the Animal Vaccine Establishment, animal lymph 'takes' with as much certainty as humanised lymph, and produces similar local and constitutional effects."

One of the earliest, if not the first, to practise animal vaccination as a source of supply for vaccinating human beings was Duquemelle, who employed the method at Rheims so early as 1800. In 1805 Troia was employing it at Naples, where in 1810 Galbiati²⁶ continued the practice. In 1840 Negri established a still more important institution at Naples for the carrying on of bovine vaccination as a substitute for humanised.

Italy was the country where this great question was earliest and most extensively worked, and it was from Italy that France first obtained a knowledge of the method and a supply of the vaccine virus. It was in 1864, after hearing addresses by Dr. Viennois and Professor Palasciano on the subject at the Congrès Médical at Lyon, that Drs. Lanoix and Chambon were stimulated to investigate the subject. They obtained a calf, which was incubating vaccinia after inoculation at the Neapolitan Institute, and brought it to Paris. From this dates the gradual large extension of the use of calf vaccine in France. Dr. Warlomont's establishment was started in Brussels in 1865, and subsequently became the Government station for animal vaccine.

In Germany the use of calf vaccine for public vaccination has become general, and all public vaccinations, as well as almost the whole of private vaccinations, are done from this source. The German Royal Commission on Vaccination, 1884, of which Koch was "reporter," recommended that as "vaccination with animal lymph has been recently so perfected as almost to equal vaccination with human lymph, the latter is to be superseded by animal lymph."²⁷

The little kingdom of Holland provides calf vaccine for public vaccination, and so do many of the American States. England, where vaccination originated, was the last country to utilise this most beneficent discovery by making general vaccination obligatory by legal enactment. It was not until 1871²⁸ that vaccination of all children was made compulsory. England, true to her conservative principles, has been one of

²⁴ Sheep-pox seems to have no distinct pathological relationship to variola or to equine or bovine pock. Human beings do not acquire true sheep-pox, nor is true variolation of the sheep possible. I experimented on the subject after successfully variolating the calf, but my results were not more satisfactory than those of others. I obtained only bastard pocks of an unsatisfactory character.

²⁵ Twelfth Annual Report of the Local Government Board; Report of the Medical Officer, p. 39. Mr. Murphy is now the distinguished Medical Officer of the London County Council.

²⁶ *Memoria sulla Inoculazione coll' Umore ricavato immediatamente dalla Vacca precedentemente inoculata*, Napoli, 1810. This is the earliest memoir on animal vaccination with which I am acquainted. See also *Il Vaccino Animale e il Vaccino Umanizzato, dei Dottori Dell' Acqua, e Grancini*, Milano, 1879.

²⁷ *Beschluss des Bundesrates vom 18 Juni, 1885; II. Beschlüsse betreffend die allgemeine Einführung der Impfung mit Tier-Lymphe.*

²⁸ By the Vaccination Act, 34 and 35 Vict., cap. 98.

²² Strauss, Chambon et Menard, *Comptes Rendus de l'Académie des Sciences*, Paris, 1890.

²³ Bernheim, *Immunität und Sérothérapie*, 1895, p. 276; also *Etude sur l'Immunité Vaccinale*, etc., by MM. Bécélère, Chambon et Menard, *Annales de l'Institut Pasteur*, T. x, No. 1, 1896.

the very last countries to introduce calf vaccine, and what the Government has done has been on the smallest scale and very tentative, and without any real effort to supply the demands of the public for vaccine from the calf. The Local Government Board established its first and only station in London in 1881.

OBJECTIONS TO HUMAN VACCINE.

The great impetus given to the use of animal vaccine has been due mainly to two causes: (1) The general belief in the existence of a tendency to degeneration and weakening of vaccine which has passed through many generations of human beings; and (2) the great alarm caused by the occurrence of cases, and even epidemics (Rivalta, etc.), of syphilis, due to vaccination from children who were suffering from infective syphilis at the time vaccine was taken from their vaccine pocks and inoculated on other children. In some cases these latter were syphilised, and gave it to their mothers, who infected their husbands. In other cases wet nurses have also been infected by suckling children syphilised when they were vaccinated, by the use of infected vaccine.²⁹ No doubt, too, (3) the great facility which the vaccination of calves offers for the rapid production of large quantities of fresh vaccine, in cases of emergency; and (4) the universal unwillingness of parents to the taking of vaccine from the arms of their children, which is no longer necessary when calf vaccine is used, have tended to encourage the use of calf vaccine.

DEGENERATION OF VACCINE.

With regard to degeneration, the question has been debated from the days of Jenner. There can be no doubt that a series of human vaccinations done one from the other would die out unless care were taken to select the best typical pocks from which to vaccinate each succeeding series. Anyone with much experience in vaccination can convince himself of this. Comparison of the drawings and descriptions of the vaccine pocks as known to Jenner and to his early followers with the average pock seen, say, at public vaccination stations to-day, certainly suggests that there is considerably less activity in the virus now than formerly. The small, pale, flabby, rather flat pocks one so often sees to-day, with little or no areola (which official authority now regards as non-essential) and containing but little vaccine, and causing little constitutional disturbance, offer a strong contrast to the large, full, plump pocks, with rosy areola and decided constitutional symptoms of the Jennerian times. Although the more inflammatory results and "erysipelatosus" appearance often mentioned by Jenner and the older writers were no doubt partly due to accidental impurities in the vaccine, and want of cleanliness and other precautions in the operation, and subsequent management of the arms, still, allowing due weight to this source of difference, there seem grounds for believing that much of the vaccination of to-day is degenerate in the sense of being done with weaker, attenuated, and less active virus. But similar difficulty exists in preserving a strain of animal vaccine (cow-pox) through many successive generations. It is essential that great care and judgment be exercised in selecting good typical pocks with which to continue the inoculations from series to series, otherwise the vaccine will degenerate and ultimately die out. But with the exercise of due care, the propagation from calf to calf may be continued, practically, indefinitely.

