Graduation Thesis
on the
Theory of Vaccination
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Sustained
On the Theory of Vaccination.

Man & most of the domestic animals are liable to a disease of which a certain form of pox is the leading characteristic.

Small-pox, the name given to the disease as it appears in man, displays itself in a general eruption over the body. Cow-pox, the corresponding disease in the cow, affects locally the teats & udder. In the horse the heels are the seat of the affection, which is known as "grease." The disease as it appears in the sheep, bear, perhaps the closest resemblance of any, to the small-pox, may be said to be characterized by a general eruption. The camel also is said to suffer from a disease of the hoof from which the ancient believed small-pox to be derived. (Popular Summary of Vaccination by S. Marshall M.D., 1830).

Small-pox, owing to the great mortality attending it, and also to the incredible disfiguring scars which it leaves on recovery, forced itself upon a people's notice. Its prevalence during the last century, together with
with the introduction of inoculation by Lady Mary Montague in 1717, especially attracted the attention of the medical profession of that time. Thus, probably due to the somewhat traditional beliefs among the farming population, that those dairy men who happened to be inoculated with cow-pox matter were absolutely protected from small-pox, began to be noticed, investigated, and finally verified.

1st. Laccord states that a small work published by Sigel in 1713, entitled "De Infection Laparum," and another by Sitton Foster in 1765, both recognized the protective quality of Cow-pox. ("Pathologie Inférieure," 2d Ed., p. 736.) L'Heritier de Saint-Hubert seems to have written on the subject about 1781, but neglected to publish the results of his enquiries.

19. Adams in his work "On Inverred Poisons" wrote thus in 1795: "The Cow-pox is a disease well known to the dairy farmers in Gloucestershire. What is extraordinary as far as facts have hitherto been ascertained, is that a person who has been infected is rendered insensible.
incredible to the various powers. Again
Dr. Beddoes in 1798, "On Inquiries concerning
" inoculation," wrote, - I have learned from
"my own observation & the testimony of some
"old practitioners, that insusceptibility to the
"smallpox is destroyed by the Compox, a
"disease from cord, which is a malady not
"unpleasant than dangerous." (A State-
"ment of the Principal Historical facts of
"Vaccinia" by S. Pearson. 1802, p. 136.)

Author many minds seem to have been
directed to this subject, still as S. Pearson
writes (op. cit. p. 20) "S. Jenner's publication
was the sole primary occasion of all the
"experiments hitherto instituted."

In 1798 S. Jenner published his "In-
"quiry into the Cause & Effects of Variola
"Vaccinae" (Copy used 2nd Edit. 1800). This
"was the result of fully thirty years laborious
"observation & experiments. Anyone who has
"carefully studied this small work of his
must admire his truly scientific spirit & pre-
cision, as a sincere searcher after truth. He
"carefully observed, accurately recorded,
"clearly reasoned upon, and with something
atant to intuition, rightly interpreted the phenomena he saw. Remarkable too is the fact, that after nearly a hundred years' experience, we have practically learned little of the art of Vaccination which he did not teach. By closely observing his directions & cautions, Vaccinators would avoid many of the errors which they now make. His descriptions & drawings of a vaccine vesicle still form our standard of comparison and the nearer we approach them the better satisfied are we with our results.

Although the human subject had probably been intentionally inoculated with Copra matter before Dr. Jenner's experiments began, still he certainly was the first to take the far greater step of vaccinating from one human subject to another. This operation he found to be as he anticipated, easy & certain of performance, free from all injurious effects, and perfectly protective from Small-pox. About this time he tacitly writes "that it (vaccination) may be continued ad infinitum (as I imagine)
from one person to another (if care be observed in taking the matter at a proper period) without any necessity of recurring to the original matter of the cow. From this small beginning we have gradually attained, thro' much misrepresentation & obloquy, to the great national & compulsory system of vaccination which we now possess.

The object then of vaccination is to protect man from his own fatal & infectious pox by giving him the benign & non-poxential pox of the cow. As R. Bouguet says, "When we look at their effects, it cannot be said that vaccine curset smallpox; nor strictly speaking can it be said that it prevents it; there is a substitution and nothing more" ("A Prize Essay on Vaccination" by Dr. Ballard, 1867, p. 114).

Vaccine lymph, when taken about the eighth day, appears to the naked eye, to be a clear, transparent & somewhat viscid liquid. When taken earlier, it seems thinner & more watery, and when taken later, looks hazier & thickly.
by S. Beale (in the Microscopical Journal for April 1864) who examined it especially during the Cattle Plague, which was at first supposed to be an epidemic of Small-pox (Murchison), vaccinia lymph consists of three structure, (a) a clear hyaline fluid, (b) a few bodies, like few corpses, and (c) small transparent particles massed together. These last he called 'germinal matter,' considered that it contained the contagious principle.

This description has been verified by all subsequent observers. Dr. Klein ("On the Contagium of Variola Orinai," Government Medical Report, New Series No. 77, 1874) has figured no less than eight different forms or structures (p. 5i). But what in Fig. I. + 1, he calls "Transparent masses of various sizes, containing granules, some of which are small, while indefinite others large & shining," he finds to make so remarkable changes when kept for some hours at incubation temperature, Fig. II. + III. "These larger masses are seen to break up into smaller ones," while the
granules become like the micrococci. Spheroids of fresh lymph. Thus probably, many of these different forms are simply the terminal matter of Beale (called zoo-locally, Cohn) in various stages of development.

