"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 time 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 by personal perusal to verify a reference I have given, 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 as regards size 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, ~~viz~~ either of which would be of sufficient magnitude and importance to form a thesis by itself, viz Inoculation 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 ~~the~~ Dr. 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.

I

C. Killick Millard

City Hospital
Birmingham
Apl 25th. 1895

Summary of Contents

Photographs

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All the above authorities have been personally consulted. In addition numerous others are referred to whose works I have not had access to.

Introduction

Variola 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 breeds true and one attack confers immunity against further attacks. It undoubtedly gains great additional interest from its relationship to vaccinia 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 horrible disfigurements and terrible mortality has been one of the most dreaded, and consequently most thought of and most written of, of

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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 now essentially a preventable disease and because the success which has attended measures for its suppression has been so signally 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 &c. are being warmly discussed. Other important public health problems arise in connection with the provision of isolation hospitals.

Nomenclature.(1) - 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 deminutive 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, **viruelas**, the Italian Il vajuolo, & the French **verole** (subsequently petite verole). The French also have a name of their own - picqueté 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 **poccadl**, derived from **pocca**, a bag or pouch. The Anglo-Saxons also adopted this word which became modified at length to **pock** or **pox**. 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 German

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(1) The facts in this section are obtained from the works quoted (v. Bibliography) of Jas. Moore, J. W. Moore & McVail.

German name is blattern or pocken; the Danish & Norwegian - kopper; the Swedish - Smittkopper and the Dutch - poe.

History.(1)

The history of variola 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 3000 years. In an authentic Chinese work entitled "A Treatise from the Heart on the Smallpox" it is stated that the disease appeared in China in the dynasty of Tcheou 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 Hindoos. It has several names in the ancient Sanscrit language and there is a special deity who presides

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(1) This section is practically a resumé of Jas Moore's standard work, with modifications from McVail's art. in Stevenson & Murphy's Work.

over it, as is also the case in China

In spite of the existence of variola in the far East at such an early period of the Worlds' 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 Ancients comparatively very limited and only accomplished by lengthy journeys whether by land or sea, so the disease was certain to have been held in great abhorence it is quite conceivable how any infection which might break out at the commencement of a journey would be stamped out before a vessel or caravan arrived at its destination.

Whatever the correct explanation may be it is probable that the disease was quite 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

Such men however as Galen and Hippocrat
es 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 variola, for we
may be certain that if it existed at all it was
very prevalent. We must therefore take the
view that the supposed references had 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 historical War of the Elephant in the
year 569, immediately before the birth of
Mahomet. During the latter part of the 6th
and the whole of the 7th centuries it was
spread, by the Arabians, together with the Measles, (which was
looked upon as a variety of the Smallpox)
over 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 & France, and the

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disease

disease gradually spread North. It had certainly reached Saxony, Switzerland and Britain by the 10th, 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 discriptions of the Plague, Erysipelas &c., most epidemic diseases being classed, during the Dark Middle 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 "fere 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. Drs Mead, Drinsdale and others maintained that the disease was first introduced into Europe at the beginning of the 12th century by

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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 has been one of the most prevalent of all zymotic 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"; Hillary 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 wide-spread 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 every one 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 endeavoured to obtain most of the more important recent works together with a sample of the ~~ot~~ older standard ones. I append at the end of the thesis a complete list of the authorities quoted from together with the titles & dates of their works.

No definite allusion to Variola is made by Hippocrates, Galen, Celsus or the other ancient ~~authors~~ authors. The first writer on ~~the~~ the subject of whom we have any record was Aaron[1] 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 Almansor or "the Great." He flourished at Bagdad at the end of the 9th and beginning of the 10th century.

The

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(1) Moore Jas. "History of the Smallpox" p. 113, l. 7.

The best known of his works, "A treatise on the Small Pox and Measles"(1) 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(2) 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 10th century two more Arabian physicians, Hali Abbas and Avicenna wrote on the subject and the latter made the important observation that both Measles and variola were contagious. Little attention however appears to have been paid to this fact, and it was soon lost sight of

The view these old Arabians held was based upon the assumption that variola was a distemper natural to every human being. They regarded it as due to a poison in the system

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(1) "A treatise on the Smallpox & Measles" by Rhazes Trans. for the Sydenham Society by Dr Greenhill Syd. Soc. 1848

(2) pp. 23 & 34

system which was excreted 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 depletive 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 in the eruption. They attributed a special virtue to the colour red and everything surrounding the patient and even the medicines he drank were recommended to be of red. They believed in opening the pustules. Of supposed remedies they had an unlimited number.