It is no uncommon thing to see on the vaccinated calf pocks which present very various appearances. Some will be perfect, typical, and mature; while others may be retarded or offer various indications of degeneration, just as we see in the infant. Calves do not all exhibit equal receptivity, nor even do all parts of the same calf serve equally well as culture grounds for the virus.

AS TO OTHER DISEASES OF CALVES.

With regard to the second cause which has stimulated the general adoption of calf vaccine instead of human, namely, the fear of the simultaneous inoculation of other diseases, especially syphilis, along with the vaccine, the use of calf vaccine is absolutely free from any danger as to syphilis, as the calf cannot be infected with that disease.

²⁹ See Fournier, *Syphilis et Vaccination*; also Simon, Papers relating to the History of Vaccination.

Efforts to prevent the apprehended degeneration of the humanised vaccine have been made many times by what is termed retrovaccination, that is by the passage of humanised vaccine through bovines. In 1837 the Government of Bavaria issued an order that this process should be regularly carried out. Retrovaccination has considerable effect in thus reviving the activity of humanised vaccine, which has begun to produce poor pocks. Where the regular employment of animal vaccine is, for any reason, not feasible, the practice of retrovaccination is to be strongly recommended. A calf should be vaccinated with the human vaccine in question, and the very best pocks on the calf should be utilised for further vaccinations of human beings.

Variolation of the calf is a still more effective means of rekindling the waning activity of vaccine, as demonstrated by the great success of Voigt's variola-vaccine referred to further on.

There has been much discussion as to whether humanised vaccine, when inoculated on the calf (retrovaccination), can be continued successfully through many passages; but success in this, like all other modes of propagating vaccine in series, depends on selecting only good typical pocks from which to continue the vaccinations, and its inoculation on healthy well-fed calves, which are not too young. Schulz has continued to propagate humanised vaccine from calf to calf in uninterrupted series for over two years.³⁰

EFFICIENCY OF ANIMAL VACCINE.

Judged by every test calf vaccine must be declared to be as active and as efficient as humanised vaccine. This is true whether we take as our standard (1) the character of the pocks, (2) the insertion success, (3) case success, or (4) the most important test of all, the protection against small-pox.

It is true that so esteemed an authority as the late Dr. E. C. Seaton held a very different opinion. He states that "Vaccination thus performed" (that is, with vaccine taken direct from bovines) "is much less successful than vaccination with humanised lymph."³¹ In another passage³² he writes as follows: "The difficulties in applying such a plan to the vaccination of the general population are, I apprehend, quite insuperable;" and again,³³ in urging that the great protection against small-pox consists "in taking care that when parents bring their children to be vaccinated, these shall be infected at once and infected completely," he adds; "and this is just what animal vaccination does not do."

These objections can no longer be alleged. Time and experience, which dissolve so many dogmatic assertions, have proved that every one of these objections can no longer be regarded as of the least weight.

Whole nations have been for many years regularly vaccinated and revaccinated with calf vaccine with success, judged by every standard. In Germany not only are all children vaccinated with calf vaccine in infancy, and revaccinated in their 12th year, but all recruits (some 300,000 yearly) are vaccinated for the third time on joining the army. The same is true of other countries, as already mentioned; so that this "insuperable" difficulty has been demonstrated, on the largest scale, not to exist.

The allegation, that by the use of calf vaccine infants are not "at once" and "completely" infected and protected, is known to-day, as the result of enormous experience, to be equally groundless.

In 1893 there were 1,518,793 infants legally liable to be vaccinated in the German empire. Of these 1,326,754, or 96.35 per cent., were vaccinated; 1,321,348 being done with animal vaccine (=87.37 per cent.), and only 5,406 with other vaccine. Of these primary vaccinations 96.35 per cent. were successful. Of 1,143,947 children who were liable to revaccination (in their 12th year), 1,107,025 were actually revaccinated, or 96.77 per cent. Of the total revaccinations, 91.71 were successful. Of the children revaccinated, 1,099,860 (=99.35 per cent.) were done with calf vaccine, and only 7,165 with other vaccine.³⁴

³⁰ *Impfung, Impfgeschäft*, etc., von Dr. M. Schulz, 1891.

³¹ *Handbook of Vaccination*, by Edward C. Seaton, M.D., Medical Inspector of (late Medical Officer to) the Privy Council. London: 1868.

³² *Loc. cit.*, p. 336, note.

³³ *Loc. cit.*, p. 337, note.

³⁴ *Blattern und Schutzpockenimpfung, bearbeitet im Kaiser. Gesundheitsamte*, Berlin, 1896.

THE EXPERIENCE OF GERMANY.

With such results already obtained, it is no longer possible to urge either that calf vaccine is not efficient, or that there is any serious difficulty in its general employment for vaccination. All the difficulties have been overcome in Germany and other countries; and the wonderful degree of immunity from small-pox enjoyed by Germany, where calf vaccine is most extensively used, demonstrates the efficiency of the vaccine. In many parts of the empire there were 100 per cent. successes with primary vaccination. Of 234,839 primary vaccinations in Posen, Lübeck, Lippe, Schaumburg-Lippe, Reuss, Waldeck, Schwarzburg-Rudolstadt, Schwarzburg-Sonderhausen, Anhalt, Sachsen-Altenburg, Sachsen-Meiningen, Brunswick, Oldenburg, Mecklenburg-Strelitz, Baden, and Saxony, the whole (=100 per cent.) were successful.

It is to the strict enforcement of vaccination, for which calf vaccine is employed, that the German army enjoys such a remarkable immunity from small-pox. Every officer and soldier in the army has been at least three times vaccinated—in infancy, during school age, and on joining the army. From 1873 to 1896 only 2 deaths from small-pox had occurred in that well vaccinated body of men.³⁵ The immunity enjoyed by the German soldier during the war of 1870, when exposed to the infection of small-pox which ravaged the French troops, who are but poorly vaccinated, is most striking. There were not 300 deaths among the German troops, while the French lost 23,400 from small-pox alone. The French prisoners interned in Germany brought the infection of small-pox with them there, and great numbers fell victims to it. These captives would have done more damage to their conquerors than the weapons of their soldiers in the field, had the population, amongst which they were themselves dying of small-pox, not been well protected by vaccination.³⁶

In Jenner's time, test inoculations of persons who had been accidentally and intentionally vaccinated with animal vaccine (cow-pox) were frequently made, and they were found absolutely immune.

