

CHAPTER 5



WORLD HEALTH ORGANIZATION
Geneva

CHAPTER 5

THE HISTORY OF SMALLPOX AND ITS SPREAD AROUND THE WORLD

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INTRODUCTION

Smallpox was a disease with such obvious and characteristic clinical signs and caused such dramatic and disastrous epidemics that it

was long the subject of myths and superstitions, and physicians and historians wrote much about it. This chapter provides a brief historical background, from the earliest civilizations until the beginning of the

20th century, of the occurrence of smallpox and its spread around the world. In compiling it we have drawn heavily on a recent book by Dr D.R. Hopkins: *Princes and Peasants. Smallpox in History* (Hopkins, 1983a), to which we refer readers interested in learning more about the way in which smallpox has influenced history, as well as about the history of smallpox and its control.

Smallpox was a specifically human infectious disease. One attack conferred lifelong immunity on survivors and neither chronic nor recurrent infectivity occurred among those who recovered from the acute illness. The persistence of such a disease in an endemic state within a human community was possible only if the population admitted a large regular accession of susceptible persons, either by birth or by immigration. Where appropriate and possible, estimates have been provided of the populations of some countries and continents at various times in the past, using the *Atlas of World Population History* (McEvedy & Jones, 1978) as a source-book. It must be emphasized that most of these population estimates are informed guesses rather than estimates based on reliable demographic data.

In order to provide an overview of the history of the world-wide spread and the subsequent control of smallpox, a list of important historical events that relate to this chapter and to Chapter 6 is provided in Table 5.1.

SMALLPOX BEFORE AD 1000

Most of the early civilizations left written records, some of which describe diseases of the time. Medical historians have been able tentatively to identify some of these diseases, but the older the records the less reliable are the diagnoses. Unmistakable descriptions of smallpox did not appear until the 4th century AD in China, the 7th century in India and the Mediterranean, and the 10th century in south-western Asia. Each of these descriptions refers to what was at the time a well-known disease. Mummified human remains provide another kind of evidence of disease, which is potentially more reliable than the interpretation of ancient writings, but suitable material is very scarce. It is therefore necessary to use epidemiological intuition to make guesses about the earliest occurrence of smallpox as a human disease.

Egypt

One of the earliest concentrations of civilized man was in the valley of the Nile and in the Fertile Crescent, which stretched from Palestine to the flood plains of the Tigris and the Euphrates. Trade and conquest made this region a single ecological unit, as far as the transmission of many human diseases was concerned. However, apart from reference to a "plague" that the Hittites were said to have caught from the Egyptians in the 14th century BC, which could conceivably have been smallpox, the written records of these civilizations, which include the Talmud and the Bible, do not refer to any disease that can be interpreted as being smallpox.

The largest and densest population in the region was in the valley of the Nile, where there may have been 1 million persons in the 3rd millennium BC and perhaps 3 million by the 1st millennium BC. As biblical and other written sources attest, Egypt was periodically visited by devastating epidemics, but none has been described which was suggestive of smallpox. However, the Egyptian practice of mummification preserved the skin, musculature and bones of a large number of royal personages, and diagnoses of the causes of death of several mummified persons have been made by palaeopathologists (Ruffer, 1921). The scientific literature mentions 3 mummies whose skin was covered with lesions that looked like those of a smallpox rash.

Ruffer & Ferguson (1911) described a smallpox-like eruption on the mummy of a middle-aged man who had died during the Twentieth Dynasty (1200–1100 BC). Section of a portion of skin showed dome-shaped vesicles in the epidermis, similar to those found in smallpox. Considering how resistant poxvirions are and how well preserved material from Egyptian mummies can sometimes be (Lewin, 1967), it is unfortunate that electron microscopy was not available at the time of this discovery, and that tissue from "smallpox" mummies has not thenceforth been at the disposal of investigators for electron microscopic examination. Ruffer (1921) mentioned that there was a similar eruption on a mummy of the Eighteenth Dynasty (1580–1350 BC) and on the mummy of Ramses V, who died as a young man in 1157 BC (Plate 5.1). Hopkins (1983a) describes some features of the burial of Ramses V that are consistent with a diagnosis of smallpox, and in 1979 he was able to examine the mummy himself:



Plate 5.1. The mummified head of Ramses V of Egypt (died 1157 BC) showing the pustular eruption that may have been due to smallpox. (From Smith, 1912.)