Prof. Cohn's description of fresh lymph and the preliminary changes is very similar (in the Pathology of the Infective Processes by Dr. Sanderson, in Med. Corp. Report, New Series, No. 77, 1844. P. 30+31).

He found no distinguishable difference between the virus of Variola Vaccinia. The spheroidal corpuscles, he estimated at about 5-000 of an inch in diameter. He also observed larger refractive bodies, but whether they were fat globules or the result of development from the spheroids, he could not say. Probably they were cells. In perfectly fresh lymph the corpuscles were found to be simple, or joined in pairs, like the figure 8. On keeping these bodies, increased into chains of four, slightly rounded together, which again formed necklaces. These
From the broken up, formed into groups, which keep increasing in size for several days. Even in a sealed glass tube this multiplication of colonies, or groups, goes on for a long time and as they ultimately get bound together by an interstitial mucilaginous-like substance, they become converted into 'Zoogloa'.

The physical properties of these particles deserve notice. Though they have the same specific gravity as the liquid, there being little or no settling on standing, and though they neither affect its refraction of light, nor its transparency, yet they remain insoluble in their own medium, or other watery fluid. They must at the same time be absolutely distributed throughout the entire fluid. In proof of their particulate or insoluble character, it has been found that they can be separated by filtration, or better still by the principle of diffusion, adopted by M. Chauveau and Dr. Sauvageau (B. Reports Op. Cit. Page 233). What may be called the common sense argument of solution.
Seems very conclusive on this point (cf. p. 240).

If vaccine virus be diluted (say) a thousand fold with water, it will be found ineffective in a certain proportion of cases when used for vaccination, but these cases which are successful will take as perfectly as if pure undiluted lymph had been used. The failures therefore are probably owing to the latest having happened to miss the particles, mechanically moving in the currents of the dilution. Had these particles been soluble, we should have expected uniform, if inferior, results; but being particulate, the results were the perfect or null. Hence M. Chauveau's dictum that "all contagia are particulate." Next comes the question, Do these constant effects of the lymph as seen in vaccination, depend upon these particles? This must be answered in the affirmative. The experiments of M. Chauveau and Woodruff already mentioned prove at once their insolubility and their irritancy, for it was only when they were present in the lymph that any results could be obtained.
obtained. Their numerous experiments had conviced chiefly in vaccinating children or cattle, with the particles, had been separated by filtration or diffusion, almost proved the point at issue (vide 12th Report, supra). On the familiar, but less subtle particles of Sepulchre fever, the virulence undoubtedly depends, and we may safely conclude that they are also the contagia of vaccine lymph. And if so, what are they? Are they complex albuminoid compounds which produce these results by a kind of chemical action somewhat after the manner of Aspergillus or are they living organisms—living in the sense of being part of a living body as B. Keal maintained, (so also B. Ross in his "Craft Theory of Disease") or living as independent animal or vegetable ferments, which produce their effects by the necessaries of their nutrient growth or by the refuse products of their vital action? B. Sanderson thinks that their power of resisting destructive agencies of continue
-ring active so long under adverse circumstances, is unknown in any chemical combination. The fact that they can be cultivated apart from the body altogether, seems inconsistent with the Graft Theory. In favour of their animal origin, Dr. Sanderson (13th Report 1870, p. 40) mentions their movements, their chemical reaction to the air—being more like the respiration of animals—and their avidity for nitrogenous substances. Hallier & Cohn, looking at the Botanists, at their mode of reproduction, development, claim them for the vegetable kingdom. Their action in many respects resembles that of a parasite. We may certainly conclude with Dr. Simon (British Medical Journal, Dec. 20, 1979) that the increase of each contagium as it acts is the characteristic self-multiplication of a living thing.

Having referred thus generally to these organisms (as we may now call them) in order to get clearer ideas of what they really are, we may study them so seen in spleenic fever, which is a disease in
In many septic's intestinal to vaccinia.

Hemorrhage and being found frequently in the lower quadrants of the symptoms, as when we have to deal with human beings. "Proper to the fluid infective disease in the blood," a series (Sanderson's, P. 53)

Still, the blood arose. Whether this always present, they were the sole ones. Always, simply in some way. However, it is connected with the fluid in which it is. Exceptional, it has always been impossible to separate, the elixir, filled by United.
satisfy all practical demands. When the leading scientific men on the Continent and such examples as Sanderson Greenfield in this country devote themselves to the study of micro-organisms in disease, and especially to proving the connection between the bacillus Anthrax and Splenic Fever, we may feel sure that after their mutual criticisms, their admitted conclusions are thoroughly trustworthy.

