

## VARIOLA AND THE VARIOLOID DISEASES OF ANIMALS.

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THE greater number of diseases, that is those pathological states dependent on deviations from the normal processes of nutrition and innervation, resulting in the conditions known as atrophy, degeneration, inflammation, etc., are common, more or less, to all animals, and in the higher grades, or warm-blooded animals, exhibit essentially the same phenomena.

It is somewhat different with what are called specific diseases; that is, certain sequences of morbid phenomena following the entrance into the organism of specific poisons or virus, which may in some cases be purely chemical bodies, but which have been proved in many, and may by analogy be assumed in more, to be of a parasitic nature, that is, micro-organisms capable of multiplication in, if not of perpetuation also out of, the body, and directly by their presence, or indirectly by the action of substances generated by them in the animal fluids, setting up changes in the blood and tissues. Some of these, as the bacilli of tuberculosis, and of several forms of septicæmia, are capable of infecting many different classes of animals, and producing in all results essentially identical, any apparent differences being easily explicable by differences of histological characters. Others are peculiar to single genera or species of animals, and either totally incommunicable to others or communicable only by direct inoculation, and then setting up phenomena for the most part strictly local and otherwise distinguishable from those of the normal form. The most typical examples of these diseases are to be found in the pustular eruptive fevers of man and beast, the mutual relations of which I propose discussing in this paper. Before advancing any theories, whether of my own or others, I shall simply state certain observed facts.

*Man* is subject to an acute specific pustular exanthem, known as variola or small-pox, highly infectious, pyrexial

and fatal, having a constant incubation period of about thirteen days when communicated by aerial infection and by fomites, but when by inoculation, presenting certain deviations from its normal type. It is not communicable to other animals, monkeys excepted, by ordinary infection, and with great difficulty by inoculation to the ox, when it presents the character of a local affection only.

*Sheep* have a variola closely resembling that of man in every respect, but clearly an independent disease, being enzootic where small-pox is almost unknown, as in East Prussia, and unknown except when imported where, as in England, small-pox is never absent. Inoculation of ovine variola produces in the sheep the same modified type of disease, and similar immunity from ordinary infection as that of small-pox does in man. Inoculated in the horse, and ox, and man, it produces only a local affection, but it appears to be communicable in a less modified form to the more closely allied goat.

*Goats*, however, have, it appears, their own variola, for in Norway, where they are numerous, it is rarely absent, yet sheep-pox is unknown. It is seldom seen in countries where goats are kept in less numbers.

*Camels* have a variola, which is not unfrequently communicated to man in a severe form. It does not, however, seem to be as fatal to these animals as sheep-pox is to the sheep.

*Swine* have their variola, a highly infectious and fatal disease, and communicable by inoculation to the sheep, goat, and man, though experiments on the ox and the horse have as yet given only negative results.

*Dogs* have a variola of their own, very fatal to young puppies, contagious and inoculable, but not very infectious. It is somewhat remarkable that they do not seem ever to contract variola from man, considering how much they are associated with him. Greve has, however, succeeded in inoculating dogs with human small-pox; but it may be said that dogs are by no means susceptible to inoculation with the variola of other animals, or indeed, as recent experiments with the tubercle bacillus have strikingly shown, are they to any forms of infectious or infective disease.

Variola of fowls and of some other animals have been described; but I forbear from enumerating more than those already mentioned. It is unfortunate that, as everyone must have felt in reading even the more pretentious works on veterinary medicine, the standard of pathological knowledge among the medical attendants of our domestic animals

is still very low, while among ordinary agriculturists we can still less look for anything like accurate scientific observation, or the capability of distinguishing between a specific pustular exanthem and a non-specific cutaneous disease as herpes, attended by vesicular eruptions and scabbing.

All the diseases we have thus far considered have the same characters of general eruption, high fever, and high mortality, as well as infectiousness by ordinary intercourse, and by fomites, within the species to which each properly belongs, and may therefore be fairly considered as so many species of the genus variola, and be called variola humana, ovina, caprina, camelina, porcina, and canina. I waive the question of a common origin in the remote past, and am content to admit that, as I am inclined to believe has been the case with certain allied, but now distinct, specific diseases incident to mankind, they have become so differentiated as to be properly described as separate and independent diseases.

