"The Natural History of Variola"

A Thesis

Presented for the Degree of Doctor of Science (Public Health) of the University of Edinburgh

By

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Preparatory Note

The following thesis has been written and composed entirely by myself.

Having been for eight months resident at the Birmingham City Hospitals, most of which Smallpox has been exceptionally prevalent, I have had very considerable opportunities of studying and observing the disease. I am therefore able from my own experience to vouch for a good many of the statements I have made. For the rest, I have given careful and exact references to the authorities and works from which I have obtained them. In the few instances in which I have been unable to verify a reference, I have given it. I have invariably quoted the authority from whom I obtained it.

A list of the literature I have consulted and read in preparing my thesis is appended.

My subject—"The Natural History of Variola" is such an extensive one that I soon found that if I wished to do justice to it and yet to keep within the compass I regard as of what I imagine to be customary
customary, it would be necessary to limit
it in some way. I therefore decided to
omit, speaking about two important branches
of the subject, any either of which would be
of sufficient magnitude and importance to
form a thesis by itself, viz. Convulsion
and Vaccination.

In a few instances the information
embodied under certain heads has been
obtained almost entirely from one standard
author, e.g. History from Mr. Moore's
classical work, and when this has been
the case it is stated so in a footnote and
all further reference to the author under that
head is avoided.

The five photographs which
accompany the thesis were taken by
myself.

City Hospital
Birmingham
4th 28th 1895
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All the above authorities have been perused.

I have not had access to

William
Introduction

Varicella is one of the most important and as regards its natural history and clinical features, one of the most interesting of all the zymotic diseases. In the first place it may be regarded as a typical member of the group of exanthemata. It possesses all the leading characteristics of this group—definite periods of incubation, invasion, eruption and decline: it spreads by infection, always leads true and once attack confers immunity against further attacks. It undoubtedly gains great—additional interest from its relationship to smallpox and from being the first disease in which protective inoculation (vaccination) was practically carried out.

It has also a great historical interest. It has existed in almost all countries from a remote period, and in consequence of the universal susceptibility to it, its loathsomeness, its terrible disfigurement, and terrible mortality has been one of the most dreaded, and consequently most thought of and most written of, of all
all the diseases that have ever afflicted the human race. From its tendency to occur with epidemic virulence sweeping through cities, countries and even continents, it has been an important factor in the history of nations, ranking in this respect with the other great plagues of history. It has been the subject of much legislation and probably has a more extensive literature than any other disease.

From the point of view of preventive medicine it takes a leading place among zymotics because it is essentially a preventable disease and became the success which has attended measures for its suppression has been so remarkably great. At the present day it is becoming specially interesting from this point of view in consequence of a popular reaction against compulsory vaccination and many points in connection with its natural history are being as, for instance, fatality, immunity, infectivity, etc., are being warmly discussed. Other important public health problems arise in connection with the provision of isolation hospitals.
Nomenclature. The word variola is not classical but was coined when the disease first became known in Europe. It is evidently derived from the Latin, *varius*, spotted, or from *varus*, a pimple. The diminutive termination is said to have been to distinguish the new malady from the buboes of true plague. From this term variola have been derived the Spanish, *variola*, the Italian, *Il Viguolo*, and the French *verole* (subsequently petite verole). The French also have a name of their own, *piqueot*, which is used by some of the older writers. When the malady spread to the North of Europe the Saxons instead of adopting the Latin word variola invented the vernacular name *poccal*, derived from *poca*, a bag or pouch. The Anglo-Saxons also adopted this word which became modified at length to *poox* or *poox*. The prefix *small* in the modern name *smallpox* is usually stated as having been added to distinguish the disease from *syphilis* (which appeared later) which was known as the *great pox*. The

1 (1) The facts in this section are obtained from the works quoted (v. Bibliography) of Jno. Moore, J. W. Moore & McTavish.
German name is blattern or poxken: the Danish & Norwegian - kopper; the Swedish - smittkopper and the Dutch pox.

**History**

The history of varicella has been the subject of much learned discussion. The earliest records of the disease come from China and Hindostan where it has existed from a very remote period. In China there is reason for believing that it has been prevalent for at least 5000 years. In an authentic Chinese work entitled "A Treatise on the Heart or the Smallpox" it is stated that the disease appeared in China in the Dynasty of T'heou which was about 1122 years B.C., and this is corroborated in other literature. In India the immense antiquity of the disease is testified by tradition, by the sacred books and by the mythology of the Hindoes. It has several names in the ancient Sanscrit Language and there is a special deity who preside
over it, as is also the case in China. In spite of the existence of
variolae in the far East at such an
early period of the World's history it would
appear that it did not spread to other
countries of the Globe until a much later
period. The most probable explanation
of this somewhat surprising fact is that
intercourse between India & China and the
rest of Asia was in the time of the
Ancient empires very limited and
only accomplished by lengthy journeys
whether by land or sea, so the disease
was certain to have been held in great
abreuve it is quite conceivable how any
infection which might break out at the
commencement of a journey would be
spread out before a vessel or caravan
arrived at its destination.

Whatever the correct explanation may be it is probable that the disease
was unknown to the Ancient Greeks
& Romans. This has been disputed, and attempts
have been made to show that the disease
is referred to, though in vague & indefinite
language, by ancient medical writers.
Such men, however as Galen and Hippocrates have given us such clear and accurate descriptions of other diseases with which they were acquainted that it is difficult to believe that they would have omitted such a definite and important disease as smallpox; for we may be certain that if it existed at all it was very prevalent. We must therefore take the view that the supposed reference has relation to something else.

About the middle of the 6th century smallpox reached the southern coast of Arabia, by means of vessels trading with India, and broke out near Mecca during the Chalilat War of the Elephant in the year 609, immediately before the birth of Mahomet. During the latter part of the 6th and the whole of the 7th centuries it was spread, together with the Measles (which was looked upon as a variety of the Small Pox) throughout the remaining countries of Asia and all that part of Africa which is washed by the Mediterranean.

In the 8th century Europe was contaminated in consequence of the Saracens invading Spain, Italy, and France, and the
disease gradually spread north to and certainly reached Saxony, Switzerland, and Britain in the 10th century and probably by the 9th century. The earliest European records are, as might be expected seeing how meagre the literature of that period is, few and incomplete. Epidemics of Smallpox were probably included in descriptions of the Plague, Erysipelas &c., most epidemic diseases being chronic during the Dark Ages, under the generic name “Pestilentia”. Two authentic detailed cases are recorded as occurring in a Flemish Prince and a British Princess in the 10th century; and in an ancient Anglo-Saxon manuscript, believed from internal evidence to have been written also in the 10th century, there is an exorcism praying for divine protection against the “fire and power of the Smallpox”. In the 11th century works were published both in Spain and Italy which included discourses on the Smallpox as an ordinary malady. Ibn Sina, Avicenna, and others maintained that the disease was first introduced into Europe at the beginning of the 12th century by
the return of the Crusaders from Palestine, but they must have overlooked the evidence I have quoted which clearly proves it of earlier origin.

