

CHINA AND THE ORIGINS OF IMMUNOLOGY

JOSEPH NEEDHAM



Centre of Asian Studies
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First S. T. Huang-Chan Memorial Lecture

9 November 1979

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FOREWORD

I cannot begin this first S.T. Huang-Chan Memorial Lecture without thanking the authorities of Hong Kong University (itself one of my *almae maters*) for the great honour they have done me in inviting me to give it. It is always a pleasure to come to the South China region, and no circumstances could be more propitious than these.

In years gone by I met Mrs. Beatrice Huang (Dr. Chan Shu-Tzu 陳淑慈) twice, and therefore mourned her premature disappearance along with many Hong Kong friends and colleagues, not least her husband the microbiologist Emeritus Professor C.T. Huang 黃啟鐸. She was a dedicated anatomist, Reader and from time to time Acting Head of the Department, particularly interested in research on the growth of the human body, and in the physiology of the bone-marrow cells. Born at Canton in 1920, she studied at the Chiangsi Medical College, and thirty years later embarked on her anatomical career in Hong Kong. Her profession took her to places as far flung as Buffalo, Birmingham, Boston, Leningrad and Tokyo, a most worthy representative of Chinese science to the world republic of learning. I hope she would approve of what I shall say today about an outstanding Chinese achievement in the field of medical biology.

Before going further, a tribute must also be paid to my chief collaborator Dr. Lu Gwei-Djen, with whom this story was worked out earlier this year. It will form part of Volume 6 of *Science and Civilisation in China*, but we have abbreviated it so as not to detain you too much, like Ancient Mariners, today. Finally we should like to thank the eminent Dr. Peter Wildy, Professor of Pathology at Cambridge, for all the help and advice he has given us.

Joseph Needham
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June 1980

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CHINA AND THE ORIGINS OF IMMUNOLOGY

Introduction

It will be generally allowed that the inoculation for the smallpox was the beginning of all immunology, one of the greatest and most beneficent departments of modern medical science. In what follows we propose to show that the practice can be documented a good deal earlier in China than in any other civilisation (i.e. from about 1500 A.D.), with a weighty tradition taking it back much earlier still (to about 1000 A.D.), so that its numerous appearances in less developed societies spread widely over the Old World may not unreasonably be interpreted as emanating from the Chinese focus. Since the beginning of the eighteenth century A.D. every Western historian of epidemiology and public health has known that something important happened in this connection long ago against an East Asian background, but almost no scholars with adequate access to the Chinese literature have made it their business to dig out the facts. We often meet with this situation; for example, all modern historians of rocketry and firearms have been aware of the half-dozen centuries of Chinese development of the first chemical explosive known to man, which occurred before the first appearance of the metal-barrel bombard in Europe, but no one (except of course the historians writing in Chinese themselves) has drawn out the treasures which the texts contain, and which the whole world ought to know about.

Now the action of the ancient Chinese physicians was again an illness which had not yet appeared, but that again was entirely in line with a medical conviction which started very early in Chinese history, the conviction that preventive medicine was the best. The most perfect physician cures a disease before it has ever shown itself at all. There are Warring States sayings which could be quoted, but the Han time is good enough for making this point. "A skilful doctor", wrote Liu An, "cures illness when there is no sign of disease, and thus the disease never comes."¹ The Chinese Hippocratic Corpus constantly makes the same point: "It is more important to prevent illness than to cure the illness when it has arisen."² And one of the best statements is in the book of the great Taoist alchemist and physician Ko Hung, written about 320 A.D.:³

Thus the adept disperses suffering (physical or mental) before they have begun⁴ and cures diseases before they have made their appearance.⁵ He practices his therapy before any untoward signs have manifested themselves, and does not have to pursue what has already happened.

With this background in mind, a setting which many further quotations would readily support, it is hardly surprising that China should have been the culture where we find the earliest evidences of preventive inoculation.

The idea itself must have arisen from the ancient folk observation that nobody ever suffered from smallpox more than once in a lifetime. In regions where it was endemic, however, everybody was due to get it once. It was one of the "gates" of life that children, or sometimes adults, had to pass through, and one could well-advisedly pray for a mild attack and a happy recovery without too much scarring. On one visit to the cave-temples of Chhien-fo-tung, near Tunhuang, we well remember finding a cave where the country people had pasted up pieces of yellow paper along the processional circum-ambulatory way round the central group of statues, where of

old the monks would pass chanting their sūtras; each paper bore the character *kuan*; "gate", and there were the names of the diseases as well, for example one for cholera, one for chickenpox, one for whooping-cough, and of course one for smallpox. Each disease that might be expected had its gate, and no doubt the children were taken there and passed along the round, with a station at each flag where the resident Taoist would say the appropriate prayers. Accordingly, with the background of preventive medicine in mind, it would have occurred naturally enough to some Taoist physician that if one could instil or "engraft" the disease artificially in a very mild form, somehow gently, ensuring a lenient attack, then the patient would have "got it over", and that gate at least would be successfully traversed. He or she could not have had the remotest conception of all that was being set in motion thereby, for the concept of active immunity (whether cell-mediated or humoral) was as yet far ahead in the womb of time. Here it may occur to the historian to wonder why this happened first with smallpox and not with any other of the exanthematous diseases, but the answer lies near to hand in the thought that smallpox produces pustules with an abundant content of infectious lymph readily available for transfer, and when these break down they are covered with scabs which are also rich in infective variola virus particles. Centuries later immunologists would make "vaccines" killed or living, sera and antisera, for many other human and animal diseases, but all would require a much more sophisticated methodology than that which sufficed for the first smallpox inoculations.

Continuing this introductory *tour d'horizon*, we may like to proceed from the known to the unknown, and take a look at the coming of smallpox inoculation to Europe. The first that anybody ever heard of it was in letters from China to the Royal Society just before 1700 A.D. But no one paid much attention to them (nor to those letters from the Jesuits in China later in the eighteenth century A.D.); the effective channel of introduction was from the

Levant in its second decade, partly through the intermediation of an aristocratic Englishwoman, the wife of the ambassador at the Sublime Porte, and the culture-area concerned was essentially Turkish, though Greeks and Caucasians had also been carrying on the technique for years beforehand. Two clear relations from Greek physicians practising in those parts then came to hand, achieving publication in the *Philosophical Transactions* and setting the stage for a whole century of inoculation, first in England and America, then more slowly in France, Germany and the other countries of the continent. The appalling ravages of smallpox — no other description is adequate — were thus for the first time checked; and then, at the end of the century, in 1798 A.D., came the discovery of Edward Jenner that cowpox lymph, which was not dangerous for man, would give almost complete protection against smallpox itself. Thus the familiar vaccination came into being.