They are, however, all more or less easily communicated to other animals, man included, by direct inoculation, when they appear variously modified, more or less localised, and far less severe or fatal than in their original form. And the same holds good, though in a less degree, of the disease produced by inoculation of the virus into animals of the same species, that is, the inoculation of man and other animals with their own proper variolæ.

Cow-pox and horse-pox differ in several essential features from the true variolæ. They have, like them, a definite period of incubation, followed by some febrile disturbance and an eruption passing through the successive stages of papules, vesicle, perhaps pustule, and scab. But so far as we know, they are communicable by direct contact or inoculation only, and not by ordinary infection, any evidence to the contrary or of their supposed spontaneous origin, if indeed a variola of any kind can so arise, being wholly negative, or at best circumstantial. They are, too, unlike the true variolæ, unattended, at any rate in their normal course, and in the absence of erysipelatous or other septic complication, by any severe febrile disturbance or any danger to life, and they are confined to a limited part of the surface of the body. In short, they are non-infectious, not dangerous and strictly local affections, standing in the same relation to the others as vaccination does to small-pox in the human species. The horse-pox is distinguished by the large size of the vesicles, those of cow-pox bearing a closer resemblance to the vaccinal eruption in man.

Inoculable in any part of the body of animals of either

sex, and of every age, those cases which are not the result of intentional inoculation, the so-called spontaneous cases, are almost invariably confined to the heels and lower part of the leg in the horse, and to the udders of milch cows, and the lips of sucking calves. They are communicable by inoculation, intentional or accidental, to man and other animals, and when so acquired, confer for a considerable time immunity more or less complete against the effects of subsequent inoculations of the kind, and of those of exposure to an inoculation with the virus of human small-pox, though they do not seem to afford a like protection to sheep or other animals against attacks of their own respective variolæ.

These are the bare facts of the case, concerning which there is a general unanimity; but on these, two strongly opposed theories have been built. Before I proceed to enunciate these theories, I must state one more fact, viz., that inoculation of the bovine race with human variola is a matter of extreme difficulty, and success when achieved is only partial, the sole result being a hard papule, with or without the development of an insignificant vesicle, lasting perhaps but a few hours, quite different from the well-marked vesicle of ordinary so-called cow-pox.

Of the two theories as to the mutual relations of the several variolæ, or it would be more correct to say the relations of horse-pox and cow-pox to the others, especially to that of man, one I shall call for the sake of convenience the French theory, since though it has found a few adherents in other countries, as Professor Bollinger in Germany, and Mr. G. Fleming in England, it is the accepted doctrine in France, where MM. Chauveau and Bouley are among its most prominent advocates. According to this view, there are two orders of variolæ, one including all that I have called true variolæ, infectious, attended by great constitutional disturbances, general eruption, and serious danger to life; and another, comprising only the equine and bovine, requiring actual contact for communication, with little constitutional disturbance, localised or partial eruption, and no danger to life. In the one, to use Mr. Fleming's expression, the virus is "volatile", in the other it is fixed. But they ask us to believe what, if their theory be sound, is an indisputable fact, paradoxical as it appears, viz., that while there is no evidence whatever that inoculation of any one of the first order or true variolæ into the bodies of animals other than those whose own variola it is, affords any protection against infection with their own, the inoculation of either of those of the second order confers, in the case, at least, of man, as great

immunity against his variola as the inoculation of small-pox itself. Or, to put it in other words, small-pox and sheep-pox have every feature in common, while cow-pox is essentially a different disease. Inoculation of small-pox protects a man against small-pox infection, and inoculation of sheep-pox protects a sheep against sheep-pox infection. But inoculation of sheep-pox does not protect a man against small-pox, a very similar disease, though inoculation with cow-pox, a very unlike one, does, and it protects the cow equally against both its own and the human form of the disease.