In proof then that the bacillus Anthrax found in the blood of animals which have died of Splenic fever is the active agent or cause of all the phenomena presented in that disease, we find the following acknowledged facts:—

If a healthy animal be inoculated with a small quantity of blood from another animal which has just died of Splenic fever, death results with all the symptoms of that disease, and bacilli are found in the blood. If a suitable fluid outside the body be inoculated with this infected blood, this organism alone develops. If the fluid be cultivated
tivated thru several generations, till all the original blood-constituents disappear, still, when inoculated, its virulence is proved by again producing Spleenic Fever with specific microorganisms. If the blood be filtered, the fluid is innocuous, and if it be boiled so as to destroy life, again it is harmless.

Again, and this is more closely allied to our subject of Vaccination, if the virus be passed through the guinea-fiy, its character is so modified, that it may safely be innoculated into a cow. And further, if this virus be cultivated outside the body in suitable media, and with certain restricted conditions of growth, it becomes what Pasteur calls "attenuated" or less virulent, and may be fearlessly used for inoculation; the animal recovering from the mild form of the disease produced; and being meanwhile rendered insusceptible of a second inoculation, or of taking the disease by the ordinary methods of infection. Behnke has found that this cultivated and
and "attenuated" virus may again recover its activity under favourable conditions and on suitable soil. ("Abstract of lecture on further investigations on Autotrace" by W. Greenfield. British med. Journ. Dec 1880 + Jan 1881.) These facts are so similar to what we see in the relationship between Small-pox & Vaccination, that we may fairly conclude that the active agent in its mode of working are of the same kind in both cases.

Since then these microzymes (the term for them adopted by Sanderson from Béchamp) are the contagia of Vaccinia, and are living organisms, have they a specific power of producing a specific disease? When we vacinate a child we can predict almost absolutely certain unvarying local + constitutional effects. So in other diseases which depend on similar organisms, we find, that from the clinical history of one, we can fairly foretell the symptoms, course, duration of another of the same kind, so distinct & constant are the effects in each. From
This we can scarcely avoid the conclusion that within certain limits each specific disease has its own specific organism.

In favour of this statement we would quote from Simon's "Medical Report to Government" for 1869 (p. 60), where he writes: "Knowing that all contagia (as such) are distinct one from the other, and believing that each of them has its essence in the so-called microorganisms which it contains, we by implication impute to the microorganisms that in different diseases they are not identical; and as we affirm them to be dynamically different, so also we assume that under well-advised differential experiments other signs of their specificity may be brought to light; and for each sort of them a definite genealogy be written."

The same authority further writes ("An Essay on Contagion," British Med. Journal, Dec. 20, 1779), "that the true unit of each metabolic contagium must either be, or must essentially include, a specific living organism, able to multiply its kind" and that "low self-multiplying forms, specific in
in each case for the particular disease which
is in question, are essential to each mode of
poison". The multiplication of terms alone,
owing to the greater differentiation of these
organisms, as illustrated by the Paper
read by Prof. Klebs before the International
Congress (British Med. Journal for 81. P. 280)
verifies part of the quotation from Mr.
Simon's Report... It also shows the great
advances already made in the study
of their forms, functions, and morphology.
Prof. Klebs believes however, as the result
of his observations "that difference of form
Corresponds as a general rule to difference
of function, and only different degrees
of functional activity occur within
the same series of forms," and that
there is "so complete an identity of form
in the parasitic organisms occurring in
the diseased part in like pathological
processes that the causal interdependence
of the two seems to be thus made certain."
This is what Sanderson & Kleii have
endeavoured to prove in their inquiries
regarding Small-pox & Sheep-pox, and
the
the results of their investigations bear out Koch's assertion that "specific communicable diseases are produced by specific organisms" (Ann. J. O.H. cit.).

Dr. Sanderson (op. cit. p. 30) thinks that the faculty which various contagia possess of maintaining their activity outside the body, is more easily explained as a function of life and organization resident in the contagium itself than in any other way. We have a strong proof of how little is absolutely known regarding this question in the great divergence of opinion amongst competent investigators. Thus, as reported in the British Medical Journal, p. 547, Prof. Folk holds that all the "viruses of contagious diseases were reproduced by organisms it was very unlikely that the organisms were specific" for the same organisms assumed different forms according to the circumstances under which they were developed". Whilst M. Pasteur (op. cit. 547) asserted that "everybody was wrong who did not believe in the specific nature"
"nature of germ"—Prof. Hallie Hohn, who have devoted much time and talent to the subject, think they have discovered in plants or their parasites, the original forms of most of the bacteria seen in infective animal liquids (12th Report of cit. p. 243 (256)).—Prof. Hochmuth has succeeded in cultivating the bacillus into a bacillus Anthracis, vice versa. These wonderful results with their equally wonderful processes are narrated by Prof. Lister in the British Medical Journal for Sept. 4, 80. He sees no reason to doubt the methods or the results of these experiments. Prof. Greenfield, who has also tried this cultivation, has hitherto not quite successful, is still hopeful of success. This would almost amount to a demonstration of the truth of Specificity. Certainly this much has been proved that bacteria in the course of many generations, and varying nutrient conditions of growth, may be so altered in character by training, that they may
finally be able to thrive in a medium in which at first they readily perished. The question as to how these organisms do affect the system is still open. Even afterwards we can only answer partly.