From the date of its introduction up till the time when Jenner's glorious discovery became generally known and made use of, variola had been one of the most prevalent of all epidemic diseases. Isaac, the Jew, in the 9th century wrote "happens to almost all persons"; Helvetius, physician to the King of France in the 16th century spoke of the "almost unavoidable necessity of undergoing it at one time or another"; Hilary in 18th century "there is no malady more difficult to guard against...". Such passages might be multiplied indefinitely and in the absence of statistics they are the most convincing proof we can have of the widespread nature of the disease. As we shall see directly, the old theories of its origin were based on the belief that it was a disease natural to man which everyone was bound to suffer at some time or other in his life.
Literature.— The literature of variola is so extensive that it is impossible in writing a thesis such as this to consult more than a fraction of all the important works that have been written on the subject. I have however endeavored to obtain most of the more important recent works together with a sample of the older standard ones. I append at the end of the thesis a complete list of the authorities quoted from together with the titles and dates of their works.

No definite allusion to variola is made by Hippocrates, Galen, Celsus or the other ancient authors. The first writer on the subject of whom we have any record was Serapion of Alexandria who lived in the 7th century. His works unfortunately have been lost, but numerous quotations from them are made by Rhazes. The next writer was Isaac the Jew who probably lived in the 9th century, but it is not certain where. Next we come to Rhazes, a famous Arabian physician, known on account of his scientific attainments as "Ararat of the Great." He flourished at Baghdad at the end of the 9th and beginning of the 10th century.

The best known of his works, "A treatise on the Small-Pox and Measles" has been published in various languages about 35 times, which proves the great esteem in which it has been held. He treats of the subject chiefly from a clinical point of view but also enters at-length into the theory and cause of the disease. He was undoubtedly a man of close observation and a lucid writer, and though his explanations and theories may now appear grotesque and absurd they evidence deep thinking, and his clinical descriptions are such marvels of accuracy and detail that they quite justify the high reputation his writings have attained. At the end of the 16th century two more Arabian physicians, Hali Altas and Avicenna wrote on the subject, and the latter made the important observation that both measles and varicella were contagious. Little attention however appears to have been paid to this fact, and it was not until the 18th century that the view these old Arabian held was based upon the assumption that varicella was a disease specific to every human being. They regarded it as due to a poison in the

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(1) "A treatise on the Small-Pox and Measles" by Rhazes

(2) p. 23 4-5

Syd., 1848
system which was expected in the variolous eruption.* Acting upon this view their treatment was directed towards expelling the morbid humour by fomenting and encouraging the eruption together with sweating, bleeding and purging and other meditative measures. They recommended keeping the patient in a close hot chamber and covering him with bedclothes. Cold was carefully to be guarded against for fear of driving it from the eruption. They attributed a special virtue to the colour red and everything surrounding the patient and even the medicines he drank were prescribed to be of red. They believed in opening the patient. Of supposed remedies they had an unlimited number.

The doctrine of the Arabian school were with some modification accepted as correct by the medical profession almost all through the remainder of the dark middle ages. Hereditary taint, miasmata, bad food and air and even astrological influence, were added.

* Isaac the Jew advanced the theory that the morbid humour was originally derived by the fetus in utero from the menstrual blood of the mother. In any case having the smallpox was regarded as a process as natural as tertian or childbearing. — *History of the Small Pox* pp. 124-125.
as possible causes. * While its infectious nature was largely lost sight of, but the same line of treatment was persisted in. Based as it was upon entirely erroneous conceptions of the disease this can be little doubt that so far from benefiting the infected patient it was distinctly injurious and must have increased the fatality of the disease. If this was natural cause as high then as it now is in immediate the normal long of life from this one disease alone must have been appalling!

Reform came at last - Soon.

In the 17th Century Sydenham appeared, revolutionised medical practice including the treatment of variola, and pointed out the distinction between the latter and measles which had previously been regarded as a variety of the same disease. Thirty years later Emo Boerhaave, whose retiring vein of speculation on the ultimate cause of the malady, was the first to insist upon the

It is interesting to note that there is a tendency in some quarters to revert to the view that the disease is caused by insanitary surroundings rather than by contagion.
all important influence of contagium. From this time on variola began to be considered scientifically. In the 18th century came inoculation and its close vaccination. The most standard of early modern works is that of Dr. J. Moore, Director of the Natural Vaccine Establishment, entitled "The History of the Small Pox," pub. in 1816. Moore wrote in a true scientific spirit, and the book contains reference to a very great amount of ancient medical and general literature. At the present day, probably Marson & Collier, both formerly medical superintendents of Smallpox hospitals under the Metropolitan Asylums Board, are regarded as the greatest authorities, both from a clinical point of view, whilst as regards the natural history of the disease, including vaccination, Dr. John C. McVickar, formerly Med. Officer of Health for the Counties of Stirling & Dumbarton, and now promoted to the Local Govt. Board for Scotland, ranks equally first. Frequent reference are made in this thesis to his monthly article in "Stevenson & Murphy's "Hygiene & Public Health"
Geographical Distribution

Like the plague, cholera and some other diseases varieola has its natural habitat at certain spots on the globe, from whence it has spread at successive epidemics to all parts of the world. Its native foci would appear to be India and Central Africa. At the present time however it exists over almost the whole of the Eastern Globe, there being but few regions that are still completely free from it. Varieola appears to be very suitable soil among colored races, especially negroes, who are not at all very susceptible amongst whom it is not only very prevalent, but also very fatal. It is endemic over large tracts of country in India and further India. Brodie writing in 1869 after 13 years medical experience in India said it was the prevalent scourge throughout the country was subject to causing "frightful devastation". Since then however the more general introduction of vaccination has limited to some extent. Australia has been very successful in keeping the disease at bay in spite of two accidental importations, one in 1838 and one in 1868. Victoria has suffered severely.

1) Hirsch Vol II p. 128, C. 24. (Handbook of Geographical Pathology)
2) " " p. 151, C. 16
3) " " p. 134
severity from the disease. It has been introduced nineteen times since the beginning of the 14th century and in many instances the resulting epidemics were of appalling severity. In America it was introduced with the first European immigrants and spread by them wherever they went. A still more terrible source for America was the importation of negro slaves. The first outbreak in America was so severe that whole tribes were swept away by it. It has been very prevalent in all the countries of South America where it was probably first introduced by the Spaniards and frequently since then by negro slaves from Africa.

(3) Loc. Cit.
Influence of Climate, Race, Season
Sex and Age.

Climate. — On this subject Hirsch says, "not many of the acute infectious diseases show in their incidence and distribution so complete an independence of the conditions of climate and soil as smallpox" and the widespread geographical distribution of the disease supports this. It certainly prevails more in hot climates than in cold but beyond that nothing can be said.

Race. — The greater prevalence of smallpox in hot climates is probably rather a question of race than of climate. As regards the negroes at any rate, this is certainly so, for it is found that they suffer severely in America as well as in the West Indies and in Africa.

Season. — This appears to have a marked influence on the disease. Most writers are agreed that whilst smallpox is certainly prevalent at all seasons, outbreaks are more common during winter and spring than during summer; in other words, it is favoured by cold. This seems remarkable after what has

(1) Hirsch op. cit. p. 144, C. 2 et seq.
been said about its prevalence in hot climates; Hirsch[1] however in a table which he gives shows that the rule as to increased prevalence during winter holds good in India and other hot countries. On the other hand the character or type of the disease appears to be quite uninfluenced by season or temperature.

Sex. — At most ages the case-mortality is slightly greater in the male sex. The exceptions are the second and third years of life and the tenth to the fiftieth years, at all of which, for some unexplained cause, the female mortality slightly exceeds the male.