The other theory, and that which I am convinced is the correct one, is that, while setting aside all questions of the evolution of diseases in times anterior to experience, the true variolæ are so many distinct and specific diseases peculiar to the respective animals, though capable of being communicated in a modified form by inoculation to other species; cow-pox and horse-pox are not independent and specific affections, but merely two particular instances of this modification by the cultivation of the virus of human small-pox in the organism of an animal to whom this form of variola is not natural. If we admit this view, the law of immunity becomes at once clear and consistent, and may be expressed by four theses:—

(1) One attack of variola of the kind proper to any animal protects the individual against subsequent infection by, or inoculation of, the same.

(2) Inoculation of any animal with the virus of its own variola produces a milder form of the same disease, but affords a protection similar to that conferred by an attack acquired by ordinary infection.

(3) Any variola inoculated in an animal other than that whose proper variola it is, gives rise to a peculiarly modified form of the disease, attended by little constitutional disturbance, merely local eruption, and no danger to life; such modified disease being no longer communicable to any other animal of the same or of different species, except by direct inoculation; and

(4) This modified disease affords a considerable degree of immunity against infection by any means whatever with the variola whence it was derived, either to the animal whose variola was the original source of it, or to others capable of being infected in any way thereby.

Jenner suggested the original identity of small-pox and the diseases incident to the horse and the cow, but did not attempt to prove it experimentally. He merely maintained;

from numerous observations given in detail in his classical work, that cow-pox was identical with, and derived from, what he called "grease" in horses; being communicated to the cows by the hands of men who milked them after having dressed the heels of diseased horses, supporting his view by positive evidence, as well as by the fact that in Ireland, where men were never employed in milking, cow-pox was almost, if not quite, unknown. Gassner and Sondermann, in the early part of the present century; Thiele and Ceeley between the years 1830 and 1840, and, more recently, Reiter, Badcock, Senft, and, last but not least, Voigt, to whose experiments I shall refer more particularly, all believed that they had succeeded in inoculating the cow with small-pox, and in producing by that means a cow-pox indistinguishable from the so-called spontaneous disease. Doubts have been cast on the correctness of the conclusions of some of these observers, but there is no denying the fact that Ceeley's lymph thus obtained was extensively employed by Schneemann, of Hanover, for the vaccination of many hundreds of children, and found by him to be identical in every respect with good humanised lymph.

In 1860, Dr. Martin, of Boston, in America, attempted to repeat Ceeley's experiments, but with the unfortunate result of setting up an epidemic of small-pox, and causing several deaths: a like disastrous experience befel an Indian surgeon; and for many years these examples deterred others from further experimentation in this direction.

The explanation put forward by the French school, and accepted by its adherents abroad, of these conflicting experiences of Ceeley and Martin is that small-pox inoculated into the cow, while producing an apparently trifling local effect, the papular, already described, undergoes no modification, or, as they would say, attenuation; that Ceeley's supposed vaccinations were really examples of mild and favourable inoculations, and Martin's of severe and fatal ones; the only difference being that Ceeley selected, as the source of his virus, favourable cases of small-pox, while Martin, as we know, took his from a virulent case, and actually after death. They maintain that cow-pox is a disease *sui generis*, and that though the local phenomena following successful inoculation of small-pox in the cow are so unlike those which follow the same operation in the human subject, the lymph yielded by the resultant vesicle has undergone no change or mitigation, and is still unmodified small-pox. But such assumption gives the lie direct to the sober statements of honest and cautious observers, and is totally irreconcilable with the successful