Jenner's discovery retains, and always will retain, a high importance in the history of medicine, but it cannot quite be regarded as the isolated peak of scientific achievement that many writers have thought it to be; and this for a number of reasons. (1) Smallpox inoculation was not really so dangerous as has sometimes been supposed, though it is certainly true that without adequate isolation of the patients it could perpetuate foci of infection in the population which might disastrously spread. But mortality with the technique was not nearly as great as has sometimes been represented. (2) Inoculation did have a powerful effect in the reduction of mortality from smallpox during the eighteenth century A.D., and indeed it is claimed that its demographic effects can be demonstrated. (3) Inoculation gave permanent protection against the disease since the active immunity gained was so strong, while vaccination (contrary to Jenner's original belief) has to be repeated every few years. (4) Jenner's cowpox lymph was quite soon "contaminated" with variola so that mixed inocula were certainly given in many thousands of cases. (5) His intervention led to

something which he himself could never have anticipated, namely the origination of vaccinia virus, a virus with no known natural host, kept going only in vaccine institutes by passages through animals or in cultivation on the chorio-allantoic membranes of hen's eggs. Serologically the three viruses are very similar though they can readily be distinguished, and the most likely current view is that vaccinia was a genetic hybrid between the cowpox virus and the human smallpox virus, variola. The general upshot of all this is that inoculation ought not to be regarded as the crude and dangerous "folkloristic" predecessor of vaccination, but rather as the real first step towards that vast armamentarium of vaccines and sera, antitoxins and toxoids, which mankind now possesses, with all its accompanying developments in a whole new science, immunology, today based on, but not originally stemming from, virology and bacteriology.

Here it is necessary to bear in mind that the exact reconstruction of what originally did happen both with early inoculation and early vaccination is distinctly difficult. The physicians of those days were not able to write with such precision as became usual afterwards, their practices were often not meticulously recorded, and there is no possibility today of examining the strains of virus which they used. Statistical information is also uncertain and imperfect, often available only in local records fitfully kept, so that it is generally not possible to be quite sure of the effects of the various procedures. But all this must not deter us from trying to fit together as carefully as possible a picture of the events which took place at the birth of immunology.

History

The history of the disease of smallpox itself is obviously indispensable for the whole discussion. Only too many medical his-

torians have airily said that "it has been known for countless centuries", but in fact a specific disease can only be identified for certain when it has been given a specific description. Neither Hippocrates nor Galen accomplished this, the former probably because he (or his group) never met with it; but there is a good account, and a differentiation of it from diseases such as measles and chickenpox, in the writings of the great Baghdad physician and alchemist al-Rāzī about 900 A.D. Again significantly, perhaps, he had been anticipated in China by Ko Hung (ca. 300 A.D.), even if his statement was subsequently amplified by Thao Hung-Ching, also a great physician and alchemist, about 500 A.D.

Many medical historians have also said that inoculation "was practised for untold centuries as a folk custom", but this assertion rested exclusively upon what we may call ethnological evidence, deriving from Central and Western Asia, many parts of Africa, and European information supposedly pre-dating the introduction of inoculation there. These facts need to be viewed against the background of the knowledge gained from the study of the Chinese texts. To summarise, therefore, what we shall later set forth in detail, the practice of smallpox inoculation begins to be documented in China in the Ming period, from the beginning of the sixteenth century A.D. onwards, i.e. from a time much earlier than any accounts of it from other parts of the world. Moreover it was then accompanied by a tenacious tradition that inoculation had first been practised towards the end of the tenth century A.D., by wandering Taoist healers from Szechuan. We believe that this tradition has to be taken seriously. From the earliest days of medicine in China, there were "forbidden prescriptions",⁶ "confidential remedies and techniques", which were handed down from master to apprentice, among the physicians as well as the alchemists, and sometimes sealed with oaths of blood. There were also books passed down in the same way, as in the case of Pien Chhio (sixth century B.C.), whose master Chhang Sang Chün conferred upon him private scrolls with warnings⁷

that their contents should not be revealed to uninitiated practitioners. In early times there had been a strong element of tabu about these "forbidden prescriptions", together with the conviction that injudicious disclosure would lead to the medicine becoming ineffective. Of course this social situation lent itself to abuse by mystagogues and quacks chiefly interested in making money, but of the existence of secret traditions there can be no doubt, and particularly where a technique was somewhat dangerous, certainly rather daring, they would have applied with particular force.

At all events, from the early sixteenth century A.D. onwards there grew up in China a specialist literature the books of which are easily identifiable because their titles usually begin with the words *Chung Tou...* "Transplanting the Smallpox", instead of *Tou Chen...* "Smallpox, Measles and Chickenpox". The secrecy was breaking down, the technique was becoming widespread, even entering royal and imperial families, and this was happening just about two centuries before the spread of smallpox inoculation in Europe. Besides, if we accept the tradition going back to the Sung, there had been eight or nine centuries for this bold exercise in preventive medicine to spread out over the Old World and Africa in all directions, and this in fact is just what we think it did.

An interesting problem arises here with regard to the method used. In China it generally involved the implantation of the pustule-contents or (more often) the scab-extract in a pledget of cotton-wool into the nose, so that the nasal mucous membrane was the point of entry. It shows great acumen on the part of the Chinese physicians to have guessed that the respiratory tract was the normal route of infection, but in the cultures between China and the West, as also in Africa, scarification and introduction of the lymph into the epidermis was the commoner method.

Theories of Smallpox and Inoculation

Another matter which we must take up is that of the various

theories developed to explain the nature of smallpox — and indeed many other epidemic diseases as well. As soon as one looks into this one finds such an extraordinary similarity between the Chinese and the European ideas that it is hard to believe there was no intellectual contact or interchange. Broadly speaking, there were two possibilities, (1) that the "morbific agent" was internal to the patient, a matter of intrinsic predisposition; or alternatively, (2) that it was external, the action of something in the human environment. The second possibility divided again into (a) an ascription to the airs or the seasons, at times unhealthy, even mortally poisonous, and (b) a belief in the activity of invisible malign animalcules in the surroundings of human beings, liable to break out from their hiding-places whenever the conditions were just right. These three possibilities could be called, the genetic, the meteorological, and the contagious respectively. Let us examine them in turn, first in the European and then in the Chinese context.

Theory of the "innate seed" of smallpox was supported warmly by many eighteenth century A.D. medical writers. It was supposed that there was some inherited contagion from the maternal blood, some virus, venom or ferment latent there, but destined to burst into the flower of smallpox whenever the conditions were favourable, and every individual would have to go through it sooner or later. It was as if there was something sinister, something almost like "original sin" inside each person, struggling to get out, or needing to be expelled; and many physicians opined that this tendency was exacerbated by luxurious living and too rich a diet. It will hardly be believed that Chinese medical writers concurred, without ever having the slightest idea, so far as we know, of what the Western doctors were thinking. The Chinese theory involved what was called *thai tu*, literally "womb poison", due to come out sooner or later in the child; and the metaphor of a flowering plant was all the more telling because smallpox in China was called *thien hua* "flowers of Heaven", a natural phrase precisely mirrored etymologically in the

term exanthematous. The aetiologists attributed it, as we shall see, to excessive pleasure in the coitus of conception, or else more naturalistically, to a blood-clot or lump of meconium not properly removed from the mouth of the foetus at birth.