Age. — The age incidence of varicola has so completely changed since the introduction of vaccination that in studying the influence of age it is necessary to look at pre-vaccination times. We find that varicola was then a disease of childhood and infancy to an extent difficult to realise at the present day. Thus in Geneva (between the years 1680 and 1760) out of every 1000 deaths from the disease, 961 were in children under 10 years of age. [2]

[2]  "   "  p. 148 (Hirsch)
of age (1).—At Kilmarnock (1768-64) 988 per 1000, and in London, (prior to the Vaccination Act of 1863) 816 per 1000. It is quite clear therefore that in a community where variola is always prevalent more or less every few years, the incidence, as far as death rates are a guide, falls almost entirely upon children; it is there in fact DESTROYED as much a disease of childhood as measles still is, and for the same reason, viz., that the disease being universal, the adult members of the population have been protected by a previous attack. (2)

It is interesting however to find that variola when introduced into a community where it was previously unknown, behaves also like measles under the same circumstances and attacks old and young alike. This was exemplified in the West Indies (2) soon after the discovery of America, and in Iceland (3) after having been absent for a century. As regard case-mortality however, age as in all epidemic has an important influence and will be discussed under the head of fatality—

(2) (3) M'Culloch p. 316. p. 391. C. S. P. Ottawa
Periodicity of Epidemics

In consequence of the disturbing influence of vaccination and other prophylactic measures for checking and stamping out the disease, it is necessary, as was the case in considering the influence of age, to revert to the last century in order to study the periodicity of smallpox epidemics. In some places, for instance Kalmthout and Geneva, the periodicity was very striking, epidemics recurring at regular intervals of time. The duration of the interval however varied in different places, ranging from 4 to 7 years. Hirsch appears to regard any apparent constant periodicity as accidental and according to him there are only two factors which determine the recurrence of an epidemic: (1) "the necessary number of persons susceptible to the poison," (2) "the introduction of the virus itself." The marked periodicity however which undoubtedly existed in many places and which even still yet manifests itself in London seems to indicate some other factor. The striking way also in which epidemics recur or decline apart from any apparent cause, at least suggests the existence

(1) Op. cit. p 145, c.10
existence of some further this at present unknown influence.
Fatality.

This term is used as a convenient substitute for case-mortality, by Dr. Barry in his well known report on the Sheffield epidemic and I shall follow his example here.

In speaking of fatality it is necessary to make a broad distinction between the fatality of the present century and that which existed in pre-vaccination times. It is very desirable in estimating the effect produced by vaccination in reducing the case-mortality of smallpox to know what the fatality was in the days when milder vaccination or inoculation was practised. Unfortunately such statistics as we have, and they are but few, vary very considerably. We know however that widespread epidemics occurred, especially when the disease was introduced into a new country or into localities where it had long been absent, in which the mortality was appalling. Thus we read of whole tribes of American Indians (1) having been entirely swept away; of places almost depopulated and of armies broken up. The ravages in Iceland, Africa and America have already been referred to. In Greenland in 1754

(1) Harrow, "Reynold's System of Med." 2nd Ed. p. 242, c. 5
1734 nearly two thirds of the entire population were swept away (1). In this country we know that the total mortality was great. The London "Bills of Mortality" show that on average 7 to 9 per cent of the persons buried in London during the 17th and 18th centuries had died of smallpox, and in epidemic years the proportion often rose to 13, 15 or even 18 per cent; but as the number of persons attacked is unknown it is of course impossible to calculate a case-mortality rate; it must however have been high.

There is one very important influence which must not be lost sight of in considering the subject of fatality, and that is the influence of age. The fatality of variola is very high during the first few years of life. Harnew states that under 5 years of age it is 50 per cent (3) it decreases steadily and rapidly till it's minimum in the third quinquennium and then rises steadily for the rest of life. Harnew (4) gives a very high rate over 40 years of age — viz. 70 per cent but the figures upon which he bases this statement are too small.

(1) Sinon, quoted from Sturman & Murphy's History p. 397. 1320
(2) Whitridge, "Hygiene & Public Health," 2nd Ed. p. 261, 13. 15
(3) "Reynold's System" p. 209, 014
(4) Ibid.
small to be quite reliable (1). It follows from this that the age distribution of a given epidemic will have a great influence upon its fatality. But the age distribution of an epidemic in a population where preventive measures are not attempted and the epidemic allowed to run its natural course, will depend entirely upon the age distribution of the susceptible portion of the population and this in turn will depend upon the time which has elapsed since the last epidemic. It is therefore to be expected that in places where the disease is introduced after an interval of 20 or 30 years the mortality will be slight as the majority of persons born since the last epidemic will be at an age at which an attack is least likely to be fatal; whereas when the disease appears after a very long interval in which the average age of the victims would be much over 10 to 15 years (as was the case in the second epidemics) or taking the other extrem when the epidemics occur at intervals of only a few years and therefore the victims mostly infant.

(1) The writer experience, based however upon vaccinated cases, is that over 50 yrs of age, the fatality of a very severe attack is comparatively rare therefore the fatality not very high. This entally to what one could expect.
infants, we should expect the fatality to be high.

In addition to the influence of age there is in variola the same inexplicable variation in the type of epidemics that we see in other symptomatic diseases.

Taking these facts into consideration we are able to give an explanation of some bore side statistics, notably those of Jurin, which make the fatality of the disease appear surprisingly low and which are consequently much used as arguments by the opponents of vaccination, as tending to minimize the benefit conferred by vaccination in rendering it less fatal. Jurin's statistics give statements as to number of attacks & deaths in about 18,000 cases of smallpox occurring between the years 1723-1729 and the average fatality was about 18 percent. McVail has shown that many of these cases (about 6000) occurred in Boston in New England and amongst these the mortality was under 10 percent, thus lowering the average of the whole. But in Boston, as shown by Hersch, the disease was epidemic in 1690, in 1702 and next in 1721, and it was from the last of these epidemics that Jurin got his figures. Consequently

the age incidence of their 6,000 cases was probably as favourable as it well could be. This probability is confirmed by the fact that in 132 of Gurina's cases occurring in Ayesha in Hotantia, where the age distribution happens to be best recorded, over 50 percent were at ages between 5 and 25, i.e., the most-resistant period of life: (2) that there is ground for believing that Gurina, for some unaccountable reason, did not knowingly include any deaths from smallpox in children under 2 years of age, attributing them rather (owing to a mistaken theory of his) to other causes; as we know that the first two years of life is a most-fatal period, such a procedure, if true, completely invalidates the whole of Gurina's figures, and it is to be observed that the known age incidence of the cases at Ayesha support his views. (1) Furthermore, for there was not a single case amongst those under two years of age!

Fortunately we are able to form a more accurate idea of the true fatality of last century smallpox from the recorded case-mortality in smallpox hospitals. Thus in the Highgate Hospital, out of many thousand cases, the average was 26.3 per cent.

(1) See p. 20.
and from during the last 25 years of the 18th century to 32.5%. It is easy to say that this heavy mortality was due to insanitary hospitals and overcrowding or to a selection of severe cases for hospital treatment and that it in no way represents the true average fatality. It is a remarkable fact however that this rate, 25% to 32.5% per cent, is almost exactly that of unvaccinated cases in present-day hospitals, and consequently it is difficult to avoid the conclusion that the case-mortality of variola in the days before vaccination (or inoculation) was known was pretty much the same as it now is in those who are unvaccinated.