The doctrine of the Arabian school were with ~~slight~~ unimportant 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 as

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* 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 teething or childbearing. v. "History of the Small Pox" pp 124 & 125.

as possible causes* while ~~and~~ its infectious nature was largely lost sight, but the same line of treatment was persisted in. Based as it was upon entirely erroneous conceptions of the disease there can be little doubt that so far from benefiting the unfortunate patient it was distinctly injurious and must have largely increased the fatality of the disease. If this was naturally as high then as it now is in unvaccinated cases the number lives of life from this one disease alone must have been appalling!

Reform came at last however. 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 came Boerhaave, who ceasing vain speculations on the ultimate cause of the malady, was the first to insist upon the all

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* It is interesting to note that there is a tendency in some quarters to revert to this view that the disease is caused by insanitary surroundings rather than by contagium.

all important influence of contagium. From this time on variola began to be considered scientifically. In the 18th century came inoculation and at its close vaccination. The most standard of early modern works is that of Dr. Jas. Moore, Director of the National Vaccine Establishment, entitled "The History of the Small Pox", pub. in 1815. 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 & Collie, both formerly medical superintendents of Smallpox hospitals under the Metropolitan Asylums Board, are still regarded as the greatest authorities ~~of the~~ from a clinical point of view, whilst as regards the natural history of the disease including vaccination, Dr. John C. McVail formerly Asst. Officer of Health for the Counties of Stirling & Dumbarton, and now promoted to the Local Govt. Board for Scotland, ranks easily first. Frequent reference are made in this thesis to his masterly article in Stevenson & Murphy's "Hygiene & Public Health".

Geographical Distribution

Like the plague, cholera and some other diseases variola 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(1). at the present time however it exists over almost the whole of the Habitad Globe, there being but few regions that are still completely free from it. Variola appears to find a very suitable soil among coloured races, and especially negroes(2), ~~who are not only very susceptible~~ amongst whom it is not only very prevalent, but also very fatal(3) It is endemic over large tracts of country in India and Further India Pringle(4) writing in 1869 after 13 years medical experience in India said it was the severest scourge the country was subject to, causing "frightful devastation" Since then however the more general introduction of vaccination has limited it 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. Iceland has suffered severely

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(1) Hirsch vol III. p. 128, l. 24, (Handbook of Geographical & Historical Pathology)

(2) & (3) " " p. 151, l. 16

(4) " " p. 134

severely from the disease. It has been introduced nineteen times[1] since the beginning of the 14th century and in many instances the resulting epidemics were of appalling severity In America[2] 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[3] 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[4] from Africa

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(1) Hirsch - op. cit. p. 135

(2) Chapman, "Lectures on the more important Eruptive Fevers" Philad 1844. Quoted by Hirsch, op. cit. p. 136 (2) Loc. cit.

(4) Hirsch - op. cit. p. 138

Influence of Climate, Race, Season Sex and Age.

Climate.— On this subject Hirsch[1] says "not many of the acute infective diseases "show in their incidence and diffusion so "complete an independence of the conditions of "climate and soil as smallpox" and the wide spread 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 variola may certainly prevail at all seasons, outbreaks are more common during ~~winter~~ winter and spring than during summer; in other words it is favoured by cold. This seems remarkable after what has been

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(1) Hirsch op. cit p. 144, C. 2 et seq.

been said about its prevalence in hot climes; Hirsch[1] however in a table which he gives shews 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.[2]

Sex.— At most ages the case-mortality is slightly greater in the male sex. The exceptions are the second and third year of life and the tenth to the fifteenth year, at all of which, for some unexplained cause, the female mortality slightly excedes the male.[3]

Age.— The age incidence of variola 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 variola was then a disease of childhood and infancy to an extent difficult to realise at the present day. Thus in Geneva (between the years 1580 and 1760) out of every 1000 deaths from the disease, 961 were in children under 10 years of

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(1) Op. cit. p. 147

(2) " " p. 148 (Hirsch)

(3) Whitelegge, "Hygiene & Public Health" 2nd Ed.