It has long been known that certain diseases, as a rule, attack a person only once in a lifetime, so that these are strongly contagious. We know, however, that microorganisms are invariably associated with such affections, and we can hardly resist the inference, that their presence has something to do with the protection afterwards attained. We think future research may find the solution of the problem on the lines of D. Sanderson's suggestion regarding pesteriaemia, "that all the bacteria are not the agents in septic infection, they are, nevertheless, the products of the septic poison." (B. M. Jones, Jnl. 1918.) Perhaps then it is some product of their vital action which so affects the system as to render it poisonous to themselves.

Rearing on this point and exceeding of
of the cultivation of the bacteria of cholera. Prof. Lister says (P. Med. Soc. Sept. 7, 1880)
"After the bacterium has grown for a certain time in a given portion of chicken broth, it ceases to develop further, and when this is the case, although the broth has lost only a very small proportion of its substance by weight, and although as at first said, it has not undergone denaturation and still constitutes an excellent culture medium for ordinary forms of bacteria, the bacterium of cholera, thus introduced from some new source, is incapable of growing in it. The fact seems highly suggestive of an analogy with the effect of vaccination, or of those of an attack of measles or scarlet fever in securing immunity from the disease for the future. Following up the analogy, he finds that by cultivating this bacterium in a particular manner its virulence is so reduced in energy, that it may be inoculated into a healthy fowl without serious result, and at the same time renders the fowl secure against taking the ordinary form of cholera."

[Signature]
form of the disease. Altho' here we have a process akin to vaccination, going on before our eyes & outside the human body, & altho' we can fully appreciate the results, we are yet unable to say exactly how it is done. It is interesting to record the theories on this subject, which have been held by un doubted authorities. Dr. Jenner, as we think, very sagaciously wrote (Inquiry Part. i) it is not the identical matter inserted, which is absorbed into the constitution, but that which is by some peculiar process in the animal economy generated by it, is it not probable that different parts of the human body may prepare or modify the virus differently? All this the skin, e.g. adipose membrane or mucous membrane are all capable of producing the various virus by the stimuli given by the particles originally deposited upon them, yet I am induced to conceive that each of these parts is capable of producing some variation in the quality of the matter previous to its appearance in the Circulation.
Mr. Mason (Smallpece, Reynolds's System of Medicine, 2nd Ed., Vol. 1.) writes: "There is in the organism, most likely, in the blood, some vitally principle or ingredient, clearly not essential to life & well-being, by which we are rendered liable to undergo these attacks... and it is this principle or ingredient which is gist-rid of during the attack.

D. Ballard (Prize Essay on Vaccination) writes: "At the spot where the virus becomes arrested, it attains its complete development, and there it generates until all the transformed material of the blood has been removed, or exhausted, eliminated as we commonly say, and thus the nervous phenomena which its presence in the blood occasioned, ceases & the fever subsides."

Dr. Simon (Writing on Contagion) (British Med. Journ., Dec. 13, 1779) says. "Each contagion operates with a chemical distinctiveness of electric affinity or some special ingredient or ingredients of the body, and (that) de-containing this particular material in febrile process, which necessarily ends where the alteration is complete, is the bodily change which the}
"the contagium specifically performs".

Dr. Ross ("A Treatise on Disease," 1872) thinks that the organisms have an affinity for a certain tract of tissue, when that tract of tissue has once undergone motion, which constitutes the disease, it is no longer capable.

M. Pasteur's theory is that these organisms simply live, grow, multiply in the body, and only perish finally when they have exhausted their sustenance, i.e., as he believes, their supply of oxygen. As in the yeast plant, the fermentation is the result of its search for sustenance. So with these organisms the changes produced by them in the animal body are simply the results of the necessity of their existence.

Prof. Greenfield, speaking of anthrax ("Abstract of lectures," Dec. 25, 1880) thinks "there must be something in the blood, which has the power of resisting the action of the bacillus," which is practically saying, that once generation of bacteria renders their favourite soil unfit for the life and maintenance of another. He also
found that quantity of virus was an important factor in overcoming this state of resistance i.e. the protection acquired by a first inoculation. The same principle holds in vaccination. For another wrote (Inquiry 6.110) that "a single cow-pox purule is all that is necessary to render the various virus efferent," still we think with Dr. Ballard (Op. cit. 1823) that "there are circumstances in which quantity of virus is a matter of importance, and it would appear that this is the case in the instance of vaccine." Mr. Marsan's statistics prove most authoritatively that size of excorix is a most powerful element in protection; still it is just possible that it is more the duration of the protection which is thus affected, than the completeness of the immediate effect. Had Mr. Marsan classified his cases, not only by the number of the scars, but also according to the lapse of time since they were produced, his statistics would have been still more instructive, especially as regards revaccination.
However, wherever those organisms act, they must act in the same manner on the same tissues in vaccination as in small-pox. We might infer this from the fact that the local effects and pathological changes are identical in both. It is only a difference of degree. We further know of no case where an attack of one disease gives immunity to the body from an attack of another & different disease.