On the other hand, in Europe there were many authors who supported a meteorological explanation, believing that unseasonable weather released "morbific seeds" or "putrefactive effluvia" into the human environment so that smallpox resulted. A perfect balance in the elements of the circumambient air, those *eu-krasias aeras* which are prayed for in the Liturgy of St. John Chrysostom (ca. sixth century A.D.) were needed for health; when it failed, epidemic diseases such as smallpox would result. Precisely the same ideas were found in China, where some physicians ascribed the greatest part in causation to the "pneumata of the season"⁸ or the "movements of Heaven".⁹ In Europe the idea went back, of course, to Hippocrates, with his "Airs, Waters and Places", but its most prominent Renaissance advocate was Guillaume de Baillou (1538 to 1616 A.D.), a French physician who was the first to describe whooping-cough and introduced the idea of rheumatism. This was in his book *Epidemiorum et Ephemeridum* published posthumously in 1640 A.D. Later Thomas Sydenham (1624 to 1689 A.D.) supported the same conception, introducing a long-lived phrase, "the epidemic constitution", which as the watchword of the atmospheric-miasmatic school, still battled with the contagionists in the nineteenth century.

The third aetiological theory was one which had rather less parallelism in China; it was that of the *contagium vivum* or *contagium animatum*, the idea of living "atoms, corpuscles, bodikins in the ayre", decisively living rather than dead. Out of this indeed, after many vicissitudes, arose the "germ theory of disease". Without question the turning-point here was the posthumous publication in 1546 A.D. of the treatise of Girolamo Fracastoro (1478 to 1533 A.D.) entitled *De Sympathia et Antipathia Rerum, Liber Unus: De Contagione et Contagiosis Morbis et Curatione. Libri Tres*. It was a

landmark in the history of pathology. He was a "seminarist" because he believed in the existence of widely dispersed seeds of disease, but he also believed in their qualitative specificity, and above all he believed in their life, for he distinguished between a poison which cannot multiply itself and an infection which can do so. Infection was the cause, epidemic disease the result; the seeds were transmissible and self-propagating. Fracastoro also distinguished between three kinds of infection, by direct contact from person to person, by carriage through the air at some distance, and through intermediate objects of Athanasius Kircher, *Scrutinium Physico-Medicum...Pestis* (1658 A.D.), and the immortal letters of Antoni van Leeuwenhoek to the Royal Society, the ground was firmly prepared on which modern bacteriology would later build.

So far as we can see at present, there was nothing quite like our *contagium vivum* in China. The classical term for epidemic disease was *i li*, and either of these words could be combined with the omnipresent *pneuma* as *i chhi* and *li chhi*. *I*, characterised by its "disease" radical, is related to the cognate word *i*, to serve, to be in bondage, to enslave, which was just what an epidemic would do to a population. *Li* combines the "disease" radical with the character denoting ten thousand, again perhaps a reference to the number of patients contracting or succumbing. *Tou*, the term for smallpox itself, was obviously derived from *tou*, a bean, because of the pustules. *Jan* means primarily dyeing, secondarily infection, but the common phrase *chhuan jan ping* is comparatively modern, and was not used in the classical Chinese literature. *Jan* itself occurs in this sense, as in the following passage from the *Pao Phu Tzu* (ca. 320 A.D.):

Man exists in the midst of *chhi*, and *chhi* is within him as well. Of all things in heaven and earth there are none that do not need *chhi* in order to live and stay alive. He who knows how to circulate the *chhi* internally can nourish his body outwardly, and there-

fore repel all evils; ordinary people use (breathing) daily, and know nothing about this.

Among the people of Wu and Yüeh there is a method of secret conjuration¹⁰ which renders the chhi more abundant. He who knows it can pass safely through the worst epidemics, and even share a bed with a sick person without being infected.¹¹ And several dozen of his companions can similarly be rendered free from fear. This shows that mastery of the chhi can do to protect against natural disasters.

It also shows how strong was Ko Hung's belief in the efficacy of the Taoist respiratory techniques, but what it shows us too is the clear understanding of person-to-person infection. The recognition of infectivity is quite clear throughout ancient and mediaeval Chinese literature; that would be evident alone from one of the methods of "inoculation" spoken of in the books, namely of enveloping a child in cloths or clothes which have been worn by a smallpox patient. But what seems to be missing is the idea of specifically living particles. Here we think it is essential to remember that Chinese thought in natural philosophy and science was perennially averse to the idea of particles at all. Atomism must have been introduced many times, as by Buddhist monastic philosophers from India, but it never seriously gained a footing, and Chinese thought remained invariably faithful to a prototypic wave theory, the rises and falls of Yin and Yang, with a conviction of the reality of action at a distance in a continuous medium. For Europe, with its background of atomist thought in ancient Greece, of which perhaps Stoic seeds were but one aspect, the idea of infective particles, and then actually living infective particles, was quite natural; but in China it was evidently much less likely to arise. And perhaps the intellectual turmoil of the Renaissance, and upheaval not paralleled in China, could have had something to do with the new perspectives which Fracastoro set forth.

But we must refine these statements about the *contagium vivum*. The particulate as such was certainly not characteristic of Chinese natural philosophy, but on the other hand the many-sided concept of *chhi* (spirit, vapour, gas, gaseous emanation, all-permeating influence) was certainly not devoid of the undertones of living. *Chhi* included many sorts of life *chhi*; living in some sense, but not particulate living "animalcules" or virulent "atomies". First of all there was the ancient term *chi*. It occurs in the *I Ching* (Book of Changes) where it means the ultimate minute beginnings of things, out of which both good and evil come; and the pictograph itself was originally a drawing of two embryos. Perhaps we find it first in the fifth century B.C., in the *Kuan Tzu* book, with the general meaning of germination; and then in the following century in the famous "evolution" passage in the *Chuang Tzu*, where we read that "all species contain certain germs (*chi*)..." and "all things come from the germs and return to the germs". This was the inspiration for many later writers, such as Cheng Ching-Wang in the twelfth century A.D., and the Neo-Confucians beginning with Chou Tun-I in the eleventh century A.D., and the word always carried a certain aura of life and the living with it.

So far as we are aware, this word was hardly ever adopted as a technical term by the physicians, but *miao* took its place in a way, and was much used by them. The dictionary meaning of *miao* is sprout(s), but our words seed(s) and germ(s) also do it justice, and the implication of life is never far off. *Ku miao* and *tshao miao* were common terms for the sprouts or cotyledons of plants and grasses, but the word was also used in animal contexts, as for *yü miao*, tiny fish fry just hatched from eggs (*tzu*). But *miao* really came into its own when it began to be used, at least from the fifteenth century A.D. onwards, in the sense of inoculum.