As it is not proposed in this thesis to take up the vast subject of vaccination, nothing will be said about the fatalities of the present day when most of the cases which occur are in vaccinated persons.

(1) Seaton, quoted by McVail, op. cit. p. 399.
Etiology

Etiology. — Smallpox is a typical member of the group of exanthemata. The most striking feature of this group is the property of infectionsness, and ever since this characteristic has been recognized, up till quite recent years, it has been a problem for scientists to solve what this property was due to and what was its essential nature. Thanks, however, to the new science of bacteriology, we now know that infection is something particular consisting of living particles — germs. Yet only a limited number of the exanthemata known has this "contagium vivum" been as yet positively recognized, but a sufficient and ever increasing list exists of them in which it has been so recognized to justify the assumption that every member of this group possesses its own specific microbe. The microbe of smallpox can hardly as yet be said to have been positively discovered. Various microscopic organisms, chiefly of the nature of Coeci & Streptocci, have it is true been found associated with the disease, but with the exception of the bacillus recently found independently by Klein and Copeman in the local lesions in the skin there has not been evidence to show their causal relationship to the disease. In the case of the Klein & Copeman bacillus however it is otherwise and only two
links in the chain of evidence laid down by Koch as necessary to prove a micro-organism the "cause noxius of any disease, viz. its cultivation outside the body through successive generations without losing its specific properties, and the production of the disease by inoculation with a pure culture. Unfortunately no means have yet been found of getting the bacillus to grow outside the living body. This subject is again referred to under the head of relationship to vaccines.

Injectivity. — The earliest approach to the discovery of the infectious nature of the disease was made 980 A.D. by the Abbas (1). Twelve years later Aricena was quite clear on the subject as regards both smallpox & measles. In this country this important property appears to have been recognized as early as 1366 (2) but it seems to have been little appreciated and even Sydenham makes no reference to it. Boerhaave (3) at Leyden (at beginning of 18th cent.) was the first to distinctly assign eczema as the exciting cause. The disease is spread from the sick to the healthy through the air as in the case with most of the acute infectious. There is doubtless an infectious atmosphere surrounding every patient whilst

(1) Northill, op. cit. p. 407, c. 28.  (2) Ibid. c. 28.
(3) Rowe J. W. op. cit. p. 70, c. 30.
he in the acute infectious stage. The contagion is generally supposed to be given off both by the breath and by the exhalation from the skin. Possibly this is the case with every free surface in the body but of this we have no proof. The person infected almost certainly receives the infection through the respiratory system. The infection, whatever its nature, can certainly be carried from place to place by families of all descriptions. A striking illustration of the ease with which this takes place in smallpox occurred in 1894 in Nottingham. Some case material at one stage of its manufacture was manipulated at his own home by an operative who together with his wife was suffering from a mild and unrecognized attack of the disease. The Case was then returned to the factory and distributed amongst a number of hands in one room. Out of 26 persons thus exposed to infection, 19 contracted smallpox about a fortnight later, all within a very few days of each other. Another striking case recently recorded was that of a young man who contracted the disease through the medium of letters received from his sweetheart—a nurse at a smallpox hospital: other possible sources of infection could

(2) The facts of this case were obtained personally from the M.O.H. for Nottingham, but will be found recorded in "Public Health für May’94, p. 286.  
(1) It has been suggested that the skin is the channel through which it enters, and perhaps corresponding to an inoculation.  
(3) Public Health 1894, p. 197, et al.
could be excluded. As we should naturally expect, all scarlet, emetic, and epithelial debris of any kind coming from a patient whilst suffering from the disease are highly infectious and capable of retaining the virus in an active condition for a long period. Like some others of the exanthemata, notably typhus fever, varicella continues to be infectious for some time after death. For exactly what period a corpse may remain infectious is unknown but certainly for several days.

Sir Thomas Watson (1) relates a case where the body of a man who had died of the disease was brought into Mr. Caesar Hawkins' dissecting room and four students thereby contracted the disease. Compared with the other exanthemata, varicella is very infectious. By this is meant that a very short exposure in an infected atmosphere is sufficient to originate the disease; a single breath will do it. As regards former, it is at least as easily carried in this way as any disease, not excepting scarlet fever. The distance at which it can infect—i.e., the "striking distance"—is exceptionally great, but I shall refer to this again. The virility of the infection, i.e., its power of resistance to external influence after it has left the body, is probably not so great, for infected horses, foals, etc., lose their power of infecting comparatively soon after recovery.

(1) Lecture on Medicine, 5th Ed. p. 935, Ch. 38.
is also more readily destroyed by artificial means, i.e. by disinfectants.

Varicella is eminently a disease which can be conveyed by inoculation, all that is necessary being to rub varicella matter into an abraded surface of skin in a susceptible person. The important feature of the disease when transmitted in this manner is that the incubation period is shortened by several days and that the type of the disease is usually mild. The ease with which varicella is inoculated is one of the most striking differences from variolna between it and varicella. (1)

The disease may be transmitted from mother to child, “in utero,” and the child may either be born with the eruption out or it, or, as in the cases the writer has seen, may develop the disease afterwards. Frequently, in the former case the child is born dead.

"Aerial Convection." — One of the characteristics of the infectivity of varicella is its remarkable carrying distance. Varicella is at the other end of the scale in this respect to typhus. The well known investigation of Power (2) in connection with the Fulham Smallpox Hospital have shown that the carrying or "striking" distance of the disease is extraordinarily

(1) I intentionally omit any further reference to the subject of inoculation for reasons stated in a previous work.

extraordinarily great. Taking the Hospital as a centre and drawing concentric lines round it at distances of ¼ mile from each other, Mr. Power prepared "spot-maps" showing the incidence of the disease in each belt respectively. The period of time which his investigation covered (3 years, 1877-80) was divided into fortnights, and the relation between the number of cases in hospital during each fortnight to the number of such cases occurring round the hospital was clearly brought out.

His general conclusions were— (1) that the hospital contributed largely to the number of cases; (2) that the incidence bore a very exact relation to propinquity to the hospital; (3) that the houses in the main thoroughfars were not especially affected; (4) that variations in the use of the hospital were followed by corresponding variations outside, but that convalescent cases were not factors in its influence; (5) that the influence was greatest when admissions to the hospital were beginning to increase rapidly; (6) that the comparison held good with regard to successive epidemics; (7) that such defects as existed in the hospital administration were not such as would account for the influence; (8) that the conditions contributing to the smallpox around the hospital, pertained...

to the hospital, and (9) that "during the present epidemic period and most probably during former similar periods, there has arisen in the atmospheric circumstances of the time, peculiar facility for the transmission in an undamaged state, of any matter that may have been given off from the hospital." These deductions based upon careful and scientific investigation are of the very greatest importance. If they are correct it follows that a smallpox hospital however well managed must of necessity be a source of danger to the surrounding population, and the Local Govt. Board have rightly refused, since Dr. Powers' investigations were made, to sanction any site for a Smallpox Hospital that is within half a mile of any public institution or any large centre of population. In a Memorandum issued by the Medical Officer of the Local Govt. Board (Dr. Thomas Thomas) at the beginning of the present year, as the subject of provision of isolation accommodation by Local Authorities it is stated that the distance at which a smallpox hospital may operate dangerously cannot be precisely established with any degree of certainty though it may be taken to be considerable. He holds however that no Local Authority should
"Contemplate the erection of a smallpox hospital:—
(1) On any site where it would have within a quarter of a mile of it as a centre a hospital, whether for infectious diseases or not, or a workhouse or any similar establishment, or a population of from 100 to 200 persons. (2) On any site where it would have within half a mile of it as a centre a population of from 500 to 600 persons..."