+ This is corroborated by McVail, op. cit. p. 395, l 9. (p. 264, l 23

of age[1]! at Kilmarnock (1768-64) 988 per 1000, and in London, (prior to the Vaccination Act of 1853) 818 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 then in fact 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. 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 W. Indies[2] soon after the discovery of America, and in Iceland[3] after having been absent for a century. As regards case-mortality however, age as in all zymotics has an important influence and will be discussed under the head of fatality-

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(1) Supp. Ann. Rep. Loc. Gov.t Board 1884

(2) & (3) Mc Vail op. cit. p. 391, l. 3 f. bottom

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, as for instance Kilmarnock 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 (1) 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 increase or decline apart from any apparent cause, at least suggests the existence

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(1) Op. cit. p 145, l. 15

existence of some further, tho' 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 variola, to know what the ratio was in the days when neither vaccination nor inoculation were ~~known~~ practised. Unfortunately such statistics as we have, and they are but few, vary very considerably. We know however that wide-spread epidemics occurred, especially when the disease was introduced into a new country or into localities whence 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. Its ravages in Iceland, Africa and America have already been referred to. In Greenland in 1734

(1.) Marson. "Reynolds System of Med" 2nd Ed. p. 242, l. 5,

1734 nearly two thirds of the entire population were swept away[1]. In this country we know that the total mortality was great for the London "Bills of Mortality"[2] shew that on an average 7 to 9 per cent of the persons buried in London during the 17th and 18th Centuries had died of small pox, 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. Marson states that under 5 years of age it is 50 per cent.[3] It decreases steadily and rapidly till its minimum in the third quinquennium and then rises steadily for the rest of life. Marson[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

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(1) Simon, quoted from Stevenson & Murphy's Hygiene p. 397, l. 25

(2) Whitelegge, "Hygiene & Public Health" 2nd Ed. p. 261, l. 15

(3) "Reynolds' System" p. 239, l. 14 (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 Iceland epidemics): or taking the other extreme when the epidemics occur at intervals of only a few years and therefore the victims mostly infant

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(1.) The writers experience, based however upon vaccinated cases, is that over 60 yrs of age, ~~the fatality~~ a very severe attack is comparatively rare & therefore the fatality not very high. This is contrary to what one would 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 types of epidemics that we see in other zymotic diseases.

Taking these facts into consideration we are able to give an explanation of some bona fide 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 minimise the benefit conferred by vaccination in rendering variola 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 per cent. M'Vail[1] however has shown:- (1) that many of these cases (about 6000) occurred in Boston in New England and amongst these the mortality was under 15 per cent, thus lowering the average of the whole. But in Boston, as shewn by Hirsch, 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

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(1) Op. cit. pp. 398 & 399

the age incidence of these 6000 cases was probably as favourable as it well could be. This probability is confirmed by the fact that in 132 of Jurin's cases occurring in Aynho in Northants., where the age distribution happens to be recorded, over 60 percent were at ages between 5 and 25, i.e. the most resistant period of life: (2) that there is ground for believing that Jurin, 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 own) 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 Jurin's figures, and it is to be observed that the known age incidence of the cases at Aynho support M'Vail's (1) supposition, for there was not a single case amongst them 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 of cases, the average was 25·3 per cent.

(1) Loc. cit. and

and rose during the last 25 years of the 18th century to 32.5 (1). 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, 26 to 32 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 fatality at the present-day when most of the cases which occur are in vaccinated persons.

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(1) Seaton, quoted by M'Vail op. cit p. 394

Etiology

Etiology.— Smallpox is a typical member of the group of exanthemata. The most striking feature of this group is the property of infectiousness, and ever since this characteristic has been recognised, 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 particulate consisting of living particles - germs. ~~Unfortunately~~ In only a limited number of the exanthemata however has this "contagium vivum" been as yet positively recognised, but a sufficient and ever increasing list exists of those in which it has been so recognised 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 micro-organisms, chiefly of the nature of cocci & streptococci, 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 shew their causal relationship to the disease. In the case of the Klein & Copeman bacillus however it is otherwise and only two

links

links, are wanting, in the chain of evidence laid down by Koch as necessary to prove a micro-organism the "causa veraus" of any disease; viz.- its cultivation outside the body through successive generations without its 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 vaccina.