THE EXPERIENCE OF ENGLAND.

During the epidemics of small-pox in Sheffield (1887-88), Bradford (1893), Halifax (1893), and Gloucester (1896) not fewer than 50,000 to 60,000 persons were successfully vaccinated and revaccinated with calf vaccine from the Bradford Calf Vaccine Institution, and not one of them took small-pox, even where they resided in poor, infected homes, in close contact with the variolous patients. Numerous cases could also be cited of nurses in small-pox hospitals who have attained complete immunity to variola by vaccination with calf vaccine.

There is no reason whatever to suppose that humanised vaccine (which is animal vaccine passed through a series of human beings) has acquired more protective properties than the original bovine virus from which it is descended. If one were to judge by the appearance of the pocks commonly seen to-day, as produced by humanised and by calf vaccine, one would unhesitatingly say the latter was the better of the two. The pocks produced by calf vaccine propagated skilfully to-day are identical with those of Jenner's time, while those produced by humanised vaccine are often very inferior.

With regard to the proportion of successful results among primary vaccinations with calf vaccine, there is no reason to suppose that it is not, in the hands of skilled vaccinators, quite equal to, if not superior to the average success of humanised vaccine.

At the animal vaccine station of the Local Government Board in London, the results with different vaccinators vary somewhat in different years. The lowest percentage of successes ever obtained since 1886 was 89.56 per 1,000; but Mr. Shirley Murphy during two consecutive years was successful in 100 per cent. This is proof enough that the success is not altogether dependent on the vaccine, as unsuccessful vaccinators like to assert. Here we have five capable vaccinators vaccinating from the same calves, at the same station, on the same days, yet while one attains 100 per cent. successes, others vary from 88.56 upwards.³⁷

During 1893-4 Dr. Cory performed 6,569 primary vaccina-

tions at this station, of which all but 37 were successful, or 99.43 per cent. There are not many stations where arm-to-arm vaccination is more successful than this.

Dr. Cory makes five insertions, and his insertion success was as follows:

Successful in 5 insertions,	5942
" " 4 "	312
" " 3 "	139
" " 2 "	74
" " 1 "	65

In the Grand Duchy of Baden there were 41,061 primary vaccinations performed in 1895,³⁸ all being done with calf vaccine; of these 40,248, or 98 per cent., were successful.

My personal experience is very limited as compared with these enormous numbers, but it is quite in accord with the results given above. It is not, as a rule, the calf vaccine which is in fault. The great difficulty, if great it can be called, lies in the recognition by the vaccinator that the physical characters of calf vaccine are not quite the same as those of human vaccine. The former is thick and glairy, the latter is thin and watery. Hence the minute scratches which suffice to allow the latter to penetrate into the tissues hardly permit the thicker material to enter the little wound, and infect. Thus it often happens that public vaccinators, accustomed for long years to be very successful with human vaccine, are disappointed when they first begin to use calf vaccine. A little experience teaches them the necessary modification of procedure in vaccination with calf vaccine, and then they get perfectly satisfactory results with it.

VACCINATION OF CALVES.

The provision of a suitable, airy, well-ventilated, and well-drained stable is a primary necessity. They should be large enough to allow of a sufficiency of stalls for changing and evacuating from time to time. The whole must be so constructed, flagged, plastered, lighted, warmed, and drained as to provide the most healthy conditions possible for the animals. These must be very carefully selected, and all which present any appearance of ill-health, or of skin irritation, must be summarily rejected. The character of the stools must be particularly noted. If they are inclined to diarrhoea the calf must be rejected, and if the animal is constipated there is also good reason for rejection, because it arouses a suspicion, often too well founded, that the calf has been physicked in consequence of having had diarrhoea, and has thus become constipated.

The best age is about three to four months (the use of calves under three weeks is not allowed in Germany), and milk calves are more satisfactory than those which have been weaned early and fed on meal and other substitutes. Where calves are unattainable, adult animals can be used. But the younger animals are best, being more manageable, and almost certainly free from tuberculosis.

The best food is new milk, unskimmed, of body-heat, with two to four eggs daily. Calves vary in the quantity they take, but an average calf of three to four months old, if taking only very little hay, will consume 2 to 2½ gallons of milk daily, or even more. It is better to give the milk ration in three rather than in two parts. It is essential that the milk be fresh.

The milk should be sterilised by boiling, and be kept so protected that, while cooling, it will not again become polluted. This is a great preservative from diarrhoea. The addition of a little lime water and salt to the milk is very desirable. Some thoroughly well-boiled gruel or a little broken bread which has been scalded is sometimes permissible, well mixed with the milk. Between meals a few handfuls of hay may be left for the calves to amuse themselves with.

Mr. Murphy, in the report referred to, seems disposed to regard female calves as more successful vaccinifers than males. I do not think there is any merit in this respect attached to the sex, but undoubtedly females are preferable from the point of cleanliness, especially if the calves are kept in small stalls, as their litter is much more likely to be kept dry and clean.

Light-coloured, if possible white, calves are preferable to others, as their skin is more delicate, and is a more kindly

³⁵ The peace establishment is nearly 600,000 men.

³⁶ BRITISH MEDICAL JOURNAL, February 29th, 1896, p. 561.

³⁷ Reports of the Medical Officer of the Local Government Board.

³⁸ I am indebted to Sanitäts-Rath Dr. Fischer, Director of the State Calf-Vaccine Institution, Karlsruhe, for these figures.

culture medium than that of dark calves, which is always coarser, and usually does not "take" so well. Of several calves inoculated the same day and with the same vaccine a considerable variation in the relative success may be found, owing to the relatively greater susceptibility of some. Some parts of the surface, selected for inoculation, habitually are more successful than others. The buttock is very generally a bad site, while the scrotum is one of the best.

METHOD OF PROCEDURE.