We can imagine micro-organisms that are very similar, or which have attained a similarity by cultivation on a specific soil, giving a partial or feeble protection for a time, but in variola & vaccinia we have a constant degree of protection, limited only by adventitious circumstances of soil & surrounding. We can decide this matter however, by a crucial experiment, for if small-pox can be inoculated into the cow, and a true cow-pox vesicle be the result, and if by taking matter from this vesicle, the human subject can again be vaccinated, a true vaccine stock being produced.
nothing else, then the Diseases must be identical. This has undoubtedly been done at least by Dr. Ceely of Allebury. ("Observations on the Variola Vaccinae" published in the Transactions of the Prov. Med. & Surg. Association Vol. VIII. Art. IV.)

His knowledge and experience of Cowpox were great and varied; his carefulness and precision entering, and his truthfulness of Description and Drawings above suspicion. Dr. Ceely here records how twice we succeeded in producing on the cow pock, indistinguishable by using variants from those of true Cowpox. (See Plate.) matter, with views obtained from it by excised he Vaccinated first, accidentally. Mr. Taylor, his Assistant, afterwards many Children, ultimately using the matter entirely in his own vaccination, distributing it amongst his professional friends, for the renewal of their Stocks of Lymph. The only Difference in Effect, which he observed by using this Vaccine, was a stronger tendency to Supplementary Fads, such as Rose, Lichen &c., and in one case, True Vari-cellae.
-cella broke out. Conspicuously amongst many others who succeeded with various inoculation of cons, stood Thiele of Kasan in South Russia; & Badcock of Brighton in this country. M. Chauveau most correctly only succeeded in producing small papules, such as Mr. Celly has figured as failures. M. Chauveau found that by using the matter from these papules he invariably produced true, tho' in most cases, modified Smallpox.

It seems probable, that, if he had humourised the lymph thus originally obtained through several generations, he might ultimately have produced a true vaccine by this cultivation; for the further removed he got from the source, the milder, more vaccinial became his inoculations. These failures of M. Chauveau must in some degree have affected the cons, for he found it impossible either to variolate or vaccinate them afterwards. We have found however that the spurious & unprotective vaccination of a child may render it
in susceptible of a second vaccination for some time. Probably small-pox may be conveyed to cattle by infection also. Dr. Sunderland of Parmen maintains that he succeeded by (in a measure) compelling cows to inhale small-pox matter from infected blankets. Dr. Celly repeated these experiments without result, but he seems to have succeeded in another way. As related by Prof. O'Sullivan in his "Practice of Medicine" 6th Ed. 1872, p. 423) of eight cows put to graze in a field where infected flocks were exposed, five had cow-pox within three days. There was no other way of accounting for it than by infection which was rendered more probable from the fact that a koifier struck affected. The Eulilleae amongst cattle in India mentioned by B. Cury (Theosophist Thomas Hospital Reports Vol. IX. 1878) seems to have been true eruptive small-pox, for from the scabs on their back, children were inoculated with true small-pox. Possibly some climatic or other
other influence rendered the person sufficiently virulent to overcome the usual modifying powers of the cold, and the natural resistance of their skin and subjacent tissues to break and in eruptions. We may here express our agreement with B. Cory's Thesis, that smallpox was the primary disease, for we have seen that it can certainly be conveyed to the cow by inoculation, and possibly also by infection. We also know that smallpox germs are capable of existing apart from the human body for an indefinite period, and that the condition of the disease as it appears in the cow, so just where we should expect to find it on this theory of origin. M. Lacord (cf. cit. 735) whilst admitting the identity of the two diseases, claims for cowpox an independent origin.

B. Seaton (Reynolds, cf. cit. 9204) notes the prevalence of "grease", cowpox, and smallpox at the same time, and M. McClellan fancied he observed some connection amongst these diseases, but not enough to establish their identity. We think
think however that we encounter fewest difficulties by regarding Small-pox as the source from which the others have sprung; and that the rarity of Cow-pox is owing to our comparative freedom from Small-pox since the introduction of Vaccination.

Believing that Variola & Vaccinia are identical, we must now endeavour to account for their differences. These are chiefly, that whilst the former expresses itself by a general eruption, and is infectious, the latter is limited to a local pustule at the point of insertion, and can only be transmitted by inoculation.

These two distinctions are so closely associated that to explain them they must be considered together, we find in the first place that all diseases are milder when produced by artificial inoculation. This principle caused inoculation for Small-pox to be introduced & adopted.

Dr. Klein found that when he inoculated a healthy sheep with sheep-pox virus, he only got a single pustule as in Vaccination, unless he inserted the matter directly.
Diseases produced by inoculation also from a much shorter course. S. Ross (op. cit.) has elaborately endeavoured to account for this difference in time as regards small-pox. It is probably owing to the micro-organisms taking longer to reach their favourite tissue. In variola vaccinia and in several other diseases in which micro-organisms play an active part, the lymphatic system seems necessary for them to produce their full effects. This may account partly for the secondary fever in small-pox. It is doubtful whether the lesions found in internal organs in small-pox are simply caused by a mechanical blocking up of the capillaries or whether they are partly mechanical, partly specific. The order in which these organs are affected would seem to point to a process of secondary infection by the blood-current.