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

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(1.) McVail, op. cit. p. 400, l. 25. (2.) Ibid l. 28

(3.) Moore J. W. op. cit p. 70, l. 30,

he is in the acute infectious stage. The contagium is generally supposed to be given off both by the breath and by the exhalations 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[1]. The infection, whatever its nature, can certainly be carried from place to place by fomites of all description. A striking illustration of the ease with which this takes place in smallpox occurred in 1894 in Nottingham[2]. Some lace 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 unrecognised attack of the disease. The lace 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[3] 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" for May '94 p. 256

(1.) It has been suggested that the skin is the channel through which it enters, each pustule corresponding to an inoculation.

(3.) Public Health Mar 1894, p. 197, Col,

could be excluded. As we should naturally expect, all scabs, crusts 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, variola 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 Thos. Watson[1] relates a case where the body of a man who had died of the disease was brought into Mr Cæsar Hawkins' dissecting room and four students thereby contracted the disease. Compared with the other exanthemata, variola 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 fomites, it is probably at least as easily carried in this way as any disease, not excepting even 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 vitality of the infection, i.e. its power of resistance to external influences after it has left the body, is probably not so great, for infected houses, fomites &c. lose their power of infecting ~~corpses sooner than~~ comparatively soon. The ~~inf~~ contagium is

(1) Lectures on Medicine, 5th Ed. p. 935, l. 38

is also more readily destroyed by artificial means, i.e. by disinfectants.

Variola is eminently a disease which can be conveyed by inoculation, all that is necessary being to rub variolous matter into an abraded surface of skin in a susceptible person. The important features of the disease when contracted in this manner are that the incubation period is shortened by several days and that the type of the disease is usually mild. The ease with which variola is inoculated is one of the most striking differences ~~from variolla~~ 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 on it, or, as in the cases the writer has seen, may develope the disease afterwards. Frequently in the former case the child is born dead.

"Aerial Convection".— One of the characteristics of the infectivity of variola is its remarkable carrying distance. Variola is at the other end of the scale in this respect to typhus. The well known investigations of Power (2) in connection with the Fulham Small pox Hospital have shewn that the carrying or "striking" distance of the disease is extraordinarily

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

(2) Append. to Hosp. Commission Rep. 1882 and Supp. to 16th Ann. Rep L.G.B.

extraordinarily great. Taking the hospital as a centre and drawing concentric lines round it at distances of ¼ mile from each other, Dr. Power prepared "spot maps" shewing 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 & the number of fresh cases occurring round the hospital was clearly brought out. His general conclusions(1) were - (1) that the hospital contributed largely to the ~~number of cases~~ prevalence of smallpox in the neighbourhood; (2) that the incidence bore a very exact relation to propinquity to the hospital; (3) that the houses in the main thoroughfares were not specially affected; (4) that variations in the use of the hospital were followed by corresponding variations outside, but that convalescent cases were not factors in the 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 contributory to the smallpox around the hospital, pertained

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(1) Epitomised from Supp. to 10th Annual Rep L. G. B. p. 322

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 ~~man~~ administered must of necessity be a source of danger to the surrounding population, and the Loc. Gov.t Board have rightly refused, since Dr. Power's 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 ~~[illegible]~~ by the Medical Officer of the Loc. Gov.t Board (Dr. Thorne Thorne) at the beginning of the present year, on the subject of provision of isolation accommodation by Local Authorities it is stated that ~~[illegible]~~ the distance at which a smallpox hospital may operate dangerously cannot at present be established with any degree of certainty though it may be taken to be considerable. He holds however that no Local Authority should

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confine plots

"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 either a hospital, whether for infectious diseases or not, or a workhouse or any similar establishment, or a population of from 150 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 ... ." Power'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, Barry found a similar radiation of infection from the smallpox hospital in that city; but unfortunately the question of personal connection could not be quite excluded which largely destroys the scientific value of the observation. More recently Priestley has published striking evidence from Lincoln[2] and in this case the question of personal connection 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

(1.) Supp. 14th Ann. Rep. Loc. Gov. Board pp. 55 et seq.