The modes of insertion are various, and each person comes to prefer the method he has been longest accustomed to. Some make single incisions about 1 inch long, arranged in quincunx; some make the incision several inches long; others make a double incision; some prefer insertion by puncture; some scarify a considerable area. The last method has the disadvantage that it is not easy to recognise the typical characteristics about the pock when it is seen covered with a large scab. Further, the large surface of such a scarified area is more likely to attract dirt, causing both a loss of valuable material and a risk of increased pollution of the vaccine.

As to the extent of surface to be inoculated decisive facts are not yet forthcoming, but there seems to be a limit to the number of insertions which can be made with success. It cannot be yet stated with certainty whether the quantity inserted affects the quality of the harvest injuriously, or if the unsatisfactory result be due to the depressing effect on the calf of being kept too long in the constrained position required in order to carry out the large number of insertions.

Both Jenner and his contemporary Pearson (Physician to St. George's Hospital) devoted some attention to this most important though neglected question of the influence of the quantity of material inoculated on the protection afforded. Jenner was undecided on the subject, Pearson thought that in the case of variola the quantity of virus inoculated had no influence on the severity of the disease.

It is a widely spread theory among practitioners that the quantity of vaccine inserted is immaterial, and tubes of vaccine are often appraised according to the quantity rather than the quality of their contents. The vicious argument is commonly stated thus: "Vaccinia is a microbic disease; as the microbes multiply in the body until it is infected there can be no difference in the result, whether much or little vaccine is used." Nothing could be more illogical in theory or worse in practice than to adopt this very prevalent line of argument as a guide. To mention only a few capital errors: it disregards the struggle for existence between the inoculated microbes and the organised elements of the body; it ignores the fact that a feeble army of invasion may be annihilated, or it may be rendered so debilitated and attenuated that its protective operations may be reduced to nothing, or next to nothing. But, above all, this theory is at variance with the established fact that the degree of protection varies directly with the number of insertions, and there can be no doubt that more vaccine is invariably inoculated with several insertions than with one. One large insertion would no doubt give as effective protection as several smaller ones of exactly the same area: but there is a distinct advantage in not making one area of insertion too large, in the avoidance of the risk of inflammation. For the same reason it is most desirable that the insertions should be made far apart. By doing so the risk of any inflammatory action extending from one area to another is minimised. Four pocks which have become inflamed and included in one area of irritation are a source of much more serious constitutional and local disturbance than four detached pocks, each of which is inflamed. On the Continent the insertions are usually divided between both arms in order to minimise this risk. A single large insertion advances rather more slowly from the commencement to the falling off of the scab. The stage of incubation is shortened when several insertions are made.

The preliminary shaving of the parts to be inoculated and the subsequent washing and disinfecting should be done with the greatest care. Bad shaving may result in seriously damaging the harvest. Most of the so-called "supplementary or supernumerary pocks" referred to by writers are really due to scratches and abrasions of the skin, leading to the unintentional inoculation of various points. A general eruption never

results from cutaneous inoculation. Pocks only appear at the points of insertion. The skin being the culture medium of the virus, it is a general law that in order to procure a general eruption, the virus must be introduced into the system by some other medium than the skin.

The whole area to be vaccinated must be thoroughly (surgically) cleansed with soap, hot water, and nailbrush; all traces of soap must be carefully removed, and the parts be subsequently disinfected before the vaccination. As disinfectants, carbolic acid, boracic acid, and perchloride of mercury all have their champions, I generally use lysol, which is excellent, both as a detergent and disinfectant. It is necessary that the skin should be free from any absorbed disinfectant before the vaccination is done, or the vaccine may be sterilised completely.

The evolution of the inoculated pock is more rapid in the calf than in the human being, possibly owing to the higher and more favourable temperature of the body, which averages 101° to 101.5° F. There are slight unessential variations in the details of the evolution of the pocks when they result from incision as compared with punctures, and usually the former advance more rapidly than the latter.

EVOLUTION OF INSERTIONS BY PUNCTURE.

Even within a few hours a puncture which is going to "take" may be noticed to be slightly elevated from infiltration of the tissues. The orifice of the puncture is filled by a minute blood clot.

On the second day a slight reddishness may be seen around the puncture, and palpation detects a little elevation of the spot.

On the third day the elevation of the spot can be both felt and seen, its centre being occupied by tiny cicatrix, around which may be already detected slight indications of a greyish ring, outside which there is a peripheral faint pink areola.

On the fourth day the specific characters of the cow-pock are distinctly noticeable. The vaccinogenic zone is of a dull, whitish colour, its borders being well elevated and distinctly outlined. The characteristic central depression (umbilication) is well marked, the areola is more pronounced, and the induration of the skin is much increased.

By the sixth day the pocks have increased greatly in size, and apparently at a much more rapid rate during the last twenty-four hours than during any similar period; the greyish, vaccinogenic zone is much more marked; the areola is of a darker colour, while the peripheral induration is diminished, and the skin feels softer.

On the seventh day the plump, full appearance is altered, and the pocks look flatter, though wider in diameter. The central depression looks less distinct, and is occupied by a crust or scab; the grey zone is duller and more yellowish in appearance. The areola and the peripheral induration are distinctly less.

During the following days the pocks grow flatter, the crusts darker and harder, and the induration and the colour of the surrounding areola become much less marked. About the fifteenth to the seventeenth day the scabs fall off, usually displaying a completely healed surface, pinkish and glistening, below.

When the insertions are made by incision, the phenomena are slightly different in some details, but are essentially the same in character. In general the process is rather accelerated.

On the second day the grey vaccinogenic zone is fairly well marked, with its reddish areola and surrounding indurated tissue.

On the third day the central linear depression is distinct, and the grey pearly margin is broader, as well as more prominent, and the areola and peripheral induration are more noticeable.

By the end of the fourth day the grey vaccinogenic zone is distinctly clear and transparent-looking, its internal margin having become irregular in outline. The central linear depression is more marked, the peripheral areola is of a bright pink colour, and the subjacent and surrounding tissues are more distinctly indurated.