Powers's deductions have since been confirmed by further investigations made both by himself at Fulham (1) and by other observers in connection with outbreaks in other parts of the country. In the case of the Sheffield epidemic of 1887-88, Begg found a similar radiation of infection from the smallpox hospital in that city; but unfortunately the question of personal contact could not be quite excluded which largely destroys the scientific value of the observation. More recently Priestley has published striking evidence from Leicester (2) and in this case the question of personal contact could be excluded. The smallpox hospital in Birmingham (to which the writer is attached) is situated in the very midst of a poor, thickly populated district of the city, and during the present epidemic,

1893

(2) Ann. Rep. of M.O.H. for Leicester 1894
1893-95, from 100 to 200 cases of variola have been treated there at a time. At the time of writing no complete report has been published but a 'spot map' has been prepared which shows with curious significance the thick clustering of cases round the hospital. Some of this may, of course, be due to other causes, but there can be little doubt that some of it at least is due to direct atmospheric connection. Within 500 yards of the hospital are the workhouse & workhouse infirmary; these institutions have suffered severely, but though many of the cases which have occurred were "secondary" one has been a considerable number of cases in which all factors except the one we are considering could practically be excluded. Cases occurred for instance in bedridden wards with which this disease had not been associated. Numerous patients who had not left their beds for months, and whose visitors were few.

Susceptibility. Variola is one of those diseases to which almost the entire human race is naturally susceptible. In the days when it was allowed to spread itself unchecked, when indeed preventive measures were unknown, its relationship to the human race remained as chickenpox & measles may still
almost be said to do that of distemper to the canine species. It was an affection with every individual had to have sooner or later and was generally contracted at the first exposure to infection. It has already been stated, colored races and especially negroes have a greater susceptibility to the disease than Europeans. It spreads more rapidly amongst them and the fatality is much heavier.

It is doubtful how far there are exceptions to the law of universal natural susceptibility. Cases certainly occur where unprotected persons, though exposed to infection, fail to contract the disease at first, but many of them are afterwards found to do so. In this respect varicella resembles many other infectious diseases. A case is recorded of a smallpox nurse who had never been artificially protected in any way yet did not catch the disease till late in life when she contracted it in a severe form which proved fatal. It would seem then that even when there does appear to exist a natural insusceptibility it may not be permanent. It is interesting to note that a similar temporary immunity exists in the case of vaccination, though judging from Camp's experiments
experience at the National Vaccine Institution, the great majority of the cases of supposed insusceptibility to vaccinia in children which are annually signed up as such, are probably rather explicable as due to inert lymph or to carelessness or want of skill on the part of the operator. The following case which came under the writer's own observation (1) would seem to be genuine and is worth recording here. A woman, in an advanced stage of pregnancy, contracted smallpox and a few days later was delivered of a healthy child. The child was immediately vaccinated but without effect and though the operation was repeated again and again with different samples of lymph it could not be got to take. The child stayed with its mother in one of the ordinary smallpox wards for upwards of 3 weeks but did not contract the disease, thus proving beyond a doubt that its resistance to vaccinia was genuine. Some months later, however, the child was successfully vaccinated by the public vaccinators. The writer has another case of (apparent-) resistance to vaccinia at the present time, it is the infant child of one woman who...

(1) The woman was a patient in the Birmingham City Hospital.
when care consists in carrying infected article to the public disinfecting apparatus. During the first eight weeks of its existence it was vaccinated at least five times (with different samples of lymph, both human & calf) but without any success. The child is now nearly 4 months old & it is proposed attempting the operation again.

As regards the proportion of persons who may be regarded as insusceptible (evenly temporarily), it is difficult to make an exact computation for obvious reasons. In the Sheffield epidemic Barry\(^{(1)}\) found that 75% of the unvaccinated persons of all ages living in infected houses contracted the disease, but from we have no knowledge as to what proportion of the remaining 25% were really exposed to infection. Crose\(^{(2)}\) found that in the Norwich epidemic of 1826, out of 603 persons, i.e. about 2%, were insusceptible, and Kilpatrick\(^{(3)}\) taking his opinion upon his experience of inoculation, found about the same.

In addition to cases of total insusceptibility, we should expect to find a larger number of cases in which the resistance was not quite complete and in which only very mild attacks developed.

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\(^{(1)}\) Report on an Epidemic of Smallpox at Sheffield, p.171, par.13.
\(^{(2)}\) Quoted from Rivet op. cit. p.402, c.22.
\(^{(3)}\) An Analysis of Inoculation, J. Kilpatrick M.D. 27 & 28, 1761.
developed. But the question arises, would these attacks take the form of "modified" variola and the eruption be abortive, or would they be merely very mild but unmodified cases? In the writer's opinion there is a clear distinction between these two alternatives. Immotified variola, i.e. variola in which the disease runs its ordinary course, its tertiles developing "maturing" or healing in a natural manner, may be of all degrees of severity, ranging from bad confluent cases to those in which the eruption is sufficiently sparse to be easily countable. Immotified variola is what we see in those who have not been protected by any of the means known to confer immunity, such as vaccinates inoculation or previous attacks. "Modified" variola may also vary in severity - I have known bad confluent cases - but is usually very mild. I use the terms severe and mild with reference to the amount of eruption. It is in severe cases however that the modified character of the attack is most evident. Instead of running the ordinary course, the eruption...
stop developing, i.e. "abuts", at some stage before the last, there is no secondary fever, and the patient quickly gets well. Now it is a question how far modified attacks occur in persons who have not been protected by any of the means enumerated; in other words, how far natural resistance alone is capable of it? It is commonly assumed that the various diseases described by the older writers under the names of "smallpox", "mickle-pock", "chicken-pock", "divine-pock", "water-pock", or were examples, many of them, of such modification, but it must be owned their true pathology is by no means certain. Many of them were undoubtedly cases of ordinary variola vera. Many were undoubtedly cases of ordinary variola vera, which we never know to be an absolutely distinct disease. Others were probably examples of various skin diseases which are still apt to be confused with modified variola; whilst the remainder are capable of being explained as cases of true variola occurring in persons who had a previous attack of the disease invaginated. Wherever the "variola vera" disease, as it is called, occurred in epidemic prevalence, as it sometimes did, if history is to be relied upon, without introduction of unmodified cases, there is strong presumptive evidence against there being variola at all, for the reason that present-
day experience shows that though different epidemics may vary considerably in fatality, there will always be a given section of population, and this even in spite of vaccination, a large proportion of individuals who if exposed to variola infection will contract unmodified attacks.

At the same time I shall not attempt to deny that genuine cases may occur, but I believe them to be very exceptional. During the present epidemic in Birmingham (1893-95) out of over 3,000 cases of smallpox admitted into the hospital, upon which I am now writing, there have been only one or two cases of truly modified or persons who apparently were quite unprotected. Unfortunately even these are not certain, as they were carefully investigated and it is possible that person vaccinated may have been overlooked. As illustrating the possibility of this, I will here insert an article published in the "Public Health" June 1895, giving particulars of a case in point.