(2.) Ann. Rep. of M.O.H. for Lincoln 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 shews with ominous 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~~ aerial convection. Within 500 yds of the hospital are the workhouse & workhouse infirmary; these institutions have suffered severely, but though many of the cases which have occurred were "secondary" ones there ~~have~~ 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 ward ~~into which fresh cases had not been admitted for over a fortnight~~ in patients who had not left their beds for months, and where visitors were few.

<u>Susceptibility</u>.– 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 resembled, as chickenpox & measles may still

almost

almost be said to do, that of distemper to the canine species. It was an affection which every individual had to have sooner or later, and was generally contracted at the first exposure to infection. As 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~~ 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 variola resembles many other infectious diseases. A case is recorded of a smallpox nurse who had never been artificially protected in anyway 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 sometimes exists in the case of vaccinia, though judging from Cory's experience

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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 however which came under the writer's own ~~note~~ 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 vaccinator. The writer has another case of (apparent) resistance to vaccinia ~~at the present time~~ under observation at the present time. It is the infant child of the man whose

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(1) The woman was a patient in the Birmingham City Hospital

whose work consists in carrying infected articles 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 (even only 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 then we have no knowledge as to what proportion of the remaining 25% were really exposed to infection. Cross[2] found in the Norwich epidemic of 1820, out of 603 persons, 10 + 5 + 1 = 16, i.e. about 2%, were insusceptible; and Kilpatrick[3], basing 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. 17, par. 13,

(2.) Quoted from McVail op. cit. p. 402, l. 22

(3.) "An Analysis of Inoculation, J. Kilpatrick M.D. 2nd Ed. 1761 Quoted fr. McVail

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. Unmodified variola, i.e. variola in which the disease runs its ordinary course, the pustules developing, "maturating" & scabbing 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. ~~I can~~. It is possible indeed for there to be no eruption at all, as in the undoubted cases of "variola sine variolis". Unmodified variola is what we see in those who have not been protected by any of the means known to confer immunity, such as vaccination, inoculation or previous attack. "Modified" variola may (2) 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 (1) stops

stops developing, i.e. "aborts"; at some stage before the last, there is no secondary fever, and the patient quickly gets well. Now it is a question how far ~~[illegible]~~ modified attacks occur in persons who have not been protected by any of the means enumerated; in other words, how much natural resistance alone is capable of it? It is commonly assumed that the various diseases described by the older writers under the names of "hornpock", "pirle-pock", "chicken-pock", "swine-pock" "water-pock" &c. were examples, many of them, of such modification, but it must be owned this true pathology is by no means certain. Many of them were undoubtedly cases of ordinary ~~[illegible]~~ varicella which we now 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 may be explicable as cases of true variola occurring in persons who had had a previous attack or ~~[illegible]~~ been inoculated. Wherever these "variloid" diseases, as they were called, occurred in epidemic prevalence, as they sometimes did if history is to be relied upon, without intermixture of unmodified cases, there is strong presumptive evidence against there being variolous at all, for the reason that present-

day

day experience shews that though different epidemics may vary considerably in fatality there will always be, in any given section of population, and this even in spite of vaccination, a large proportion of individuals who if exposed to variolous infection will contract unmodified attacks.

At the same time I shall not attempt to deny that genuine cases may occur(1); but I believe them to be very exceptional. During the present epidemic in Birmingham (1893-95) out of over 3000 cases of Smallpox admitted into the hospital whence I am now writing there have been only one or two cases truly modified in persons who apparently were quite unprotected. Unfortunately even these are not quite certain, as they were not carefully investigated and it is possible that previous vaccination may have been overlooked. As illustrating the possibility of this I will here insert an article published in the "Public Health" Jan 1895, giving particulars of a case in point.

(1.) The writer has been informed by Dr Priestley, the Med. Off. 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.]

"Public Health" Jan 1895

Incubation Period.- Variola 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 variola appears on the day fortnight (i.e. 15th 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 375 cases are given by Dr Saville (1)

(1.) "On the Diagnosis of Smallpox in its early stages" by Thos. D. Saville M.D. B.M. Journ. Ap 29. 1893. pp. 888 & 889, Col 2.

Date of appearance of eruption.