The evolution proceeds rapidly during the ensuing twenty-four hours; the clear, transparent appearance of the pearly-grey zone is altered to a dull whitish colour, its internal

border being uneven and jagged, and the external contour more wavy and irregular; the central depression looks less marked, being more filled with yellowish crust; the areola is commencing to be of less lively colour, and the induration more diffuse.

The fifth day may be in general regarded as the point of maximum growth and vigour of the pock, whether resulting from puncture or incision, and after this date it begins to show decadence, becoming less plump, flatter and drier every day, though the total quantity of material which may be collected is greater on the sixth than on the fifth day.

CAUSES OF FAILURE.

The evolution of the pock may be accelerated or retarded by various agencies, not all, unfortunately, well understood. In general the growth is more rapid in hot than in cold weather, but the excessive heat of summer easily leads to the complete degeneration of the culture. On the Continent stations have sometimes to be closed during the heat of summer, owing to this cause. In this climate it is necessary to heat the stables artificially during many months of the year.

The success of the inoculations may be unfavourably affected by the age and health of the animal, and by the condition of the skin (harsh, inflamed, scurfy, etc.). Diarrhoea is a serious cause of failure. The sanitary condition of the stables, want of cleanliness, defective supply of fresh air, emanations from drains, bad dietary—all these things may spoil and finally destroy the finest strain of vaccine. Indeed, the calf is a delicate creature, and the successful propagation of cow-pox calls for continuous care and observation.

Should a culture, from whatever cause, begin to decline in activity in its passage through any particular calf, it is always possible to restore it to its primitive excellence if it be at once passed through a good calf before it is too late. But it is only by constant watchfulness and care as to the selection and condition of the calves; by careful attention to their dietary and hygiene, and by the judicious selection of the best typical pocks for further propagation, the vaccine being taken on the day of maximum virulence, that successful propagation in continuous series can be attained.

The fifth day is undoubtedly, as a rule, the day of maximum virulence (Pfeiffer says $3\frac{1}{2}$ to $4\frac{1}{2} \times 24$ hours), and it is on this day that the vaccine should be collected for further propagation in other calves if, as is usually the case, the pocks are seen to be in their best condition then. On the sixth day the quantity of vaccine is larger, but the quality is not quite so good, so far as activity.

At some stations the vaccine is collected habitually on the fourth, and even on the third day. It would seem to be possible to evolve a strain of vaccine which matures quicker than the fifth day.

When the pocks have undergone a decided degeneration in appearance; if small and dry, with little or no areola; if they become crusted over too early; or if, on the other hand, they become purulent on the fourth day, instead of plump, elevated, and vigorous, then no material must be taken from such pocks for further use, either on man or beast.

For the purpose of vaccinating and of collecting the vaccine the calf must be securely attached to a specially-constructed table, so that it cannot by violent movements injure itself or the pocks. Such pocks as are on the sides may, indeed, be dealt with while the animal is on its feet, but not so those on the belly and other parts out of easy reach. The original Dutch (Rotterdam) table is still the best for the purpose, though I have found it desirable to effect some changes in its construction.

THE VACCINE.

Before the vaccine is collected the whole surface must be carefully cleansed, and the whole surface wiped with disinfectant. As already mentioned, the specific seat of the culture of the unknown organism, to which vaccine is undoubtedly due, is not the blood, or the lymph, but the dermal integument. The so-called "vaccine-lymph" (which is not lymph at all) is therefore not the primary or special seat of the virus, but is only a secondary receptacle of serum, with which some of the virus has become absorbed. The quantity of virus con-

tained in this serum may vary enormously, from none or very little, up to sufficient to render it very virulent and active.

From the structure of the pock, and the thick, glairy character of the liquid in it, the latter will not flow freely when the pock is punctured, as is the case with human vaccine, which is, as compared with bovine, thin and watery in physical character. Therefore, in order to cause the exudation to flow, it is usual to employ special compression forceps, of which there are several forms in use.

Some persons collect this liquid as it exudes, direct into capillary tubes, either straight, or furnished with a central dilated chamber. In any case tubes for this purpose must be two or three times the size of those used for human vaccine, otherwise coagulation of the serum in the tube is pretty certain to occur, and it is almost impossible to extract such coagulated material from very fine tubes. Coagulation does not affect the quality of the vaccine. Others, again, collect the vaccine from several pocks in a suitable receptacle, and when flocculi of fibrin have formed in it, carefully remove each particle, and then fill the tubes with the defibrinated liquid. Thus the annoyance and loss caused by coagulation in the tubes is avoided.

Having obtained all the liquid which can be expressed in this way, some persons are content to leave the pocks undisturbed. But they still contain the great bulk of the most active virus in their tissue, probably deposited within the cells of the surface layer.

The best procedure, therefore, is to collect this infective tissue by removing the surface of the pock by scraping. The expressed liquid contains some virus, the pock contains it all. Therefore, by dealing in this way with the surface of the pock, the most active material is obtained. By means of suitable appliances the abraded material should be reduced to a perfectly homogeneous creamy consistence. It may be ground in a mortar, or, better still, in one of the machines specially constructed for the purpose.

GLYCERISED VACCINE.

To prevent this finely-ground pulp from drying quickly, it is necessary to add some liquid. As the result of large experience, and on the recommendation of no less an authority than Koch, pure sterilised glycerine, free from acid, is universally employed for this purpose. Though Koch's high authority has led to the use of glycerine for this purpose being sanctioned by law in Germany, it has been used in Italy for sixty years. My experience is that the best form is sterilised glycerine which has been three times redistilled. Some persons dilute it with more or less water. Obviously if any water is used it should be distilled and sterilised. Vaseline has been proposed as a substitute for glycerine, and Surgeon-Major King employed lanolin in India; but these substances have found few to favour them besides those who originally suggested them, and pure sterilised glycerine is still at the present time the best medium known.