transmission of Ceeley's lymph through a long, and, perhaps, still unended, succession of Hanoverian infants. If Ceeley were mistaken in a few instances, Schneemann could not have been in hundreds. That Ceeley did what he believed he did, has been, as I shall soon show, conclusively demonstrated by Voigt, and the true explanation of Martin's misfortune is that he failed to do the same. He did not succeed in infecting his cow at all; he put in variolous pus, and after producing maybe some local irritation, he took it out again, and inoculated his patients with the worst type of small-pox, as directly as if his lancet had never touched the animal. The difficulty of inoculating the cow with small-pox is so great that Ceeley did not succeed until after numerous failures; and Reiter failed in fifty trials, extending, with characteristic German pertinacity, over ten years, when, in the fifty-first, he succeeded not only in inoculating the animal operated on, but also in accidentally communicating the disease to two others in the same stall, obtaining from these latter a lymph with which he successfully vaccinated a number of persons. We need not be surprised that Frenchmen, wanting in such perseverance, and either failing in the attempt or leaving the work unfinished, should, *more Gallico*, prefer to discredit or ignore the evidence of Englishmen and Germans rather than allow the honour to a foreigner; but that, on no better evidence than the conclusions of the said Frenchmen, Englishmen should do the same, is strange.

In the year 1881, Leonhard Voigt, Director of the Vaccine Institute at Hamburg, resolved to investigate the entire question afresh. Though not personally doubting the correctness of Thiele's facts, he felt that his observations were somewhat wanting in scientific accuracy and precaution; but he was unwilling to believe, with Chauveau and his admirers, that Ceeley and Badcock, Senft and Reiter, were deluded or dishonest, or were, as the Frenchmen would have it, both fools and knaves; and he has achieved triumphant success, vindicating the reputation of our immortal Jenner, and demonstrating beyond the possibility of dispute the conversion of typical variolous pus into a vaccine lymph of the utmost purity. Taking the virus from the pustules of a confluent small-pox in an unvaccinated girl, he inoculated with it four cows in succession. In the first three attempts he attained but partial success, the inoculations ending abortively—that is, producing papules, but yielding no lymph. The fourth was more fortunate, a small vesicle appearing for a few hours. This he secured, and chose as a *corpus vile* an ill-nourished child, under treatment in the hospital for

itch, but being unvaccinated, in imminent danger from the appearance of small-pox in the same ward. The result was what he had apprehended; intense febrile disturbance, axillary bubo on the side of the vaccinated arm, eczema, and some half dozen discrete nodules leading to fluctuating tubercles, though no truly variolous eruption. Happily for both parties, the child survived. Meanwhile, Dr. Voigt continued his inoculations of the calves with lymph taken from one to another through fifteen successive generations—in fact, carrying out Pasteur's idea of attenuation by successive cultivations, and with steadily increasing facility, the vesicles obtained rapidly assuming the appearance characteristic of so-called genuine cow-pox. The lymph of the second cultivation he did not venture to use. With that of the third he vaccinated four children, one twice without result, the other three successfully. The fever ran unpleasantly high, and the axillary glands were enlarged, but there was nothing abnormal in the vaccinations. It is true they suffered respectively from erysipelas, tonsillitis, and pneumonia—mere accidents, which he attributed to the unusual severity of the weather, and the insanitary conditions of their homes. He did not attempt further experiments until he had reached the eighth cultivation. This gave entirely satisfactory results, and an intercurrent eruption of measles subsided in two days. The lymph of the ninth and subsequent cultivations was employed without hesitation by the other surgeons of the Institute in their ordinary vaccinations, the appearances presented by the animals and by the children vaccinated from them being undistinguishable from those produced by the best Beaugency or other animal lymph from accredited sources.

Evidence more conclusive it is impossible to conceive or desire, and even if all former alleged successes be rejected as uncertain or unproven, Voigt's results must convince anyone not absolutely blinded by prejudice. According to Voigt, then, every case of alleged spontaneous cow-pox is either one of accidental variolation or retro-vaccination of the cow. In pre-vaccination times, when small-pox was everywhere present, the numerous opportunities for variolation made up for the difficulty of thus inoculating the cow, or we may suppose that the horse was more susceptible, and, as Jenner held, the cow was infected from the horse. Now-a-days, retro-vaccination, which is notoriously easy, is the rule, mothers proceeding to milk the cows after attending to their recently vaccinated infants. We do not believe that small-pox ever originates *de novo* in the human being, or otherwise than by infection or inoculation of some kind; though, amid

the ceaseless movements of a population and exchange of possible fomites, it is often difficult or impossible to trace the actual source of infection. If cow-pox arise spontaneously, as I admit it must do were we to reject Voigt's explanation, the fact would remove it still further from the variolæ; and if it be as remote from human as from ovine variola, why is it protective against the one and not against the other?