31.00%	on	3rd day
26.4	"	4th "
15.7	"	5th "
15.7	"	2nd "
4.8	"	6th "
4.0	"	1st "
2.6	"	7th "

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 Variola 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 after 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 ~~exanthemata~~ of the exanthemata. In the City Hospital Birmingham all cases are kept in for a minimum of 18 days (or of 21 days if the eruption has been thick) from the first appearance of the eruption even if all scabs have come away before that, (in mild cases they may have all disappeared in ten or twelve days) or as much longer as may be necessary for the process of scabbing to become complete. In confluent attacks this often takes 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 sinus or "sore place". For this latter reason exceptional cases are sometimes kept in for several months. How far

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these 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 "return" cases and those were not at all certain. It may therefore be fairly assumed that the period during which the infection continues 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 Asylums Board in their smallpox ships require almost exactly the same as is done 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, that 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 nethertheless not yet absolutely proved, though the evidence pointing to such a conclusion is, in the writer's opinion, almost irresistable. Edward Jenner himself believed it, though he had far less positive evidence than we now have. On the otherhand 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.) smallpox

The arguments against the view I have stated, viz.- that the two diseases are due to the same essential virus are :-

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1. Great dissimilarity between their symptoms and characteristics; whilst the one is very dangerous to life, highly infectious and accompanied by a generalised eruption, the other is so mild as to seldom prove fatal, is not infectious (in the ordinary sense of the term) and has no generalised 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 photo appended, where a young girl, (vaccinated in infancy) is shewn with variola 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[1] experience in 1878 may be quoted. In that year he carried out some extensive researches upon the variolation of bovines at the Brown Institution for the Loc. Gov't Board. Altogether he inoculated some 33 cows and heifers with variolous matter 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

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(1) Supp. Ann. Rep. Loc. Gov't Board 1878-79 p. VII

results. Many other workers have had a similar experience or indeed have obtained results which rather pointed against the theory. The best-known of this is Chauveau[1] who maintained that he produced in the cow a papule (years 1863-65 and again in 1871) but the matter taken from the papule produced only similar papules in other cows, whilst in human beings in ~~three~~ instances it produced, ~~never~~ sometimes vaccinia, but variola. A similar result is said to have been obtained in ~~St~~ Massachusetts[2] in 1806, at Munich[2] in 1839 and at Berlin[2] 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 characters of true smallpox. This remarkable fact appears to the writer the strongest argument of all, for when we consider analogous modifications in other viruses produced by change of host or environment we find that virulence is quickly regained on returning the virus to its original conditions of growth.[3] ~~The bacillus~~

All these arguments however can be met. Thus:-

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(1) Crookshank, quoted by Vaillard, op. cit. p. 423, ℓ 33

(2) Ibid

(3) cf. Bacillus Anthracis

1. However great the apparent differences may be we have no right, a priori, to put any limit to the extent to, or manner in, which a virus may be modified. It is a point which with our limited knowledge of the subject can 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 (cf. Hydrophobia). Moreover the true differences are not 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 localised 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~~, for it is generally assumed that the infectiousness of a case of variola is ~~in part~~ caused by and is 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

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the (alleged) existence of cases of "generalised vaccinia" or vaccination accompanied by a more or less general eruption. On the other hand there are many points of ~~the other~~ great similarity between vaccinia and variola 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 ~~both~~ are inoculated, the local lesion resulting[1] ~~is exactly identical~~ is very similar in either disease. and this similarity is apparent not only on macroscopic, but on microscopic examination[2]. The clinical symptoms also are similar differing only in degree. Lastly there is the all important and undoubted fact that the one confers immunity[3] against the other. This is 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. Collins, Creighton and Crookshank) deny that this immunity conferred by the one against the other exists attributing any apparent experimental results to what they call "temporary antagonism"; as this is only

tripping

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(1) For a full description with illustrations of the vaccine eruption, v. Supp. Rep. Ann. Loc. Gov. Board 1889 and also 1892-93.

(2) Ibid. Report by Dr. Klein p. 139 l. 2 p. bottom

(3) The immunity conferred by vaccinia is certainly not so complete and permanent as that given by variola itself, but

trifling with phrases, and as the whole weight of scientific evidence ~~is~~ goes ~~entirely~~ to prove the ~~the~~ ~~[illegible]~~ ~~of the~~ immunity conferred by vaccinia against variola, and vice versa, nothing further need be said.