Glycerine acts not only as an extractive, and as a means of keeping the vaccine moist, but it is an excellent disinfectant for the purpose, destroying the ordinary moulds and fungi, and also the three microbes which are commonly found in fresh vaccine as collected; these are the staphylococcus aureus, a greyish micrococcus, and a white one, to which Antony has given the name of the "porcelain micrococcus."³⁹ At the same time the glycerine in proper proportion does not attenuate the vaccine virus; on the contrary, by its destructive action on the extraneous organisms accidentally present, it prevents their injurious interference with the specific virus. The glycerised compound therefore, when properly prepared, is much purer, and less likely to produce any inflammatory results than vaccine taken from the calf and inoculated direct on the child. I have never seen severe inflammation follow its use, though I have frequently seen such where the child was done directly and immediately from the calf. The result of the great experience now acquired on this subject is that the direct use of vaccine from calf to arm is almost entirely abandoned. So beneficial is the action of the glycerine, that two large institutions in France for the propagation of calf vaccine, habitually send out no vaccine for use which has not

³⁹ *Rapport sur le Fonctionnement du Centre Vaccinogène au Val-de-Grâce.* Par M. le Prof. Dr. Antony.

been kept for four to six weeks. During this interval, their proprietors assert, all extraneous organisms from the air, etc., which may have got into the vaccine while it was being collected, are killed, and the vaccine thus sterilised they consider gives the best results when used on either human beings or calves.

This glycerised pulp is the best form of calf vaccine, and the one which is in almost universal use. It is what is exclusively employed, and with the best possible results, in Germany. It is what is used for our own army and navy, it is also what is recommended and chiefly sent out from the Bradford Calf Vaccine Station. This form, like the liquid vaccine, should of course be put up in sterilised, airtight tubes, vials, or other receptacles.

Calf vaccine is also used dried on ivory points by a few persons. But it is not by any means the best mode of preservation. It cannot be as pure, and if not kept thoroughly desiccated, decomposition may readily occur. The pulp (unglycerised) is also sometimes dried rapidly and ground to a fine powder and kept for use. It must, like points, be moistened before being employed.

BLOOD IN VACCINE.

It will be evident that during the process of collecting calf vaccine, whether by scraping or by expressing the fluid from the pock by means of special forceps, some blood must get into it. But no matter how limpid the clearest human vaccine may appear, it always contains blood corpuscles. Persons who are not familiar with the use of calf vaccine and the conditions under which it is prepared, are sometimes astonished and alarmed if they see a minute flocculus of fibrin or blood clot in it, and reject the vaccine on that account. It seems, however, rather refined criticism to use without hesitation vaccine which contains blood cells, if only it be colourless, but to feel alarmed if a little colouring matter be present. Indeed, to employ the serum which has exuded from the pock on the calf or calf, and object to a particle of the colouring matter of the blood in it seems like straining at a gnat and swallowing a camel. If the vaccine exuded from the living tissues be fit for use, if the particles of tissue which must adhere to the vaccine and get carried into the tubes, or conveyed by the lancet from arm to arm, as well as the pulverised pulp, are free from danger, then the blood cannot be dangerous. Anyhow, it is always present, as represented by some of its elements, in the most translucent and transparent vaccine, whether human or animal.

The following statements on the subject by two of the officials of the Local Government Board are taken from the Report (1890) of the Royal Commission on Vaccination, now sitting. Dr. Cory, Director of the Government Animal Vaccine Station, was examined as follows:

- Q 4423.—Did you get clear lymph in that way (from the calf) free from blood? No, it is always mixed with blood more or less.
A 4652.—You cannot obtain the calf lymph without taking also a certain quantity of blood.
Q 4483.—You told us that you were obliged to use the clamp to get lymph from the calf? Yes.
Q 4484.—And that very frequently blood comes with it? Yes.
Q 4485.—In what proportion of cases, roughly speaking, does blood come with the lymph? I think in the majority of cases.
Q 4486.—Do you use that? Yes; we must use lymph with a certain mixture of blood.
Q 4487.—You have no hesitation in using lymph from the calf, though it contains blood? No; none whatever.
Q 4488.—The rule as to the examination for blood before it is issued does not apply to the calf lymph? No.

Extract from the evidence of Mr. Farn,⁴⁰ Examiner of Vaccine for our Government (*loc. cit.*).

- Q 4119.—Is blood in calf lymph recognised as an objection? I believe not. My instructions are not to that effect.

CULTIVATION OF VIRUS ON ARTIFICIAL MEDIA.

Many attempts have been made to cultivate the virus on artificial media; and many men, like myself, have felt confident they had attained that glory which "*miscet diis immortalibus*" by successful culture on agar, gelatine, broth, egg, etc., I once produced perfect Jennerian pocks on a child with a culture of calf vaccine on agar. But as I had simultaneously inoculated the child with humanised vaccine (com-

pare Ceely's and Voigt's combined inoculations in variolating bovines), I was not satisfied that the result was certainly due to the culture. Up to the present no satisfactory success has been attained. It probably is entirely erroneous to assume that the specific organism belongs to the schizomycetes or can be cultivated in the familiar manner employed for propagating such organisms.

Le Dantec⁴¹ claims to have discovered and isolated the "*variola coccus*," which, he says, is to be found in the pock, blood, bones, viscera, muscles, spinal cord; indeed, it is ubiquitous. There are serious difficulties in accepting the conclusions of the author of this supposed discovery, namely, the abundance and ubiquity of the organism and the extreme facility with which, amidst so many unsuccessful searchers, Le Dantec solved the whole difficulty. Copeman⁴² claims also to have discovered the bacillus, not only of vaccinia, but of variola. His organism, however, is not the same as Le Dantec's, and is utterly different from the sporozoa of Pfeiffer⁴³ and the cytoryetes variolæ of Guarnieri.⁴⁴

EMPLOYMENT OF ANIMAL VACCINE FOR HUMAN VACCINATION.

As animal and human vaccine contain the same virus, and only differ slightly in their physical properties, the modes of using them present no essential differences. Little differences of detail of the operation, corresponding to the differences in character of the two, will make the use of calf vaccine as successful as arm-to-arm vaccination. Only a little more trouble is required to get a good result, but with that little full satisfaction can be attained.