The direct inoculation of the cow with human variola is, as I have said, a matter of extreme difficulty, and the only result obtained in the event of success is a papule which more often than not fails to lead to a vesicle or to contain any fluid; but if it do, and the minute quantity of lymph be secured, and used again, each succeeding inoculation is easier than the preceding, and the resulting vesicles assume in the third or fourth term of the series the appearance of those of so-called spontaneous cow-pox, *i.e.*, of cases of unknown origin. Once more, I repeat that though the French may choose to set aside as "abortive" the blind papule, or at best, rudimentary and imperfectly developed vesicle I have described, it is the normal characteristic and constant result of successful variolation of the cow, and that it is idle to look in such cases for a well-marked vesicle such as we get in retro-vaccination.

Now the position assumed by M. Chauveau, and accepted by those who agree with him, is simply this. Because a few Frenchmen, in a few experiments undertaken with a view to confirm a pre-conceived opinion and foregone conclusion, have either failed in an attempt which is notoriously difficult of achievement, or, having succeeded, have obtained just the result that they were told beforehand they might, and not that which they had no right to expect, and being thus proved wrong by the evidence of their own experiments, have resolutely refused to proceed further, and to verify or refute the doctrine of their opponents, they flatly deny that others in England and Germany have done what they themselves have not even attempted to do. They ask us to believe that Ceely, Badcock, Senft, Thiele, and Reiter did not, as they believed they did, transmute variolous into vaccine lymph by passing it through the bovine organism; that these observers were so ignorant or so prejudiced as not to see that their vaccinations were really cases of inoculated small-pox; that not only were they deceived in a few instances, but that Schneemann and others were, in hundreds, practising inoculation of small-pox on infants for years without discovering it or its being discovered; or what if less charitable would be more reasonable, that Ceely, for example, palmed a different

lymph on Schneemann from what he stated. As to Voigt's brilliant performance, they, so far as I have read, ignore it, maintaining a discreet silence.

But from a pathological point of view their doctrine leads us into hopeless confusion, involving what Augustus de Morgan would have called a veritable "bundle of paradoxes". We are asked to believe that while the variolæ proper, a well-marked and closely allied group of diseases, are not mutually protective, two, which, as they admit, differ in every circumstance of origin, symptoms, course, and mode of communication from the true variolæ, are protective against not all, but one only of the other group, and that though they exactly resemble the local manifestation produced by the inoculation of true variolæ on other animals than those to which they properly belong, the resemblance is illusory, and they really have nothing in common; but we are told that though the "bouton abortif", the mostly dry papule which follows successful variolation, appears so unlike the small-pox pustule, the matter it contains, if it contains any at all, is unaltered, unmitigated small-pox virus which, contrary to all analogy, undergoes no attenuation by cultivation, even in the most diverse soil. But I forbear to pursue further the exposure of these fallacies. Voigt's facts are irrefragable. Either Chauveau and Co. are too prejudiced by national jealousy to be impartial, or Voigt is the last and most mendacious of a succession of impostors! *Credat Gallus non Ego!*

One word, in passing, on horse-pox. I have said that it is equally protective with cow-pox against small-pox, being, like it, merely a modification of that disease obtained by transmission through the organism of another animal; but both in the horse, and when communicated to man, the local symptoms are more severe, and the vesicles so very much larger than those of cow-pox, that it cannot be recommended for the purpose.

But the matter is one of the highest importance in its bearings on the present and future practice of vaccination. Two questions are frequently presented to us, one of which again involves two others. The first is, have we any reason to fear that humanised lymph has undergone any enfeeblement in its passage through many thousands of infants, and, if so, can we revivify it by passing it once more through the calf, or shall we from time to time seek a fresh and virgin supply in what certain persons allege to be spontaneous cases of cow-pox? The second question is, whether in view of the possible communication of syphilis by the use of lymph from the human subject we may not avert the danger, or

satisfy the scruples of those who object to vaccination on this ground, by passing it through the body of an animal insusceptible of syphilisation? To this last question, apart from all consideration of the relative activity of the vaccine lymph as such, I answer unhesitatingly, "Yes".