As we already know, inoculation was always termed *chung tou*, using *chung miao*, the implantation, or better the transplantation, of the sprouts or germ. This linguistic usage is easier to under-

stand when one recalls the procedures of rice farming, particularly the planting out of the seedlings at much larger intervals from each other than they had when first sprouting in the seed-bed paddy-field (*miao thien*). Chao Hsüeh-Min, in the *Pên Tshao Kang Mu Shih I*, says in his section on "treasuries of perfume-like influences" (*tshang hsiang*) that "the scabs (*yen* or *chia*) of the smallpox pustules are called *miao*, and the outbreaking of the smallpox is called *hua*." So also Chêng Wang-I, in his *Chung Tou Fang*, says that those who choose the *miao* are careful to take the scabs from children who have already been inoculated,¹² and these are the true *chung miao*, in contra-distinction from scabs taken from natural or epidemic smallpox cases, which are called *shih miao*. Chu I-Liang, in the *Chung Tou Hsin Fa*, recommends as the best ripe *miao* that which has been transformed (*lien*) by seven passages through inoculated persons. This, then, is *shu miao*.

Read in the opposite sequence, and with *chung* pronounced in a different tone, the words *chung miao* meant various "species" of sprouts. And indeed a great part of the skill and expertise of the earliest inoculators consisted in selecting or choosing the scabs (*tsê miao*, *hsüan miao*). Yü Mou-Khun says that one should select scabs which are hard and thick, with the form of a snail; thin damp irregularly shaped ones are to be avoided. Chu I-Liang says that the size matters little, but they should be thick, rounded and of a clear purplish colour. The *I Tsung Chin Chien* recommends those which are large and thick, waxy and slightly bluish in colour. Greatly to be avoided was the *shih miao*, scabs taken from the pustules of severe epidemic smallpox patients, and many warnings were given against the use of such material. The best kind of inoculum was termed pure, *shun miao*, or medicinal, *tan miao*; other names were *shen miao* (numinous transplant) or *hsien miao* (transplant of the holy immortals). Judging from the later descriptions these must have meant an attenuated virus, either obtained from the scabs of patients who had already been inoculated, or artificially weakened

in virulence by special methods shortly to be described. Finally, after Jenner, there was *niu tou miao*, cowpox sprouts, an appellation which shows the continuity between inoculation and vaccination in the minds of the Chinese physicians.

There is something to be said for the suggestion that in their careful choice of the "best" scabs the Chinese inoculators were selecting for variola minor as against the major form. Al-Rāzī may have already noted the difference, but the Chinese physicians were certainly aware that there were two types of the disease, as we see in Shih Chin-Kung's *Tou Kho Ta Chhüan*, where he distinguishes between the light (*chhing*) and the heavy (*chung*) affliction. This selection may not have been conscious. But it was certainly a classic example of the widespread phrase *i tu kung tu*, using poison to combat poison. As we have seen, the beneficent "poison" had to be most carefully chosen, and all the books give strict instructions that inoculation should never be undertaken when natural smallpox is already within the house, only under suitable conditions of relative isolation some time beforehand.

It may come as something of a surprise to see how elaborate was the theorising in traditional Chinese medicine about the nature of the inoculation process. To elucidate this, we have to recall a conception already encountered by us in the context of urinary endocrinology, that, namely, of *yin tao*, "leading something out by the same way that it previously came itself". It was maintained that urine — and a *fortiori* the protein, steroid and other hormones isolated from it — can "lead out the undue heat (*yin huo*) which is the cause of the illness, downwards to be excreted and got rid of"; because they had already passed that way themselves. If it was their very nature to follow the path of urinary excretion then they could perhaps combine with another substance or *chhi* which was causing the trouble, and lead it forth. These ideas originated rather early, because we find a clear statement of them in *Chhu Chhêng I Shu*, the writings of the physician Chhu Chhêng, who died in 501

A.D., and they are expressed again in the works of Sun Ssu-Mo (ca. 650 A.D.) and Chu Chen-Hêng (fourteenth century A.D.).

The Earliest Mentions of Inoculation

There can be no doubt that smallpox inoculation came out into the open, as it were, some time during the first half of the sixteenth century A.D. To see clearly what happened afterwards, the story has to be pieced together from flashbacks and hindsight, traditions reported by medical writers, and statements about the practice of families in which the calling of physician — and inoculator — had been passed down through several successive generations. The very earliest reference (apart from the Taoist tradition which we discuss separately below) seems to be in the book of Wan Chhüan on smallpox and measles, *Tou Chen Shih I Hsin Fa*, first published in 1549 A.D. but reprinted as late as 1687 A.D. Speaking of treatments, he casually mentions that smallpox inoculation is liable to bring on menstruation unexpectedly in women. His book has no section on that subject, but from this remark it is clear that the practice must have been quite common in his time, even though no one was seeing their way to writing about it. By 1727 A.D., the date of Yü Mou-Khun's book *Tou Kho Chin Ching Fu Chi Chieh* (Collected Explanations of the Mnemonic Verses entitled 'Golden Mirror of Smallpox and Related Diseases'), much was being written on it, and here there was a section entitled *Chung Tou Shu*. In this we read:

Smallpox inoculation arose in the Lung-Chhing reign-period (1567 to 1572 A.D.), especially at Thai-phing hsien in Ning-kuo fu. We do not know now the names of the inoculators, but they got it from an eccentric and extraordinary man who had himself derived it from the alchemical adepts (tan chia). Since then it has spread widely all over the country. Even down to now the inoculating physicians come mostly from Ning-kuo, but

not a few Li-yang people have learnt it and appropriated it. The strain of inoculum (miao chung) which was obtained from the strange and eccentric man has been kept and used to this day, but you have to pay two or three pieces of gold to get enough for inoculating one person. Physicians who want to make some profit pass it through the children of their own relatives in winter and summer, and have no mishaps. However, others who want to make money steal away the scabs from (severe) smallpox cases and use the material directly; this is called pai miao (bad inoculum), and in such cases there will be 15 deaths in 100 patients.

Thus we can say with fair confidence that inoculation for smallpox was a general practice in China in the time of Thomas Linacre, John Caius and Henry VIII, which was certainly long before the days of Lady Mary Wortley Montagu at the turn of the seventeenth and eighteenth centuries A.D.

The next step concerns the Chu family, who practised medicine one after the other. Inoculation is described in the book of Chu Shun-Chia entitled *Tou Chen Ting Lun* (Precise Discussion of Smallpox and Related Diseases) and printed in 1713 A.D., but Chu himself had lived a good deal earlier, having been born before the end of the Ming in 1644 A.D. Furthermore, his book was added as an appendix to a similar book by an older Chu, Chu Hui-Ming, dating from about 1580 A.D. and entitled *Tou Chen Chhuan Hsin Lu* (Records of Personal Clinical Experience of Smallpox and Related Diseases). This was one of those cases where the profession of medicine ran in families through several generations, so it is highly probable that the elder Chu knew and practised inoculation, though living at a time when it was not generally written about. Again, in 1621 A.D. there appeared a novel (written in 1610 A.D. by Chou Hui) entitled *Chin-Ling So Chih* (Troublesome Affairs in Nanking); this mentions two cases of

inoculation during the Wan-Li reign-period (1573 to 1619 A.D.) in which the children got the infection badly. Similarly, the *Chêng Tzu Thung* dictionary, published in 1627 A.D., has this to say about smallpox:

Smallpox (tou chhuang).