2. It is certainly true(1) that a person may suffer from variola and vaccinia simultaneously. This however proves nothing. It is probable that two or more stocks of the virus of any(2) inoculable disease will develope and run their course simultaneously in the same person provided they are inoculated at the same time or so nearly at the same time that the last may have time to develope before immunity has been set up by the first. These are just the conditions which obtain when variola 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 ~~period~~ interval, usually at least 4 days, if the smallpox be contracted in the usual way.

3. Although numerous experimenters have failed in their attempts to produce cow-pox.

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foot-note from → by considering the great attenuation the virus has undergone in other
last page contin. directions it is a is surprising and certainly a most fortunate thing for humanity that the protection is as complete & durable as it is

(1) See photo appended, No. V

(2) As instances we have Syphilis. also vaccinia & variola as regards themselves

by inoculating smallpox, their negative evidence proves nothing against the positive evidence of those who have succeeded; it merely shews that the positive result is difficult of achievement and depends upon chance or rather upon conditions at present not understood. Both Ceely[1] and Badcock[2], especially the latter produced in many instances in heifers, by inoculation 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 (Ceely & 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 complication naturally provided a loop-hole by which the opponents of the theory could escape from the otherwise logical conclusion as to the true relationship of cowpox and human smallpox, for it was at once suggested that the results obtained were in some way or other really attributable to vaccinia and not variolous inoculation. This it must be allowed was a valid objection. Several present day

Scientists

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(1) Marson, op. cit. vol I, p. 476, l. 14

(2) " " " " " l. 19

Scientists[1] however have successfully repeated the experiment (notably Surgeon-major W. G. King, of the Madras Med. Service, ~~and~~ Dr. T. W. Hime, formerly Med. Off. Health for Bradford and now Director of a Calf Vaccine Establishment, and Dr. S. Monckton Copeman, now Med. Inspector under the Loc. Gov.t Board) but with this difference that they omitted the questionable method of simultaneous vaccination. King's[2] results may be epitomised as follows:- He inoculated a calf with variolous matter from a human being suffering from smallpox. From the resulting lesion matter was obtained wherewith to inoculate a second calf, and so on through seven calves in succession. From the seventh calf a ~~child~~ child was inoculated, and the resulting lesion was in no way distinguishable from that produced by ordinary calf vaccination

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(1) A very complete chronological list of the names of those who have carried out variolation experiments on bovines is given by Copeman 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 almost all these workers with the exception of Chauveau and his colleagues on the Lyons' 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.

(2) Vide reference marked * at foot 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 his old strain of calf vaccine.

Dr. Hines'(1) experiments though not so extensive were equally successful. He inoculated a calf in 14 places with human variolous 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 ~~the first~~ one or two of his incisions. 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 and course of normal vaccinia. Both calves were afterward found to be insusceptible to the action of ordinary calf vaccine. Dr. Hime refers the failure of Chauveau and others to their experimenting upon cows and heifers instead of upon calves which appear to be more susceptible to variolation. Himes results are remarkable in that he apparently obtained true vaccinia from variola at the first remove. Dr. Moreton — Coperman working at the Brown Institution made

from

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(1) Brit. Med. Journ. 1892 Vol. II, pp. 116 et seq.

* Recorded in the Transactions South Indian Branch Med. (v. last sheet) Service Vol. IV, No. 1. June '91, referred to in Brit. Med. Journal 1892, Vol II p. 217, col. 1, l. 26 (fr. bottom).

four attempts[1] but only one of these was an undoubted success. In none of his experiments did he obtain anything approaching to a true vaccine vesicle in the calf first inoculated as happened in ~~Klein's~~ Hime's case.[2]

Since this thesis was commenced the results of a second series of experiments on the variolation of bovines has been published by Dr. Klein.[3] ~~His~~ These results coming from a scientist like Klein are of the highest importance, especially as they are quite different from the negative results he formerly obtained. His latest researches entirely corroborate those of King, Copeman, Simpson & others. By using calves instead of cows he obtained a positive local result from which he obtained matter wherewith to inoculate other calves until at the 4th remove he ventured, together with Dr. Cory, to vaccinate a child, the result being the production of typical vaccinia. This, retro-vaccinated into unvaccinated calves, produced typical cow-pox, but fail altogether to affect calves previously vaccinated. It is noteworthy that the local result he obtained in the calves first-

(1) Journ. Path. & Bacteriology, Vol 2. pp 413 to 426

(2) Other important workers in this field are Haccius in Geneva (1890-91) and Simpson in India (1892). Simpson's results resembled Hime's.