The first question is a more complex one. I believe that there is no trustworthy evidence that, so long as humanised lymph is taken from selected and well-marked typical cases, with every precaution known to vaccinators for ensuring its freedom from syphilitic or septic or erysipelatous contamination, or from deterioration in storage, its efficacy undergoes the least diminution by cultivation in the human organism.

On the other hand, the experiments of Voigt show that for a certain number of generations it does tend to attenuation in the foreign soil of the bovine organism, at least when developed immediately from variola humana; but whether, as Voigt thinks, this attenuation is progressive, is a question still *sub judice*. Is it revived by a single re-transmission through the calf, as the Frenchmen assert? I trow not. Indeed, holding the views of its origin that I do, I can see no conceivable reason for supposing that it should be. The instructions issued with the calf-lymph supplied by the Local Government Board, state that it does not take so readily as human lymph, though I myself have never failed in a single insertion, in my limited experience of it. Some persons, on the other hand, maintain that the use of what they call genuine cow-pox, that is, cases of unknown origin, is attended by constitutional and local disturbance far greater than that which follows vaccination either with humanised lymph, or with the product of retro-vaccination of the calf, or vaccination of the calf from an infant. Such experiences admit of two explanations; it is possible that, as Voigt suggests, some cases of spontaneous cow-pox, so-called, may be really variolation, and others retro-vaccination, either infection being effected unawares. The former, as he found in the case of the unfortunate child with the itch, are fraught with the greatest danger, several cultivations being necessary to render such lymph mild enough to be used with safety; but it is also highly probable that the development of the vesicles in the calf being less regular than in the infant, the surroundings of the stall less cleanly than those of the cradle, and for other obvious reasons, the risk of erysipelatous inflammation may be greater. Retro-vaccination, therefore, of the calf, or the use of lymph taken from accidental retro-vaccination, or so-called spontaneous cow-pox, may be of use in the elimination of syphilis, but does not add to, and may detract from,

the efficacy of the lymph, which is not to be measured by the intensity of the local and general constitutional disturbance, since these may be but evidence of the presence of bacteria other than those of the vaccine proper. If, however, we are really desirous of obtaining a stock of virgin vaccine, we have but to repeat the process of transmutation of variolous into vaccinal lymph, following in the steps of our respected countryman, Ceely, with the care shown by Leonhard Voigt, and the precautions he has indicated for the performance of the operation. Three years have elapsed since his experiments were performed, and the lymph of that stock still shows some superiority over that of remoter origin, though not so marked as it did at first. It would, however, be advisable, as he himself suggests, to select the original variolous lymph from a case which, though typical, should not be malignant, and the subject of which should be otherwise healthy.

A few words in conclusion as to the time at which the lymph should be taken from the arms of children in the routine practice of vaccination. The conventional eighth day presents several advantages of a practical kind. The vesicle is then at its height, the lymph is most abundant, and the custom is convenient, as it does not require more than one weekly sitting. But we all know that in a certain proportion of cases leucocytes have made their appearance by that time, and as the recent investigations of Dr. Joseph Acker have shown, microscopical examination reveals the presence of a multiplicity of other bacilli; whereas the lymph of the seventh, sixth, and even the fifth day, while containing abundance of vaccinal micrococci, is quite free from extraneous microzoids, and gives the very best results, as I can vouch for by personal experience. Nay more, experimenters with less conscientious scruples than we in this country entertain, have found that while lymph from syphilitic infants taken on the eighth day has proved infective, that taken from the same subjects on the earlier days has been used without any unpleasant consequences. I would not justify the repetition of such experiments, but knowing that one does occasionally meet with degrees of erysipelas, interfering with the subsequent process of scabbing, and in no way enhancing the value of the operation, I would suggest that in private practice we should select the sixth or seventh day in preference to the eighth, leaving the public vaccinators, with their wider choice of subjects, to follow the established custom.