In order to understand the eruptive process we must follow the course of an ordinary vaccination or variolation.
On the 2nd or 3rd Day after the insertion of the virus, we have a papule. By the 3rd or 4th Day this has become a vesicle, of a bluish white colour, with a raised edge, a central depression. On the 8th Day these characteristics are more marked, & the pock is ripe for taking lymph. Now also an inflammatory areola begins to form & this continues to spread for two or three days. About this time there is some glandular swelling, and a rise in temperature. By the 10th Day the disease has reached its height. The areola which must always be present in successful vaccination does appear. The vesicle dries up & forms scabs which fall off about three weeks after the operation. These leave an indelible cicatrix, which ought to be circular, depressed, & foetid.

Prof. Huxley (in his Address as reported by Dr. Ogbell in his "Report on the Progress of Medicine" for 1870-300) gives a graphic description of the more minute changes which take place after Vaccination.

Dr. Allan (Medical Report No. III. 1874. P. 3366)
and Dr. Braidwood Wacker ("Contagium Vivum" British med. Journal 1879) have microscopically examined, & fully described the anatomical & pathological changes which occur in the production & maturation of the pock. They find first local effects, especially in therete Malpighii, which become divided (by what in a further stage Dr. Klein calls the "horny layer", which he considers the cause of the mobilization of the vesicle). Next the pustule same in the excitement & becomes altered, chiefly in its papilla. Then the lymphatic canalici & hence the lymphatic vessels become distended, with "what resembles coagulated plasma, but which ultimately becomes organized teeming, like micrococci. (Klein) whose further interpretations are not trustworthy"). Vacuolated vesicles begin to form with a consequent corpuscular infiltration. The adjacent structures become devitalized ("a sort of necrosis, without inflammation" Santorso) and destroyed. Finally enclosed by this altered tissue, we have the abscess or pus.
title of Small-fox or Vaccination.

Dr. Weigert (as quoted by Sanderson in his "Lectures on Inflammation". B.M. 1. April 1834) has observed similar phenomena in such internal organs as the liver and spleen in cases of Small-fox, just before or during the secondary eruption.

We know that in different diseases microzymes affect different parts of the body. They are chiefly found in the stool in intestinal complaints, in the blood in recurrent and scarlet fever, and also in syphilis, in the pustula in measles and in around the pustule in variola vaccinia.(1st Report Sanderson. Foot note)

This close constant connection between the microzymes and the pustules suggest the relationship of cause & effect. Whilst the bacillus of spleenic fever affects the blood current, the microzyme of Small-fox has nothing for a more restful life, chooses probably the "Astroid" tissue of his. Sanderson. This tissue is distributed in patches throughout the whole body, & possibly forms a suitable habitat for the aggregation of multiplication.
multiplication and consequent destruction of its structure which bring about the general eruption of small-pox. In vaccinia they are probably carried freely through the system and have less virulent irritative properties than their destructive tendencies at the point of introduction. Calf lymph, according to Ward, most, shows a greater indication of spicing than humanized lymph, and may thus account for the frequency with which subsidiary rashes follow its use. We conclude therefore that the eruption in small-pox depends on the number, aggregative tendencies, and poisonous or irritative properties of the microzymes, and that the seat of a fistula within the limits of the cellular tissue, is more a matter of accident than pleuritic arrangement.

As regards the infective quality of small-pox, we shall find that it probably depends on the morphological differences of the microzymes—T. Sanderson write (op. cit. p. 3758) "there are facts relating to spleen fever, which show on the one hand, that the contagious property as
"it exists in the circulatory fluid, is very transient, and on the other, that there must be a form or state of the contagium, in which it is remarkably persistent". For the blood loses its infectivity the moment decomposition sets in. Prof. Greenfield discovered that many of his experiments gave negative results unless performed immediately after the death of the animal affected.

Yet from the distribution of the disease amongst cattle, the contagium must be able to exist for years. At page 39 (of cited) Dr. Sanderson further says "Bacteria have two modes of existence, the one characterized by permanence and resistance, the other by rapid development and short duration. So in regard to smallpox and Vaccination we may have in the former, an organism permanent and resisting, and in the latter an organism whose life is short, active and fleeting, whose lethal properties are weak, and whose attack the human system can throw off with impunity."

M. Pasteur (Brit. Med. Journ. 1881. B. 284) found that he had more difficulty in pe-
During the virulence of his anthraxoid cultivation than in that of four cholera. On closer observation he saw two modes of generation in his culture of the bacillus, only fission, the other by budding. By the latter mode after the culture fluid had been freely exposed to the air for about forty-eight hours, the translucent filaments of the bacillus had corpuscles germs distributed in series more or less regular along them. "All around these corpuscles, matter is absorbed little by little all connection between them disappear, presently they are reduced to nothing more than germ dust. If you make these corpuscles germinate, the new culture reproduces the virulence peculiar to the thready form; which has produced these corpuscles, and this result is seen even after a long exposure of these germs to contact with the air. Recently we discovered them in pits in which animals dead of spleenic fever had been buried for twelve years, and their culture was as virulent as that from the blood of an animal recently dead." Worms he found.
found b. play a prominent part in the resurrection of germs.

M. Pasteur discovered that this budding process could be stopped by maintaining the culture in contact with the fumes at 40° or 43°, and he thereby produced a "mycelial culture of bacteria entirely free of germs." This virus gradually lost its infectiveness until about six weeks afterwards, it became completely sterile. In this we observe that microzymes are highly sensitive. Two degrees of temperature make a less. A free exposure to oxygen is otherwise wise, or an inorganic medium may be a matter of life or death to them.