(1) The writer has been informed by Dr. Priestley, the Med. Off. of Health for Leicester, that there were several cases during the last epidemic in that town.
MODIFIED SMALL-POX IN THE UNVACCINATED.

By C. Killick Millard, M.B., B.Sc. (Pub. Health), Senior Assistant Medical Officer, City Hospitals, Birmingham.

It is stated by some, especially by those opposed to vaccination, that modified small-pox occurs in persons who have never been vaccinated, nor yet partially protected by a previous attack. By "modified" small-pox, I mean small-pox which fails to run its usual course, the eruption drying up, or "aborting," prematurely. Such cases are usually extremely benign, and are very common in persons whose vaccination has failed to protect them completely. They also occur, and are the rule, in second attacks of variola. I do not wish to deny that these cases may occur in persons unprotected by either of these means, but I can only assert that if they do ever occur, they must be extremely rare, for in all our experience of the present epidemic of small-pox in Birmingham, numbering now over 3,000 cases, we have not seen a single instance.

The following case, for permission to publish which I am indebted to the courtesy of the Medical Superintendent, Dr. Meredith Richards, helps, I think, to explain some, at least, of the supposed cases. Annie G——, aged 18, was admitted to the Birmingham City Hospital on June 2nd, 1894, suffering from an extremely mild attack of typical modified variola. She had a few scattered papules, chiefly on the face and wrists, but barely a score altogether, which early aborted, quickly drying up and disappearing. There were absolutely no constitutional symptoms either before or after the appearance of the eruption. She stated positively that she had never been vaccinated, the reason being, she said, that she had been in ill-health at the time when as an infant she ought properly to have been done. Except for this and an attack of measles she had never had any illness before—certainly not small-pox. Careful examination of both arms failed to detect the slightest sign of vaccination, nor were there any traces of a previous attack of variola. Not being satisfied, however, I wrote to her mother, and inquired as to the facts from her. Her reply corroborated the daughter's own statement. Annie had never been vaccinated, her doctor certifying when she was three months old that she was unfit for the operation, in consequence of an attack of bronchitis. The family subsequently changed their address, and the child was doubtless lost sight of by the vaccination officer, for I have since ascertained that she was never signed up as having been successfully vaccinated.

On the strength of these facts, we came to the conclusion that this was a genuine instance of modified small-pox in an unvaccinated person, and I showed a photograph I had taken of her to several of my friends as such.

Last month, however, nearly five months after the patient had left the hospital, we received a visit from the vaccination officer, who told us the following story:—In the course of his duties he had called at the house where Annie G—— was living, after she had been discharged from hospital, and inquired as to the facts of her vaccination. Being somewhat sceptical, he examined her, and observed a small cicatrix, about the size of a threepenny piece, immediately below the lower lip, a likely site for a burn. This scar, I must confess, had not struck me as of any importance. The vaccination officer, however, inquired as to its origin, and was thereupon informed by Mrs. G—— that that was the sore place she got when a few years old from nursing her baby sister at the time the latter's arm was bad with vaccination! Further inquiry as to the appearance and history of the sore which formed, and inspection of the scar which it left, made it quite clear that Annie G—— had unwittingly vaccinated herself.

[EDITORIAL NOTE.—The photograph sent with this article shows very well the modified character of the variola, and also the foveated cicatrix on the chin.]
Incubation Period. — Varicella has a more constant and exact latent period than most acute specifics. Speaking generally, it is twelve times twenty-four hours after the infection was taken into the system before the first symptoms of the disease manifest themselves. Occasionally it may be a day more or less. There is more variation in the time which elapses after the appearance of the first symptoms before the eruption appears. Though commonly stated in the books as being on the 3rd day of the disease, it is almost as often on the 4th, and probably in at least 25% of cases it is on neither of these days, so that the rule sometimes stated that the eruption of varicella appears on the 3rd day oftentimes (i.e. 2nd day) after exposure to infection, though convenient for rough and ready reckoning, cannot be relied upon and indeed is only quite true in a minority of cases. The following figures, based upon an analysis of 3750 cases, are given by Dr. Saville (1)

(1) "On the Diagnosis of Smallpox in its Early Stages" by T. D. Saville M.D. B.M. Journ. Apr. 29, 1852. pp. 888 to 889, ed. 2.
Date of appearance of eruption.

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In Variola after which has been inoculated the incubation period is shortened by 3 or 4 days.
Period of Infectiousness — It is difficult to say exactly at what stage of its course Varicella becomes infectious. There is no evidence pointing to its being so during the latent period, and it is probably only slightly so during the pre-eruptive stage. In practice it is usually considered that the disease is infectious from the first appearance of the eruption till all the scabs have fallen off. This time varies from two to five weeks according as the disease is mild or severe. The infectious stage is therefore of much shorter duration than in Scarlet Fever and many other acute exanthemata. In the City Hospitals Birmingham all cases are kept in for a minimum of 18 days (or of 21 days if the fever has been high) from the first appearance of the eruption, even if all scabs have come away before that, in mild cases they know all disappeared in ten or twelve days) or as much longer as may be necessary for the process of healing to become complete. In confluent attacks this often takes weeks from four to five weeks. We also refuse to discharge a patient so long as the skin remains markedly rough or whilst there remains any discharging sinuses or sores place. For this latter reason exceptional cases are sometimes kept in for several months.
their precautions, and the minimum stay in hospital which we prescribe are necessary, is a little doubtful. The experience at the above-mentioned hospital has been singularly happy; out of over 3000 cases of smallpox discharged during the past 2 years, there have not been more than 1 or 2 "future" cases and these were not at all certain. It may therefore be fairly assumed that the period during which the infective remains is certainly not greater than that stated above, though it may possibly be less.

It would be interesting to know the result of reducing the minimum to say 14 days. It must be confessed that many hospitals require a considerably higher minimum than 18 days, but the Taylors' Board in their smallpox ships require almost exactly the same as we do here in Birmingham.
Relationship to Vaccinia.

Ever since vaccination has been known it has been suspected, and indeed believed, that cow-pox was in reality the bovine form of variola, such differences as exist between vaccinia and smallpox in the human subject were due to modification of the virus in its passage through the cow. This theory, whilst very attractive, and as we shall see probably correct, is nevertheless not yet absolutely proved, though the evidence pointing to such a conclusion is, in the writer's opinion, almost irresistible. Edward Jenner himself believed it, though he had far less positive evidence than we now have. On the other hand, many early advocates of vaccination absolutely denied its possibility, and at the present day there are still some who at least think it improbable. This is especially the case with those who fail to see, or refuse to acknowledge, the efficacy of vaccination as a prophylactic against vaccination.

The arguments against this view I have stated, viz. that the two diseases are due to the same essential virus are:
1. Great dissimilarity between their symptoms and characteristics; whilst the one is very dangerous to life, highly infectious and accompanied by a generalized eruption, the other is so mild as to seldom prove fatal, is not infectious (in the ordinary sense of the term) and has no generalized eruption.

2. A person may suffer from both diseases not only at different times, but at one and the same time. This is well exemplified in photograph, where a young girl (vaccinated in infancy) is shown with variolae and vaccinia (the result of re-vaccination) running their course contemporaneously each apparently but little modified by the presence of the other.