Human vaccine may possibly take, on the human subject, with somewhat greater readiness. But if so just a little additional trouble will cause the difference to disappear. Calf vaccine, which has become somewhat attenuated in reference to the human subject, may often be inoculated on the calf with perfect success. It is possible that, in an analogous way, human vaccine may have a greater affinity for the human subject, and take with somewhat less trouble and greater facility than calf vaccine. But evidence is wanting to prove this. The practical results show that good vaccinators get as satisfactory results with calf as with humanised vaccine.

It has been my experience to witness the initial attempts of many men to use calf vaccine instead of human, which latter they had long been familiar with. It is almost a rule that men become more and more skilful after their first attempts, which may have been unsatisfactory. With increased experience increased success has come, until the results have been perfect. The results attained by the individual men at the Government Animal Vaccine Station in London, during a series of years, prove the influence of the "personal equation" in vaccination, as in other things. Why should one man never get more than 96 per cent. success, while another gets 98 per cent., and a third gets 100 per cent., year after year, with thousands of cases, though all three are using the same vaccine direct from the calf to child? Year in and year out some men cannot get beyond a certain proportion of success, perhaps just below perfection, while others attain perfection apparently without any special effort. But obviously it is not the vaccine which is in fault.

It is not a little remarkable how readily men blame the vaccine they have bought, if they should fail with it, while they never blame the vaccine they take direct from the arm if it should fail. Yet 100 per cent. successes are by no means the rule even with arm-to-arm vaccination.

I am constantly consulted as to the keeping property of the various forms of calf vaccine. I invariably answer that to keep it long in stock without necessity is to sacrifice needlessly one of the great advantages of the supply of calf vaccine, which is, that within a few hours it can be procured in practically any quantity required, and fresh and active? Why, then, use part of the contents of a tube to-day and store up the remainder for use after a lapse of months? Calf vaccine will, however, keep apparently as long as human.

⁴¹ *Archives de Médecine Navale*, No. 6, 1895.

⁴² *BRITISH MEDICAL JOURNAL*, 1, 1896.

⁴³ *Centralbl. f. Bakt.*, No. 25, 1895; *Die Protozoa als Krankheitserreger*, Jena, 1890, and various other writings of this eminent authority on vaccinia.

⁴⁴ *Archivio per le Scienze Med.*, No. 22, 1892.

⁴⁰ This gentleman is employed by the Government to examine the vaccine procured from various sources, including that from the Animal Vaccine Station, in search of blood, microbes, etc.

I have used it with perfect success after a year. I have sent it to Algiers, Egypt, India, tropical South America, and it has given perfect results under most unfavourable conditions of time and climate.

Where storing is unavoidable, the vaccine should be kept in the coolest available place and in the dark. Points and the dry powder should be kept perfectly desiccated. The glycerised form, which I term "conserve," may be opened and used, and the vials may be resealed and re-used many times without diminishing the activity of the vaccine.

Attempts have been made to employ other aseptic and disinfectant substances—for example, small quantities of salicylic acid and of boracic acid have been added to the vaccine—but these methods have not been generally approved by experienced men.

It is impossible to state what is either the case or the insertion success of public vaccinators generally with arm-to-arm vaccination, much less to give the average for the whole country, which would be a good deal lower than that of public vaccinators. The general standard must be very far below that attained at the Animal Vaccine Station in London, where, as stated already, some of the vaccinators attained to 100 per cent. successes. Seaton gives it as his opinion⁴⁵ that, "while one practitioner is disappointed if one case out of ten exhibits a number of vesicles short of the number of insertions of lymph which have been made, another is very well content if he get the full number of vesicles in only half his cases." I could name many men who during several years have systematically never failed in one case with calf vaccine conserve.

Seaton mentions several stations as being particularly successful, and yet he adds that the insertion success was only "considerably more than 90 per cent.!" He mentions that at Lincoln, of 150 persons who caught small-pox, 18 said they had been vaccinated [with human vaccine], but that the vaccination had not taken, that is, only 88 per cent. had been successful!

The following suggestions for successful vaccination with animal vaccine are offered as the result of my own experience, and as approved, after considerable experience, by large numbers of medical men who have asked my advice:

PRACTICAL HINTS FOR VACCINATORS.

1. Satisfy yourself the child is in thoroughly good health; always examine the body and buttocks before vaccinating.
2. Vaccinate only with lancets kept for that special purpose. Disinfect them thoroughly before and after use. The lancet blade, without any handle, is most convenient. Have a separate lancet for each child (they cost about 6d. each, and last a lifetime).
3. Disinfect the arm before vaccinating.
4. Use soft tissue paper, which may be kept cut in packets of a suitable size, about 4 square inches, for washing and drying the arm, lancets, etc. Such paper "napkins" cannot be used more than once; whereas people become so attached to bits of rag that they are loth to part with them. The packets should be sterilised by baking from time to time, and be kept in a well-closed vessel.
5. Use blunt lancets rather than very sharp ones.
6. Have the child's arm completely uncovered.
7. As the evolution of the pock takes place, mainly in the rete Malpighii and upper portion of the papillary bodies, the surface tissue must be removed so as to enable the vaccine virus to be deposited there; it is useless and disadvantageous to go deeper. By making too deep a wound some of the vaccine is deposited where it will not infect (in the deeper layers), and some is swept away by the hæmorrhage which is needlessly caused.
8. It is disadvantageous and unnecessary to cause blood to flow.
9. As animal vaccine is so thick and tenacious, it will not penetrate readily into such minute scratches as suffice for the thinner and more watery human vaccine, therefore a slightly larger raw surface is necessary.
10. The best method is to rub off the surface of the skin by frequently passing the edge of the lancet rapidly over it. The spot should be about this size . Do not make clean cuts or incisions.

11. Allow a few minutes for absorption, before the child is dressed.

12. Instruct the mother carefully (a few printed rules are a great assistance) to avoid irritating the pock, breaking it, poulticing, applying wet cloths, etc., and as to keeping the pocks scrupulously clean. About the seventh day it is advisable to have the sleeve ripped up to the shoulder, or taken off entirely to prevent rubbing the pock.