Sanderson thinks they may even acquire specificity from the soil in which they grow. Koch found the difference between a horse, mouse, and a field mouse enough to destroy the bacillus of malignant (J. Med. Ost. 3063)

M. Chaumeau observed that the Algerian breed of sheep could resist a very large quantity of anthracoid poison. Curiously too is his observation that when he inoculated a ewe in the last months of pregnancy, the fetus
Sears was insusceptible of the anthrax
poison. Greenwood & others have found the
blood of the fetus free from bacilli when
the mother suffered or died—a fact used
by Sanders as a proof of the particu-
lar character of contagion—the bacilli
being prevented from passing by the
fetale placental membrane. But in
M. Cieau's case we have protection
without the presence of the bacilli. This
seems to prove what we have already
stated that micro-organisms protect
by means of their products—also the
fatal mode of life may not be able to
duly supply their necessities. The transmision
of smallpox, even of the effects of vac-
cination from mother to fetus has been noted,
the subsequent vaccination of the child
being used as a test. And this is not probable,
for Lennec stated that "smallpox does not
entirely prevent persons from having oxy-
plax" & I have myself successfully vaccinated
persons who had had smallpox and bore
its scars. Dr. Cory (thesis) mentions one
seven others of children successfully vaccinated after birth, although the mother had suffered from small-pox during pregnancy. On the other hand, Dr. Greenaway (Peters.), relates a case where the child was born with small-pox vesicles upon it, as was proved by a microscopic examination of the skin. He also incidentally verified Dr. Clinton's opinion regarding the "horny layer," for in this case it was wanting, and the vesicles were not complicated. How then can we account for "one of the least explained facts in pathology" viz. the "change which this ferment undergoes in passing thru the tissues of the cow," a change which renders it incapable when transmitted to the human system, of any longer propagating itself by effluvia, while it retains its capability of propagation by subcutaneous introduction, and its power of protecting the system by its own further action upon it? (Ernst Hart. "Truth about Vaccination," from J. Seaton's "Handbook," p. 110).

Is this mystery cleared up by supposing that the virus of variola, when cultivated in the cow, is not only restricted in its aggregative
ative & irritable properties on which chiefly
the eruption depends, but is also restricted
in its mode of reproduction as seen in the
anthracic culture fluid of M. Pasteur.

The confluent gums escape which alone the
permanency & consequent infectious power
of a disease depend may be prohibited
in production, or somehow rendered sti-
de or in the process. This the lasting self-
multiplying gums of variole may be modi-
ified by the cow into the transient & shot-
lived microgymes of Vaccina. This
change when once accomplished remains
for the two viruses may flourish together
in the same body & even in the same cell
at once yet remain distinct & produce
each its own specific effects.

On this theory of infection it ought to be
possible to cultivate small pox virus into
a true vaccine. Dr. Thiele (as mentioned
by Dr. Long) found that by mixing it with
milk & keeping it for some days, and
then using it in vaccination he produced
a modified small pox. Treating the lymph
thus obtained in the same way for ten gen-
ations,
ations, he knew could produce a disease indistinguishable from Blank fox. In W. Adbell's experiments (13th. of Feb. 1774), they render many things probable, prove little or nothing. As we have discovered in the cow the true cultivating medium of variolous virus, we may hope similarly to discover in other animals the proper cultivator of other human poisons, and in this way find the vaccine of all our virulent diseases, or in other words, the means by which these permanent self-replicating germs may be robbed of their power of independent existence by reproduction, so that they may no longer be infectious, and capable of perpetuating themselves of their specific diseases.

Summary.

We have undertaken to show:

1. That vaccination was first performed accidentally, and without a due appreciation of its full significance.

2. That Dr. Jenner first studied and practiced it scientifically.

3. That roughly speaking, vaccine might consist of
of three parts viz (a) a hyaline fluid (b) coccus-like particles (c) small particles.

4. These particles are the active principle.
5. That they are living organisms, on whose growth and well-being depend the effects of vaccination.
6. That they are the specific cause of a specific disease.
7. That they protect the system from a second attack of the same disease, or of themselves, by the 'refuse' of their vital functions.
8. That Varicella and Vaccinia are identical diseases, Varicella being probably the primary.
9. That their differences are owing to some modifying power in the cowpox, whereas, the micropores of Varicella have their tendency to aggregation & specific destruction impaired by their freemasonry of life & power of reproduction restored.
10. That we yet be able to apply this principle of vaccination for smallpox, to other analogous disease.
The subject is so extensive, that we refrain from applying these conclusions to the explanation or removal of many of the objections to Vaccination. We shall merely indicate the line of argument with regard to first:

1. Tuberculosis
2. Eruption
3. Syphilis
4. Smallpox
5. Non-protectiveness

1. Tuberculosis, Smallpox. Whatever Variola does, Vaccinia will tend to do. This is a necessary result of their identity. Hence the stimulus sometimes given to a dormant tubercular or seropulmonary constitution by Vaccination. The "Reports of Farre & Greenhow, however, prove that these diseases are less fatal now than formerly, which verifies Dr. Alloz's observation (quoted by Seaton in his "Handbook") that whatever small-pox in a population will save many of that population from Seropulmonary tuberculosis, otherwise to be fatal to them. We believe this to be true of Vaccination.