3. Failure (?) of experimental attempts to produce vaccinia by inoculation of cows with variola as a well known instance of this. Klein's experience in 1875 may be quoted. In that year he carried out some extensive researches upon the variolation of bovines at the Brown Institution for the Soc. for the Poor. Altogether he inoculated some 33 cows and heifers with various materials from persons suffering from smallpox at various stages, but in spite of perseverance and of modifying the method of inoculation he only obtained negative results.

results. Many other workers have had a similar experience or indeed have obtained results which rather pointed against the theory. The best known of these is Chauveau (1) who maintained that he produced in the cow a papule from 1865–66 and again in 1871 but the matter taken from the papule produced only similar papules in other cows, whilst in human beings it produced vaccinia, not varicella. A similar result is said to have been obtained in Massachusetts (2) in 1806, at Munich (2) in 1839 and at Berlin (3) in 1847.

4. Vaccinia, though cultivated through an infinite number of generations in the human subject, never takes on, even in the slightest degree, the character of true smallpox. This remarkable fact appears to the writer the strongest argument of all, for when we consider analogous modifications in other animals produced by change of soil or environment we find that virulence is quickly regained in returning the virus to its original conditions of growth. (1) The body all these arguments however can be met. Thus:

(1) Crooke’s Bank, quoted by Vivian, op. cit. p. 423, l. 33
(2) Ibid
(3) cf. Bacillus Anthrax
1. However great the apparent differences may be, we have no right, a priori, to put any limit to the extent to which a virus may be modified. It is a point which will only be settled by experience. As a matter of fact, we know that some diseases may be enormously modified, especially in the direction of reduction of virulence and incubation period (e.g., hydrophobia). Moreover, the true differences are really so great when we come to examine them, and are rather matters of degree than of essential characteristics. Take, for instance, the absence in vaccinia of a generalised eruption and of the property of infectiousness. Both are explicable on the theory that the microbe, whatever it may be, is in consequence of its modification localized to the seat of inoculation. I am aware this is only a theory and has not yet been proved, but it is quite a reasonable one. If it be true, it is sufficient to account for the absence of eruption and the latter fact in turn may probably account for the non-infectiousness of the former, as it generally assumed that the infectiousness of a case of varicella is in part caused by and in proportion to the amount of eruption. We have an important link in helping the direction of bridging the apparent difference in this respect in
the (alleged) existence of cases of "generalised vaccinia" or vaccinisation accompanied by a more or less general eruption. On the other hand there are many points of similarity between vaccinia and varicella which are quite obvious. They both belong to the group Exanthemata, with the characteristic features of incubation, invasion, eruption, and defervescence, followed by immunity for a time against further attacks. If people are inoculated, the local lesion resulting from the disease is very similar in both diseases, and this similarity is not only macroscopic but microscopic as well. The clinical symptoms also are similar, differing only in degree. Lastly there is the all important and undisputed fact that the one confers immunity against the other. This is probably the most suggestive of all the evidence in favour of the causal relationship of the two diseases. It is true that some, but they are very few, (notably J. Collie and Crookshank) deny the immunity conferred by the one against the other and attributing any apparent experimental results to what they call "temporary antagonism"; as this is only

(2) Ibid. Report by T. Klein p. 139, l. 2 p. q.v.
(3) The immunity conferred by vaccinia is certainly not as complete and permanent as that given by varicella itself, but
talking with phrases, and as the whole weight of scientific evidence is in favor of the
immunity conferred by variola against varicella, and vice versa, nothing further need be said.
2. It is certainly true(1) that a person may suffer from varicella and vaccinia simultaneously. This
however proves nothing. It is probable that two or more stocks of the virus of any(2) inoculable disease
will develop and pass their course in the same person provided they are inoculated at the same
time or nearly at the same time that the
fect may have time to develop before immunity
has been set up by the first. These are just the
conditions which obtain when varicella and
vaccinia occur together, the shortened incubation
period in the latter requiring of course that the
vaccination be performed at some time, at least 2 or
3 days, subsequent to inoculation with the former,
and at a still longer interval, usually at least 7 days,
if the smallpox be contracted in the usual way.
3. Although numerous experiments have
failed in their attempts to produce convulsions
by
considering the great attenuation the virus has undergone in att
travels, it is sufficient and certain a most fortunate thing
for humanity, that the protection is as complete & durable as it is.

(1) See plate appended, No. V.
(2) As instance we have Syphilis also vaccinia & varicella

some weeks.
by inoculating smallpox, their negative evidence
favors nothing against - the positive evidence of
those who have succeeded, it merely shows that
the positive result is difficult of achievement and
depends upon chance or rather upon conditions at present
not understood. Both Calk (1) and Badcock (2), especially
the latter, produced in many instances in hogs, by
association with human variolous matter, a vesicle,
and lymph taken from such vesicle was found
by experiment to have the properties of ordinary
vaccine. These workers (Calk & Badcock) failed in
a large proportion of their attempts but thought
that they succeeded better if they simultaneously
inoculated the animal (at a different part of the
body) with true vaccine. This unnecessary com-
plication naturally provided a loophole by
which the opponents of the theory could escape
from the otherwise logical conclusion as to the
true relationship of cow-pox and human smallpox
for it was at once suggested that the result
obtained were in some way or other really
attributable to vaccine and not variolous in-
oculation. This it must be allowed was a
valid objection. Several present day

(2) " " " " " c. 19
Scientists have successfully repeated the experiment (notably Surgeon-major W. J. King, of the Madras Med. Service, and Dr. T. W. Hines, formerly Med. Off. Health for Bradford and now Director of a Calf Vaccine Establishment, and Dr. S. Moncton Copeeman, now Med. Inspector to the Local Gov't Board) but with this difference that they omitted the question of method of simultaneous vaccination. King's results may be epitomized as follows: he inoculated a calf with variolar matter from a human being suffering from smallpox. From the resulting lesion matter was obtained which it inoculated a second calf, and so on through seven calves in succession. From the seventh calf a child was inoculated, and the resulting lesion was in no way distinguishable from that produced by ordinary calf vaccinati.

A very complete chronological list of the names of those who have carried out variolation experiments on cows is given by Copeeman in his paper on Variola and Vaccinia in the Journ. Path. & Bact., vol. 2, p. 416. It contains the names of some 23 observers, commencing at the year 1801 and continuing down to the present time. It is a noteworthy and significant fact that all these workers, with the exception of Copeeman and his colleagues on the Lynn Commission, claim to have obtained positive results as regards the production of typical vaccinia after one or more passages, as the result of variolation of the cow.

The reference marked * is part of next sheet.
vaccination. From this child other children were vaccinated and the results were so excellent that Surgeon-major King gradually substituted this new lymph for the old strain of calf vaccine.

Dr. Hume's experiments though not so extensive were equally successful. He inoculated a calf in 14 places with human variola matter in an area of the abdomen previously made surgically clean. In the course of a few days he found a few papules in proximity to four, one or two of his inoculations. These became vesicular and the lymph from them was used to successfully re-vaccinate a man and to vaccinate a calf. This second calf was inoculated in 29 places. They all took and had the appearance of normal vaccinia. Both calves were afterward found to be insusceptible to the action of ordinary calf vaccine. Dr. Hume refers the failure of Chauveau and others to their experimenting upon cows and buffaloes instead of upon calves which appear to be more susceptible to variolation. Hume's result are remarkable in that he apparently obtained true vaccinia from variola at the first removal. Dr. Martin Cooperman working at the Brown Institution made


four attempts (1) but only one of these was an
undoubted success. In some of his experiment-
did he obtain anything approaching to a true
vaccine vesicle in the calf first inoculated as
happened in (2) Hone’s case.