13. As the scab is a natural protector for the raw surface below, the mother should be instructed to take every care to avoid knocking it off.

14. Avoid "shields." The dry clean scab is the best protector.

15. Do not be too economical in the quantity of vaccine used.

16. Make at least four insertions well apart.

ALLEGED DISADVANTAGES OF ANIMAL VACCINATION.

We may dismiss the older allegations that persons vaccinated direct from animals, acquired physical and other characteristics of the vaccinator, gradually developing the voice of the bull, bovine stupidity, or good promise of a tail!⁴⁶

The only alleged danger which it is worth considering is that of the possibility of tuberculosis being inoculated. It is inconceivable that an animal suffering from anthrax, or any other disease offering obvious symptoms, could by any accident be used as a vaccinator. That such a thing should happen means that the animal must pass muster when first obtained; that it should undergo the handling and observation unavoidable during the preliminary days it is under observation, while it is being shaved and vaccinated; that during five to six days after vaccination it could be fed and tended and no one know it was ill, and that ultimately it should be again placed on the table, and the vaccine collected, without anyone knowing it had a serious disease such as anthrax! To assume all this is, of course, to assume what is absurd. That apparently normal pocks would rise on such an animal is improbable; but that any medical man could be found to collect vaccine from pocks on such an animal, knowing it to be diseased, is incredible.

TRANSMISSION OF TUBERCULOSIS A GROUNDLESS FEAR.

As to the possibility of tuberculosis being acquired, supposing it to exist in the animal: (1) Such a case has never been known, although millions have been vaccinated for some years past with animal vaccine, and there are suspicious persons on the watch who would be only too glad to proclaim the discovery of such a misfortune; (2) tuberculosis in the young calf is so rare as to be a curiosity; (3) the existence of tuberculosis can be diagnosed now with great certainty by means of tuberculin, and its presence has never been detected in this way in calves; (4) the calves can be slaughtered, and a *post-mortem* examination made before the vaccine is used; this practice is in force in some places; (5) all attempts to produce tuberculosis by experimentally inoculating susceptible animals with vaccine taken from human beings in the last stage of general (not merely local) tuberculosis have failed; the tubercle bacillus does not exist in the vaccine even in such advanced cases as these, which were selected because they were of the most marked and general form of tuberculosis.

The immunising power of vaccine shows itself earlier and is more powerful than that of the inoculated virus of variola. The primary fever in variola discreta begins on the twelfth day of inoculation; after inoculation with the virus of variola on the eighth day; after vaccination on the fifth day. Active virus can be obtained from the pock of inoculated variola on the fifth day, from the vaccine pock of the child on the third or fourth day. There is an interval of eight days from the commencement of the primary fever until the commencement of the secondary fever, in varioloid of six days, in inoculated variola of six days. From vaccination until the falling off of the crust about twenty-one or twenty-two days elapse. After vaccination there are but three days of febricula (sixth, seventh, and eighth), and the patient is saved not only the high fever of these days, which occurs in all three classes of variola (discreta, varioloid, and inocu-

⁴⁵ Loc. cit., p. 160

⁴⁶ I possess an early print of 1802 in which all these sequelæ of vaccination are represented, pictorially and otherwise, as in process of evolution!

Chart showing the relative course of small-pox, spontaneous and inoculated, and vaccinia.

lated), but the whole of the secondary fever and the more or less intense fever which lasts during the stage of intermission.

But the fact that while the use of calf vaccine in Germany and some other Continental countries has increased yearly until it is practically universal, while tuberculosis has greatly diminished, shows how groundless the fears of infection by calf vaccine is.

ABSENCE OF SERIOUS SEQUELÆ.

Serious sequelæ after vaccination with animal vaccine I have never seen. They are certainly not more common than after the use of humanised vaccine. Of course, if obvious precautions be neglected, if dirt be inoculated along with vaccine, if the wound be kept foul and be irritated by friction, if injurious dyes from the clothing be allowed to get into the open sore, then we must expect the necessary bad results to ensue; but such results are not due to the animal vaccine as such, but to the dirt and other preventable causes.

POPULARITY OF ANIMAL VACCINATION.

It is quite certain that in this country the public is becoming every year more determined to use animal vaccine instead of humanised vaccine. The quantities consumed increase enormously every year. The country is flooded with cheap stuff, "made in Germany" and elsewhere, of unknown nature or origin. It is cheap, and therefore sells. That serious danger may arise from the reckless employment of material of such absolutely unknown origin is obvious. There are clamorous demands against the importation of beef or articles manufactured abroad, unless they bear the label of the place of origin. Surely such an important matter as the vaccine which is to be incorporated direct into the substance of the body should not be saleable without some guarantee as to its being at least harmless.

Public vaccinators begin to find that their stations, which had become deserted while they used humanised vaccine, soon are gladly visited by parents when they learn that calf vaccine is used. In Halifax the vaccination station had been closed for years, as no children were brought for vaccination. Small-pox came, still the station was deserted. Calf vaccine was then provided, and within a few weeks some 1,000 persons flocked to get vaccinated in this, one of the most antivaccinating towns in England. The same thing has been observed in many places, notably in Bradford, and more recently in Gloucestershire and the neighbourhood. The poor certainly have a legitimate grievance in the fact that they are prevented from enjoying the use of calf vaccine, which all the better-off persons use, and which abroad has been generally adopted in place of human vaccine. To add to the hardship, the poor man is obliged to pay for the humanised vaccine which he refuses to use, just as his rich neighbour does. The poor man pays for his "free vaccination" in his poor-rate, even though he does not make any use of it. If further irony could be imported into the case, it would be merely to mention that the poor man in London can get vaccinated with calf vaccine, which the poor man out of London has to help to pay for, while he cannot get it for himself or his child, as the Government station in London is paid for out of the taxes, and not out of the London rates. Our soldiers and sailors are vaccinated with calf vaccine by our Government. What good reason can then be urged why the respectable civilian should be forced to get done with humanised vaccine?

The great objection to vaccination which the general public has is to the use of humanised vaccine, and it would be a most wise step if the Government would take steps to remove it.