2. Eruptions. We have seen that Variola is essentially an Eruptive Disease. Hence the frequency with which Vesicular, Eczematic, Erythematous, &c., rashes follow the
use of fresh & robust lymph, especially when primary. (Cecily). These eruptions are but the shadows, as it were, of the original fox. When present they merely indicate that the virus has affected the system, or that there was a latent irritability in the child which the stimulus of the Vaccine called into action (Sir J. Paget). They are seldom worse than inconvenient or alarming.

3. Erysipelas. This we believe to be really a septic inflammation, having all the characters of disease. (Sanderson). It occurs most when epiglottitis, scarlet fever, or other allied diseases prevail, and is more an accident common to any abraded surface than any thing peculiarly Vaccinal. With a careful vaccinator, a more careful mother this sepsis would scarcely rank amongst the objections.

4. Syphilis. This is the great unspoken "Achard of Vaccination. "Whenever a popular opinion continues for any length of time to be widely spread amongst a community, it will be found to have had its origin in some truth or other, however amiss that truth may ultimately
ultimately have been distorted." (H. Lee, "Lectures on Syphilis," 2d Ed. 1842, p. 116, 1st Ed.)

and the full acknowledgment of the danger is the real essence of safety. (33.) Briefly then (a) Syphilis is inoculable both when congenital & acquired, with the former we have chiefly to do in Vaccination. (b) It may be transmitted by the blood (Experiments of Palpizzare, 1860 & 1862), and also by muscular & suppurative poxes & tissues. This, we might expect from our knowledge of the specific microbes found in this disease, & their action of tissue. By whatever means they are inoculated, will Syphilis be transmitted. And (c) Syphilis has been transmitted in the act of Vaccination, but never in leucine when blood, pus, or other products of de-vascularized tissue have been avoided.

As these are always avoided in careful vaccination, therefore, with Mr. Seaton, we think it "cannot occur unless as the result of malpraxis." In the famous Keralta period, we find the vaccinator was suffering from a recently acquired Syphilis.
Syphilis, whilst blood was drawn from a tenth-day vesicle. Thus we had all the elements of infection present: active Syphilis, blood, suppuration, and a careless vaccinator. The wonder is that any escaped. Ballard (op. cit. 353; Simon C.M.D. 1817-79, Wardmont (op. cit. 1817-79) (and I have frequently noted the same thing) maintain that a highly syphilitic child may show a perfectly irreproachable vesicle yet, I believe, children may be that many thousands must have been vaccinated from such, with absolute impunity. The reason may be found in the influence of their microorganisms or indeed in the simple fact that they are diseases caused by these specific organisms. Most we may more easily agree with Whinnow when he says that a typical Jennerian vesicle is a vesicle which only one modified influence can produce, which no secondary influence can concur in producing, for the contagion of which no second principle of infection can possibly reside. So also think Mason Leese, Sir W. Jume.
Sir J. Paget & L. N. Hutchinson.

We should suggest the limited introduction of animal vaccination as an "ejecto" to popular prejudice. Since seeing Dr. Wardomont at work with his caldesm in the garden at Brussels during the summer of 1880, our conviction is fixed that, under skilled management, an unlimited supply of lymph can be continuously produced, without recurring deterioration. The principal objections to its general use are (1) that it keeps badly, (2) it takes less readily, (3) requires more careful cultivation after a few months, than does the humanized lymph.

In about 5,000 vaccinations performed during the last ten years, my proportion of failure, from arm to arm vaccination, has scarcely been one per thousand with calf lymph. The rate would be unattainable, even when used direct from calf to arm, and as tubes, sprouts must be the chief means of transmission, the number of failure, would seriously interfere with our present results.
6. Non-protectiveness. This, if true, is the most serious objection of all. Dr. Jenner believed that vaccination would give the same immunity from small-pox as a previous attack of that disease. The protection at this early stage was generally lost by subsequent small-pox inoculation. It seems as if we had somewhat degenerated from this standard, for recent epidemics have proved us sadly wanting in our protection. The remedy seems to lie in a more careful cultivation of the vaccine lymph—i.e., the microzymes, so as to prevent the natural tendency to deterioration, with its consequent inefficient vaccination. This could best be done by appointing skilled vaccinators over large districts, who could devote their time and skill more fully to the matter. Better keep up a perfect supply of lymph. Still a more complete system of re-vaccination must be our main stay against small-pox, for the rapid tissue changes during childhood greatly certainly reduce the protective quality of...
of vaccination. A quasi-compulsory re-vaccination before entering an appren-
ticeship or being permitted to work with a penalty on the employers,
might do much with the less intelli-
gent members of society. It is cer-
tainly, by educating the community up to the due appreciation of the
value & safety of re-vaccination that
we can expect finally to stamp out the 'Small-pox'.

I hereby certify
that this Thesis was composed and
written by myself.

George Keith Bremner
M.B., Ch.M. - 1869.

April 22/82.