The treatises of the adepts (fang shu) attribute it to an innate flaw or toxin of the womb (thai tu). Some people never get the disease (in spite of this). As for the numinous magical way of dealing with smallpox (shen tou fa), they take the liquid pustule contents (tou chih) and instil it into the nose, so that simply by breathing the patient will get infected with a light eruption (and be protected).

Apart from its early date, this passage is interesting in its explicit recognition of the role of the respiratory passages in the infection. At this point we are entirely contemporary with the physician Ong Chung-Jen, whose "Golden Mirror of Smallpox" with the famous mnemonic verses accompanying it, was the basis for the work of Yü Mou-Khun already mentioned. Implications of inoculation occur in his text, but with Yü they become highly explicit.

Attenuation

Perhaps the aspect most interesting scientifically about all the old Chinese descriptions is the measures that were taken for the attenuation of virulence of the inoculum. Today we know that the attenuation phenomenon includes two things, on the one hand reducing the population of fully active virus particles or bacteria, on the other, inducing the appearance of genetically distinct strains or clones of organisms with intrinsically diminished virulence. The old Chinese methods probably involved mainly the former of these two, but the fact that they discovered the attenuation principle is

most remarkable in itself. Here are the directions given in the *Chung Tou Hsin Shu* of Chang Yen (1941 A.D.):

Method of Storing the Inoculum (Tshang Miao Fa).
Wrap the scabs carefully in paper and put them into a small container bottle. Cork it tightly so that the activity (chhi) is not dissipated. The container must not be exposed to sunlight nor warmed beside a fire. It is best to carry it for some time on the person so that the scabs dry naturally and slowly. The container should be marked clearly with the date on which the contents was taken from the patient.

In winter the material has Yang chhi within it, so it remains active even after being kept from thirty to forty days. But in summer the Yang chhi will be lost in approximately twenty days. The best inoculum is that which has not been left too long, for when the Yang chhi is abundant it will give a 'take' with nine persons out of ten; but as it gets older it gradually loses its activity, giving perhaps a 'take' with only five out of ten people — and finally it becomes completely inactive, and will not work at all. In situations where new scabs are rare and the requirement is great, it is possible to mix new scabs with the more aged ones, but in this case more of the powder should be blown into the nostril when the inoculation is done.

Substantially the same directions are given in other eighteenth-century A.D. books. In the *Chung Tou Chih Chang* for example, we read that the inoculum, whether lymph (*chiang miao*) or scabs (*yen miao*) should be put in a small bamboo tube between two septa, and carefully corked up. It should then be carried round regularly in one's pocket so that it can acquire adequate human energy (*jen chhi*). But if the weather is very hot then the container with lymph or

scabs should be stored in a relatively cool place. There follow the usual directions about grinding and extracting the material if dry, and implantation into the nostril on the cotton-wool plug. The writer was clear that lifelong protection would be afforded by inoculation, which was more than could be said, in spite of Jenner's initial optimism, about vaccination.

Thus the general system was to keep the inoculum sample for a month or more at body temperature (37°) or rather less. This would certainly have had the effect of heat-inactivating some 80 per cent of the living virus particles, but since their dead protein would have been present, a strong stimulus to interferon production as well as antibody formation would have been given when inoculation was done. There is no way of telling how far back these attenuation procedures may have gone, but perhaps it would not be an unfair guess to suppose that they were gradually developed as clinical experience increased from that time in the mid sixteenth century A.D. when inoculation began to come out into the open and take its place in medical writings. Many of these, of course, ignored the matter, as in fact did the *I Tsung Chin Chien* itself.

Europeans could have got information about inoculation from the reports of Westerners in China from about 1700 A.D. onwards, but in fact they paid little attention to these in comparison with the powerful influence exerted by the Turkish version after 1720 A.D. Attenuation was not a conscious part of that technique, so it remained unknown. In 1726 A.D. the Jesuit missionary, d'Entrecolles made a report which did include news of attenuation,¹³ yet once again no one took it seriously. He told how Chinese inoculators had been sent to Tartary at urgent need in 1724 A.D., and how he himself had got an account of the secret techniques from certain lesser court physicians, for communication to Europe only. D'Entrecolles knew of the long keeping of the scabs in the sealed tubes, and remarked: "il suffit de les tempérer par la douce transpiration d'un homme plein de santé qui les porte sur lui quelque tems avant qu'on

en fasse usage".¹⁴ He also knew of other methods of interfering with the virulence of the particles, saying: "les écailles recentes ont besoin d'une préparation pour tempérer leur acrimonie".¹⁵ For example, the scabs were steamed in one method with black salsify (*Scorzonera albicaulis* or *austriaca*, *yen tshung chü*) and "liquorice" (presumably *Glycyrrhiza glabra*, *kan tshao*); this doubtless did a good deal of inactivation, "pour dissiper la malignité du vénéin".¹⁶ D'Entrecolles also reported the use of waste silkworm cocoons as the plug for the nostril. He included a translation of a lost manuscript tractate, *Chung Tou Kan Fa* (Dry Inoculation Method), which described the close sealing of the scabs for as much as a year, then treatment with realgar before implantation in the nose. Finally he gave his opinion that the nostril method was much better than the deep incisions which inoculators were using at this time in Europe. Many years later, in 1779 A.D., another Jesuit, Cibot,¹⁷ also wrote an account of smallpox and the inoculation for it, including a précis translation of the five chapters of the *I Tsung Chin Chien*, but saying practically nothing about attenuation.

No, the Europeans had to find out about attenuation by themselves, the hard way. In the middle of the eighteenth century Kirkpatrick¹⁸ knew that some attenuation occurred when pustule lymph from an inoculated person was used upon another ("arm-to-arm" transfer), but he did not believe that this was in any way necessary or desirable. The first clear statement of it was made by de la Mettrie¹⁹ in 1740 A.D., but he did not positively recommend it. Angelo Gatti did, however, in writings with Morellet²⁰ from 1763 A.D. onwards; he used the lymph dried in air and pulverised, then serving successively for several inoculations, as also aqueous extracts of scabs in the Chinese manner. He was followed by the Dane, Rottbøll, and others, but by the nineties the era of Jenner was approaching, and the attenuation of variola did not have much future.