Since this thesis was commenced the
results of a second series of experiments on the vari-
dation of bovine has been published by Dr. Klein (3)
who far recent coming from a scientist like Klein of
the highest importance, especially as they are quite
different from the negative results he formerly ob-
tained. His latest research entirely corroborate that
of King, Jenner, Simson & others. By using calves,
instead of cows, he obtained a positive local result-
from which he obtained matter which will to in-
oculate other calves until at the 4th premun
he ventured together with Dr. Cong, to vaccinate a
child, the result being the production of typical
vaccinia. This post-vaccinated into unvaccinated
calves, produced typical cow-pox, but paid atttention
to affect calves previously vaccinated. It is note-
worthly that the local result be obtained in the calves

(1) From Path. & Bacteriology, Vol. 2, pp 415 to 426
(2) Other important workers in this field are Vaccins
in Germany (1880-91) and Simpson in India (1893).
Simpson results resembled Hone’s.
(3) Supp. to 22rd Amb. Rep. Sec. Govt. India, 1897,
first inoculated (i.e., prior to passing through the child) did not, even at the 4th removal, exhibit to any extent the appearance of vaccinia. The lesions remained papular without any trace of vesication and matter, for further inoculation had to be obtained by scraping and clawing.

Dr. Klein's important research did not end here. He went on to look for the long-sought-for microbe of vaccinia and variol. Thinking over the known facts that lymph taken from a ripe vaccine vesicle, though thoroughly dried or "points" can retain its activity for a great length of time, whereas lymph taken in a very early stage, though fully potent for "direct" vaccination is comparatively useless, when dried and stored, it occurred to him as a likely explanation that the microorganism, whatever it might be, was a spore-forming one. Thus the early lymph containing the organism prior to the formation of spores would much readily become inert than the late and spore-containing lymph. He accordingly obtained lymph from the budding vaccinia vesicle (3rd and 4th day) and on examination in "cover-glass" specimens stained in alcoholic gentian violet found a minute straight bacillus in almost pure culture. On the 5th day

(1) Loc. Cit.
of the vacuole this bacillus was still present, but in
for less numbers, whilst on the 6th or 8th day
it was scarce and appeared to be replaced by
granules taking the fuchsin stain and which he
sensibly were spores. The same result was obtained
in either human or calf lymph. Turning next to
varicella and proceeding to the same methods he
obtained a bacillus in no way to be differentiated by
the means at his disposal from the one he had
previously found in vaccinia. This is strong reason
for assuming that this bacillus is the true microbe
of varicella and vaccinia, but unfortunately Klein
does as yet entirely failed in his attempts to culti-
vate it in any artificial nutrient medium. A
great variety of media have been tried but all in
vain. This is very unfortunate as it prevents the
demonstration of the causal relationship to varicella
and vaccinia. At the same time the fact is in itself an
argument against the organism being merely adventi-
tious, for other of organisms found in lymph and vac-
inc proved to be only adventitious cause all be cultivated
outside the living body.

Shortly before F. Klein's discovery was
made public, Dr. Copenman(1) working quite
independently, but on the same lines, had dis-
covered

(1) Paper on 'Pathology of Vaccinia... read at 62th
discovered a bacillus in early vaccinal and variolous lymph apparently identical with Klein's. Though he published shortly before Klein, the latter's work was done first and therefore the first place as discoverer of the bacillus properly belongs to Klein (1). Like Klein, Dr. Copeman has quite failed to cultivate this bacillus in any artificial medium.

Before leaving the subject of relationship to vaccinia we must refer to the experiments that have been made, notably by Charvex, with the object of attempting, by successive inoculation, to reduce variola to the "mutter-naht" which forms at the actual seat of inoculation. In the days when inoculation was practiced, and especially with the more approved Suttoman method, it was no uncommon thing for the general eruption to be reduced to a few pustules only. Working on the same lines Charvex succeeded in some of his experiment in producing merely a few minute pustules-principles in the immediate vicinity of the "mutter-naht."

(1) The writer had the privilege of working with Klein in his laboratory at St. Bart's Hosp. during the spring of 1893. Klein's work had already been completed as early as that the writer himself saw the bacillus in Leptin's slides. Only, however, to the delay of the Government Printing Depot the results were not published till toward the end of 1894.
But these results were so uncertain and sometimes gave rise to such untoward results, that he was forced to abandon them. Whether, if these attempts had been pursued in long enough, they would ultimately have been successful, it is impossible to say, but if it be true that vacinum is only modified variola, it seems at least possible that the conversion of the latter into the former might be accomplished by means other than the passage of the various virus through a bovine animal.
Alleged Relationship to Varicella

It is hardly necessary at the present day to insist upon the absolute distinction between varicella and varicella. Smallpox is smallpox and never under any circumstances gives rise to chickenpox, and vice versa, chickenpox never gives rise to any form of true varicella affection. Each disease invariably stands true and is quite independent of the other.

Nevertheless, as similar sometimes as superficial observation is the eruption of the one disease to that of the other that it is not surprising that in the early days of medical science the two diseases were regarded as one; indeed it was not till about the middle of the 18th century that Fellu(1) and then Heberden(2) became convinced of their non-identity. The latter wrote a paper on the subject in 1867, which has become classical, and from that time the belief in their separate existence has gradually been accepted. At the same time there have always been some who continued to maintain their identity, and of them the most notable were Hebra of Vienna and Thoms of Edinburgh.

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(1) See, Reynolds' System of Medicine, 2nd Ed. p. 520
(2) Morus Jr. Hist. of Pract. of Vaccination 1817,
   p. 93, C.7
It is indeed remarkable that such a really eminent man as Herba should have been so misled, especially after the real points of distinction had been accurately pointed out.

The arguments in favour of the non-identity of the two diseases are briefly:

1. Variola and varicella are not interchangeable, (a) by infection; the supposed authentic cases of the one giving rise to the other were undoubtedly the result of a mistaken diagnosis or a false deduction. At the present time, with improved diagnosis and more careful deduction, such a thing is never observed. (b) By inoculation varicella is not inoculable. This has been proved by Breyer, Trousselot and many others. Smallpox is readily inoculable but never gives rise to varicella. The supposed instances are explicable as in (a).

2. Variola and varicella are not mutually prophylactic; a person may suffer from both even at the same time.

3. According to those who collected a long series of cases in 1820 a small minority of inoculation experiments appear to succeed but doubt has been thrown on the validity of these observations. (Dr. Fogg 1820, Vol. I, p. 244, col.)


(2) Varicella occasionally spread in smallpox hospital when accidentally introduced.
3. Vaccination has no influence on varicella; vaccinated and unvaccinated children are affected with equal severity and commonly those who have had varicella are just as susceptible to vaccination as those who have not.

4. The natural history of the two diseases are greatly different.

Other arguments might be adduced, but the above are amply sufficient. (1) The theory of the identity of the two diseases, however, gained considerable ground after the first introduction of vaccination. The advocates of its practice having a firm belief (which we now know was a mistaken one) in the permanence and completeness of its protection refused to acknowledge that the modified fever (which occurred in vaccinated persons was true varicella, but declared it to be "varioloid", varicella, etc. As these cases would naturally give rise frequently to the unmodified and therefore unmistakable disease, it is easy to understand the confusion which would arise.

(1) An excellent chapter on the subject is given in Morii "History and Practice of Vaccination"