(3) Supp. to 22nd Ann. Rep. Loc. Govt. Board Append. B No 3. pp. 391 & seq

first inoculated (i.e. prior to passing through the child) did not, even at the 4th remove, exhibit to any extent the appearance of vaccinia. The lesions remained papular without any trace of vesiculation and matter for further inoculations had to be obtained by scraping and clamping.

Dr. Kleins important research did not end here. He went on to look[1] for the long-sought for microbe of vaccinia and variola. Thinking over the known facts that lymph taken from a ripe vaccine vesicle, though thoroughly dried on "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 micro-organism, whatever it might be, was a spore-forming one. Thus the early lymph containing the organism prior to the formation of spores would much more readily become inert, than the later and spore-containing lymph. He accordingly obtained lymph from the budding vaccine 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 of

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(1) Loc. cit.

of the vesicle this bacillus was still present but in far 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 suspects were spores. The same result was obtained in either human or calf lymph. Turning next to variola and resorting 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. There is strong reason for assuming that this bacillus is the true microbe of variola and vaccinia, but unfortunately Klein has as yet entirely failed in his attempts to cultivate 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 of the bacillus to variola and vaccinia. At the same time the fact is in itself an argument against the organism being merely adventitious for other ~~of~~ organisms found in lymph and since proved to be only adventitious can all be cultivated outside the living body.

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

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(1) Paper on "Pathology of Vaccinia..." read at 62nd Ann. Meeting Brit. Med. Assoc. Bristol Aug. '94. Pub. in Brit. Med. Journ. Sept 22. 1894

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 his 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 Chauveau, with the object of attempting, by successive inoculations, to reduce variola to the "mother-pustule" which forms at the actual seat of inoculation. In the days when inoculation was practised, and especially with the more improved Suttonian method, it was no uncommon thing for the general eruption to be reduced to a few pustules only. Working on the same lines Chauveau succeeded in some of his experiments in producing merely a few minute papules or pimples in the immediate vicinity of the mother-pustule.

But

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(1) The writer had the privilege of working with Klein in his laboratory at St. Bart. Hosp. during the spring of 1893. Klein's work had already been completed as early as that - the writer himself saw the bacillus on Lantern slides. Owing however to the delay of the Government Printing Dept. the results were not published till towards 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 persevered in long enough, they would ultimately have been successful, it is impossible to say, but if it be true that vaccinia is only modified variola, it seems at least possible that the conversion of the latter into the former might be ~~performed~~ accomplished by means other than the passage of the variolous virus through a bovine animal.

Alleged Relationship to Varicella

It is hardly necessary at the present day to insist upon the absolute distinction between variola 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 variolous affection. Each disease invariably breeds true and is quite independent of the other.

Nevertheless, so similar sometimes on 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 Fuller[1] and then Heberden[2] became convinced of their non-identity. The latter wrote a paper on the subject in 1767, which has now 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 these the most notable were Hebra of Vienna and Thomson of Edinburgh.

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(1) Gee, Reynolds' System of Medicine, 2nd Ed. p. 520 l. 13

(2) Moore Jos. Hist. & Pract. of Vaccination 1817 p. 95, l. 7

It is indeed remarkable that such a really eminent man as Hebra should have been so mis-led, especially after the real points of distinction had been ~~[illegible]~~ 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 ~~[illegible]~~ is not inoculable. This has been proved* by Bryce(1), Trousseau(1) 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 one after the other or even at the same time(2)

3.

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* According to Hesse who collected a long series of cases in 1829 a small minority of inoculation experiments appear to succeed but doubt has been thrown on the validity of these observations (v. Fagge 2nd ed. Vol I. p. 244, l. 21.)

(1) Quoted by McVail. op. cit. Vol II. p 462, l 21 & 24

(2) Varicella occasionally spreads in Smallpox hospitals when accidentally introduced.

3. Vaccination has no influence upon varicella; vaccinated & 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 & clinical features of the two diseases are different.

Other arguments might be adduced but the above are amply sufficient.(1) The theory of the identity of the two diseases doubtless gained considerable ground after the first introduction of vaccination. The advocates of the 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 smallpox which occurred in vaccinated persons was true variola, but declared it to be "varioloid", varicella, &c. 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.

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