The Background Tradition in China

The moment has now come to examine the persistent conviction that before the earliest extant writings on inoculation for smallpox there had been some five centuries of its practice under conditions of restriction and secrecy. The central figure round whom the tradition revolved was Wang Tan (Wang Wên Chêng Kung, 957 to 1017 A.D.), a famous prime minister whose civil service career covered the reigns of two Sung emperors, Thai Tsung and Chen Tsung. He got his first office in 990 A.D. and became a Han-Lin Academician in 998 A.D. In 1004 A.D. he helped to negotiate peace with the Chhitan Liao Tartars, and throughout his life he was a leader of the anti-war party, so much so that he acquired the popular name of Thai-Phing Tsai-Hsiang, the peace-seeking premier. His chief troubles arose in connection with the imperial Fêng-Shan sacrifices and the fabrication of the "heavenly missives" (*thien shu*), but he eventually joined in these celebrations of the State religion, and himself superintended the ceremony in 1011 A.D., the last time in Chinese history that it was ever held. Wang Tan was particularly good at organising the bureaucracy and the imperial examinations, and on the whole went down to posterity as a virtuous prime minister.

His connection with smallpox inoculation came about because his first son had died of smallpox, so when Wang Su came, the father sought everywhere for some means of preventing a similar calamity. He invited all kinds of physicians and shamanic technicians (*wu fang*) to show him what they could do, till finally the gods were compassionate and sent him a Taoist hierophant (*shen jen*) who carried out inoculation; after which the technique was handed down from one practitioner to another with stringent confidential precautions. Such is the account as Chu I-Liang gave it in his *Chung Tou Hsin Fa*, but all the books on inoculation have the same, albeit with numerous

variations. The oldest statement may go back to about 1680 A.D. as it occurs in Chu Shun-Chia's *Tou Chen Ting Lun*, not printed till 1713 A.D.; here the inoculator is called a *shen i* (holy physician) or a *thien mu* (numinous old woman) or a *chi hsien* (planchette immortal). Whoever it was came from O-mei Shan, that famous mountain in south-western Szechuan, mainly, though by no means wholly, connected with Buddhism. This information was repeated by Chang Yen in his *Chung Tou Hsin Shu* of 1741 A.D., and incorporated in the *I Tsung Chin Chien* two years later, which gave it a certain seal of official orthodox approval. Chang Yen himself had been the inoculator of the imperial princes in 1681 A.D., and the tradition was accepted on all hands.

Many other accounts occur. The writer of the *Chung Tou Chih Chang* says that the medical attendant of Wang Tan's family was a *ku hsien san pai chen jen*, a "three-white adept of the school of the ancient immortals", while the great medical historian Hsü Ling-Thai in 1757 A.D. in his *I Hsüeh Yuan Liu Lun* calls him just one of the holy immortals (*Hsien*), in other words, a numinous Taoist. It might be relevant too that Wang Tan himself asked to be habited as a "monk" after his death.

If we look a little more closely at the O-mei Shan tradition, we can see that the Buddhist connection may be rather misleading. The syncretistic tendencies in Chinese religious life were always so strong that there are many evidences of a Taoist presence on and around that mountain. There are place-names, such as Hsien Fêng Shih (the rock of the peak of the holy immortals), and buildings such as the Chiu Lao Hsien Fu (palace of the nine ancient immortals). There are caves of Taoist hermits such as Li Hsien Tung and Ko Hsien Tung; there was a tradition that the great alchemist-physician Sun Ssu-Mo did some of his alchemy at O-mei Shan, as witness a Wan Tan Shih. Moreover, Taoist books or inscriptions are named, such as an *I Shan Wu Khou Tao Jen Shu* commemorating five passes through the range, or a *Tan Ching* (alchemical manual) of Yin

Chhang-Sheng. All in all, there is a strong, if subordinate, element of Taoism about O-mei Shan and its neighbourhood.

Certainly there were votive temples for inoculators. The *Huchou Fu Chih* tells us that towards the end of the Ming there was a young man of that city who ran away from his family in 1644 A.D. because of his irresistible urge to become a physician. His name was Hu Phu and he carried out many inoculations before disappearing in 1712 A.D. He was supposedly seen in 1723 A.D. in Nanking, though that would hardly have been possible. More interesting perhaps is the fact that at least since the time of Khang-Hsi's accession in 1662 A.D. there were votive temples (*miao*) in Huchow and Suchow dedicated to the "immortal teacher of inoculation" (Chung Tou Hsien Shih) and to the "mountain recluse of O-mei Shan" (Sung O-mei Shan Jen). The image, says the writer, often looked very like that of Shun-Yang Tsu Shih, i.e. the famous adept and alchemist Lü Tung-Pin, whose dates are rather uncertain but belong in the eighth century A.D., the Thang time. Here perhaps is another thread linking inoculation with the activities of the Taoist alchemists.

Naturalistic and Theological Attitudes to Disease

Lastly there is a singular comparison to be made between China and India here. It revolves round the question of whether sickness was to be considered a divine punishment for former misdeeds and transgressions, and how far it was to be accompanied by feelings of guilt or sin or shame. We have already seen how in China one theory of the "innate seed" (*thai tu*) of smallpox was that it arose from excessive erotic pleasure in the procreating parents. One could also touch upon the preparation of altars in the family where sacrifices and oblations were to be made to the smallpox deities; and sacrifice generally implies repentance, and repentance implies the recognition of former wrong-doing. Over against this lay the con-

viction of the rational physicians that the causes of smallpox were natural, and that the illness could be nursed through and cured, or at least alleviated and moderated, by therapeutic actions. Still more daring was the conviction of the earliest inoculators that by inducing the disease in mildest form they could give lifelong protection against even the most dangerous forms of it; and the paradox is that this technique arose precisely in a milieu saturated with religion. But perhaps the Taoist religion was not quite so resigned to fate as other religions? Although fundamentally a nature-mysticism (even after it provided itself with personal deities, indeed a Holy Trinity) and one which always believed that Nature's way was best, perhaps it could generate the idea of borrowing tools from Nature's workshop?

The contrast comes out in a particularly instructive way if one studies the remarkable book of Chattopadhyaya²¹ on science and society in ancient India. What it is really about is the struggle that took place in that civilisation for a rational medicine. The classics called *Suśruta-saṃhitā* and *Caraka-saṃhitā*, greatest of the ancient Indian medical works, both have an ambiguous character, partly scientific, partly not. When this is dissected, it reveals an intense struggle between the physicians on the one hand and the theological philosophers on the other, who wanted to attribute everything to the "law of *karma*", regarding all illness as necessarily caused by ethical and moral infractions or sins in previous existences. Since the idea of reincarnation was never so strong in China as in India, this piling up of sins was not so overwhelming either, but it was certainly there. On the other hand, the rational physicians in India were striving for a truly scientific view of the world; they believed that diseases were not caused or sent by the gods on account of sin, but rather arose from distinguishable natural causes, and these they were anxious to seek out. The admixture of science, magic and religion is as clear in the *Caraka* book as in China, for it defines *yukti-vyapaśtraya bheṣaja* as therapeutic

systems based on the use of natural material substances such as drugs and diets, as against *daiva-vyapaśraya bheṣaja* or therapeutic systems based on incantations, charms and sacrifices, whether propitiatory or penitential. This is just the distinction which we find in China between apotropaic techniques and rational scientific techniques; but although there the former always existed through the centuries, they took second place to pharmacy and physical therapy. Once again comes the paradox that inoculation arose precisely among them.

A key word in the ancient Indian literature is *svabhāva*, which could be translated "inherent nature", "innate thus-ness", or "the essential nature of things". It must have had close relations with *ṛta* and even *dharma* in some senses, meaning "the Order of Nature" or the way in which Nature works — all recalling Tao in Chinese. The physicians were seeking the pattern-principles in Nature, the ultimate reasons (ultimately of course inscrutable) why things are as they are and behave as they do. It is interesting to see how these Sanskrit words came out when the Buddhist philosophers needed to translate them into Chinese. *Svabhāva* was rendered as *hsing*, and defined as embodied cause, the unchanging, independent, self-dependent, fundamental "nature" behind the manifestation or expression of anything. Sometimes this was amplified as *tzu hsing*, "the primary germ [verb.sap.] out of which all material appearances are evolved, the first source of the material world of phenomena". Other more curious locutions were *ssu-pho-pho* and *tzu-thi-thi*, "own state", essential or inherent property, innate or peculiar disposition, natural state or constitution. So much for the nature of Nature as it passed from Sanskrit into Chinese, and there it found a natural home in Taoist philosophy.

What about *karma* in China however? The remarkable thing is that ideas very like it were clearly current in early Taoist religion. In the *wu tou mi tao* parishes, part of that Taoist church which flourished from the second to the sixth centuries A.D., all

illness was thought of as a visitation on account of previous misdeeds or transgressions, and sick persons were "imprisoned" to meditate on their past mistakes in quiet chambers (*ching shih*). The hierarchs presided at sessions which today we should call "faith-healing"; and recovery (in most cases natural anyway) was effected by confession of faults, sometimes publicly, together with expiation through good deeds in the form of fines for worthy purposes, assisted by charms, talismans and incantations. In Chang Chio's time (ca. 180 A.D.) the patient went into retreat to reflect on his wrong-doings, while at the same time prayers were made on his behalf, with his name and history written on papers despatched to the gods, then he paid money to the public funds and so gained cure and release. Psychological catharsis was achieved by means of quasi-orgiastic rites such as the *san yuan chai*, the "mud and charcoal ceremony" (*thu than chai*) and the hierogamic celebration (*ho chhi chai*).

There has been much discussion, which we can do no more than mention here, concerning the question whether Chinese culture as a whole should be thought of as a "sin-and-guilt society" or as a "shame society". *Kuo* can certainly be translated "transgressions", but how far *tsui* may be taken as "sin" in anything like the sense of the People of the Book (Israel, Islam and Christianity) is highly doubtful, for monotheism was never characteristically Chinese. On the other hand, words involving shame are very prominent, e.g. *chhih*, which was essentially connected with blushing; *ju*, which derived from "dirty", hence "disgraced"; *hsiu*, which started as "ugly" and came to mean "shame", like its equivalent, *tshan khuei*. And there was always too the characteristic *shih lien*, "loss of face", so well known to Old China Hands and so combated in modern China. To examine all this carefully would take us far away from our present theme; here we need only recognise that the idea of sin or *karma* as the prepotent cause of disease did make its appearance in China during a certain period, though in so far as it was

thought of as shame rather than theological sin or guilt it could have come near to psychosomatic pathogenesis, and an organic naturalism which refused to make too sharp a distinction between soul and body was always typical of Chinese medicine.

But here comes the dénouement. While in India the theological conception of *karma* tended to dominate all through the centuries, in China, that more rationalistic culture, it did not gain the day in the long run. Although, as we have seen, the cure, and even more the prevention, of smallpox, was closely associated through the ages with Taoist religion and magic, that did not stop the appearance of the inoculation technique precisely in that milieu. Surely this must go back to the nature-mysticism of Taoist philosophy on which the Taoist church was founded, the idea that everything goes best when least interfered with by man. For a time the idea that illness was a punishment for evil-doing could flourish — indeed one wonders whether it was not essentially an Indian importation, perhaps connected with Buddhism — but before long Taoist technical élan reasserted itself, and the inspiring thought arose that man could borrow some of the tools in Nature's workshop, and by following her, bring about something effectual for human benefit. After all, the great Taoist doctrine of *wu wei* — "do nothing contrary to Nature" — avoided the setting of a hundred men to work on water-raising machinery when the same result could be achieved by taking the water off higher up the river and leading it by a lateral derivate canal to its desired destination along a higher contour level. So also by using sagely Nature's own variola virus under just the right conditions permanent protection against the worst forms of the disease could be conferred. If this was "thinking God's thoughts after him", as some pious Western Christian might have put it, who would begrudge the Taoists their candles and incense?

Conclusion

The subject of inoculation for smallpox is a highly important one for the world history of medicine and science, because it constituted the very first of all immunological procedures. As Weichardt said: "Die Variolisation war dem Grund-experiment aktiver Immunisierung".²² But the general pattern of what we have been able to describe is rather different from any other that we have encountered hitherto. There are four key turning-points: 1800 A.D., approximately the time when Edward Jenner's heterologous cowpox vaccine inaugurated the era of almost complete safety in immunisation; then 1700 A.D., the time at which the Turkish practice of inoculation was introduced to England and thereafter to all Europe and North America; then 1500 A.D., when the practice came out from the shadows of secrecy and began to be written about in Chinese medical books; and finally 1000 A.D., the start of the procedure according to persistent (and, as we believe, rather trustworthy) Chinese tradition. We have described above the ambiance of Taoist religion, magic and medicine, in which it seems to have had its origin. There can be no doubt that the Chinese documentary evidence goes back much further than in any other civilisation, and before that begins there is still a background of five centuries of cryptic confidential practice.

Two centuries, then, were available, if not seven, for the inoculation of smallpox to reach the Ottoman Turks in time for them to hand the discovery on to the Europeans, as we know happened. The Old Silk Road was a ready means of communication along which the practice could have been transmitted westward. Similarly, there were no impediments to the passage of the technique to India. But the data in both these cases, and in all the others without exception, are essentially ethnographic. No assured textual evidence exists to generate historical datings. Certainly one cannot rule

out a whole series of independent originations, perhaps especially the use of lymph, scabs, or clothes of one kind or another, without the deposition of the virus on a mucous membrane, or its introduction into the epidermis and skin capillaries, but without further discoveries in the accounts of mediaeval travellers, that will be extremely difficult to prove. The only hope for literary references other than the Chinese is in India, and there the philological difficulties of dating references, even if they could be found, are well known. In sum, the most judicious conclusion seems to us to be that the inoculation for smallpox did indeed originate in a Taoist milieu in or shortly before the early Sung, and that from that focus it spread outwards by diffusion, sometimes as a developed practice but often in dilute and fragmentary forms, throughout the Old World and many parts of Africa. It had certainly two centuries to do this, and most probably seven or more were available.

We think that McNeill did a grave injustice to the physicians of China when he wrote:²³

Even if, as seems probable, smallpox inoculation had been demographically significant in China and other parts of Asia for centuries before +1700, it had been a matter of folk practice analogous to the innumerable other customs and rules of hygiene that human beings had everywhere worked out and justified to themselves by a variety of naive and ingenious myths.

But we like well enough what he said on the following page:

Wherever the practice first developed, one may easily suppose that caravan traders heard of it, tried it, and thereafter propagated it as a folk practice throughout the parts of Eurasia and Africa where caravan traffic constituted the main form of long-distance trade.

NOTES

1. liang i chhang chih wu ping chih ping, ku wu ping 良醫常治無病之病，故無病。 See Liu An, *Huai Nan Tzu*, Chapter 16, p. 4b.
2. fang ping chung yü chih ping 防病重于治病。
3. Ko Hung, *Pao Phu Tzu (Nei Phien)*, Chapter 18, p. 4b.
4. shih i chih jen hsiao wei chhi chih huan 是以至人消未起之患。
5. chih wei ping chih chi 治未病之疾。
6. chin fang 禁方。
7. chieh 戒。
8. shih chhi 時氣。
9. thien hsing 天行。
10. chin chou 禁咒。
11. kho i ju ta i, yü ping jen thung chuang erh i pu jan 可以入大疫，與病人同床而已不染。
12. pi yao yung chung chhu chih tou 必要用種出之痘。
13. F.X. d'Entrecolles, Lettre du 11 Mai, 1726 au Pire Duhalde; "De l'Inoculation chez les chinois," *Lettres Edifiantes et Curieuses*, 1731.
14. "it suffices to temper (the scales) by the mild transpiration of a healthy man who carries them in his pocket some time before they are to be used".
15. "recent scabs need some preparation to moderate their acrimony"
16. "to dissipate the malignancy of the poison".
17. P.M. Cibot, "De la petite Verole," *Mémoires concernant l'Histoire, les Sciences, les Arts, les Moeurs et les Usages des Chinois*, 1779.
18. J. Kirkpatrick, *An Essay on Inoculation*, London, 1743.
19. J.O. de la Mettrie, *Traité de la Petite Vérole, avec la Manière de Guérir cette Maladie*, Paris, 1740.

20. A. Gatti, *Lettre à Mons Roux.....*, Paris, 1763; A. Gatti and l'Abbe Morellet, *Réflexions sur les Préjugés qui s'opposent au Progrès et à la Perfection de l'Inoculation*, Brussels, 1764; A. Gatti and l'Abbe Morellet, *Nonvelles Réflexions sur la Pratique de l'Inoculation*, Brussels, 1767.
21. D. Chattopadhyaya, *Science and Society in Ancient India*, Calcutta, 1977.
22. "Variolisation was the fundamental experiment in active immunity", quoted in A.C. Klebs, *Die Variolation im achtzchnnten Jahrhundert; ein historischer Beitray zur Immunitätsforschung*, Töpehnam, Giessen, 1914.
23. W.H. McNeill, *Plagues and Peoples*, Blackwell, Oxford, 1977.

GLOSSARY

- Chang Chio 張角
 Chang Yen 張琰
 Chao Hsüeh-Min 趙學敏
 Chêng Ching-Wang 龔景望
 Chêng Tzu Thung 正字通
 Chêng Wang-I 鄭望頤
 Chhang Sang Chün 長桑君
 Chhi 氣
 Chhien-fo-tung 千佛洞
 Chhih 恥
 Chhing 輕
 Chhu Chhêng I Shu 褚澄遺書
 Chhuan jan ping 傳染病
 chi 幾
 Chia 痲
 chi hsien 乩仙
 Chiang miao 漿苗
 Chin-Ling So Chih 金陵瑣事
 Ching shih 靜舍
 Chiu Lao Hsien Fu 九老仙府
 Chou Hui 周暉
 Chou Tun-I 周敦頤
 Chu Chen-Hêng 朱震亨
 Chu Hui-Ming 朱惠明
 Chu I-Liang 朱奕梁
 Chu Shun-Chia 朱純嘏
 Chuang Tzu 莊子
 Chung 重
 chung miao 種苗
 chung tou 種痘
 Chung Tou Chih Chang 種痘指掌
 Chung Tou Fang 種痘方
 Chung Tou Hsien Shih 種痘先師
 Chung Tou Hsin Fa 種痘心法
 Chung Tou Hsin Shu 種痘新書
 Chung Tou Kan Fa 種痘乾法
 Chung Tou Shuo 種痘說
 fang shu 方書
 Fêng-Shan 封禪
 ho chhi chai 和氣齋
 hsien 仙
 Hsien Fêng Shih 仙峯石
 hsien miao 仙苗
 hsing 性
 hsiu 羞
 Hsü Ling-Thai 徐靈胎
 hsuan miao 選苗
 Hu-chou Fu Chih 湖州府志
 Hu Phu 胡璞
 hua 花
 i 疫, 役
 i chhi 疫氣
 I Ching 易經
 I Hsüeh Yuan Liu Lun 醫學原流論
 i li 疫癘
 I Shan Wu Khou Tao Jen Shu 一山五口道人書
 I Tsung Chin Chien 醫宗金鑑
 i tu kung tu 以毒攻毒
 jan 染
 jen chhi 人氣
 ju 辱
 kan tshao 甘草
 Ko Hsien Tung 葛仙洞
 Ko Hung 葛洪
 kuan 關
 Kuan Tzu 管子
 ku hsien san pai chen jen 古仙三白真人
 ku miao 穀苗
 kuo 過
 li 糝
 lien 鍊
 Li Hsien Tung 李仙洞
 Liu An 劉安
 Li-yang 潯陽
 Lü Tung-Pin 呂洞賓
 Lung-Chhing 隆慶
 miao 苗, 廟
 miao chung 苗種
 miao thien 苗田
 niu tou miao 牛痘苗
 Ning-kuo fu 寧國府
 O-mei Shan 峨眉山
 Ong Chung-Jen 翁仲仁
 pai miao 敗苗

Pao Phu Tzu 抱樸子
 Pen Tshao Kang Mu Shih I 本草綱目拾遺
 Pien Chhio 扁鵲
 san yuan chai 三元齋
 shen i 神醫
 shen jen 神人
 shen miao 神苗
 shen tou fa 神痘法
 Shih Chin-Kung 史晉公
 shih lien 失驗
 shih miao 時苗
 shu miao 熟苗
 shun miao 純苗
 Shun-Yang Tsu Shih 純陽祖師
 ssu-pho-pho 私婆婆
 Sun Ssu-Mo 孫思邈
 Sung O-mei Shan Jen 宋峨眉山入
 tan chia 丹家
 Tan Ching 丹經
 tan miao 丹苗
 tao 道
 Thai-phing hsien 太平縣
 Thai-Phing Tsai-Hsing 太平宰相
 thai tu 胎毒
 Thao Hung-Ching 陶弘景
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 wu fang 巫方
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