"It is one of the best preserved royal mummies in the [Cairo] museum. Inspection of the mummy revealed a rash of elevated 'pustules', each about two to four millimeters in diameter, that was most distinct on the lower face, neck, and shoulders, but was also visible on the arms. Over the shoulders especially, these pustules were pale yellow against a dark brown-reddish background, the latter partly due to cosmetic compounds used in royal mummifications during that period. On his upper face, only smaller raised pimples (one to two millimeters) could be seen, which might have been shrunken more by tighter wrappings over the forehead. It was not possible to examine the palms or soles where the presence of pustules would be highly characteristic of smallpox, because his arms were folded across his chest with the palms down, and the shroud was stuck to his soles. No such rash could be seen on the chest or upper abdomen. Earlier photographs of this mummy, published by G. Elliot Smith (1912) show that the rash is also prominent on the lower abdomen and scrotum ... Three folds in the skin over the left cheek suggest that his face may have been swollen when he died. The appearance of the larger pustules and the apparent distribution of the rash are similar to smallpox rashes I have seen in more recent victims."

One might have expected that an epidemic disease as distinctive as smallpox, which killed

pharaohs and nobles as well as the common people, would have been described in the extensive writings on medical subjects left by the Egyptians, or by their northern neighbours in Asia Minor. However, no such description exists, although in the Ebers Papyrus there is a passing reference to an illness affecting the skin which Regöly-Mérei (1966) suggests may have been smallpox.

There remains the tantalizing speculation, based on these 3 mummies, that smallpox may have occurred among the inhabitants of Egypt more than 3000 years ago, which is well over a thousand years earlier than any reliable references to the disease elsewhere in the ancient world. From here it could well have been carried to India during the 1st millennium BC, either overland by caravan or, more likely, by sea.

India

Although there may have been a population of some 5 million in the Indus valley during the 2nd millennium BC, this civilization collapsed and disappeared about 1600 BC. A thousand years later another civilization, based on rice-growing, developed further east, and by 500 BC the Indian subcontinent had a population of about 25 million, of whom some 15 million lived in the Ganges basin, which has remained the demographic centre of the subcontinent ever since.

Holwell (1767), a physician of the British East India Company who survived imprisonment in the Black Hole of Calcutta, suggested that smallpox had existed in India from "time immemorial", and stated that it was mentioned in the most ancient Sanskrit writings, the *Atharva Veda*. Holwell's suggestions have been quoted by Hirsch (1883) and Hopkins (1983a), among others, as evidence of the occurrence of smallpox in India from very early times. Nicholas (1981), a scholar of Indian history and anthropology, contests this view.

He noted that *masūrikā*, the word used for smallpox, is found in many medical compilations produced in India since the beginning of the Christian era, but not in the more ancient *Atharva Veda*. It first appears in the compilations of Caraka and Suśruta, which were begun before the Christian era and put into their final forms in the 4th century AD. But according to Nicholas these texts say very little about *masūrikā* and refer

Table 5.1. Important events in the history of smallpox, from ancient times to 1900

Period	Africa	Americas
2nd millennium BC	? smallpox in 3 Egyptian mummies.	
1st millennium BC		
1st century AD		
2nd century		
4th century		
5th century		
6th century		
7th century	Ahrun of Alexandria describes smallpox (622).	
8th century		
10th century	Smallpox probably spread to western Africa by Arabs.	
13th century	Variolation by cutaneous route introduced into Egypt by Mamelukes.	
14th century		
15th century		
16th century	Smallpox epidemic in eastern Africa (1589). Smallpox introduced into coastal ports of western Africa.	Smallpox introduced into Caribbean (Hispaniola) (1507). Smallpox spreads from Hispaniola to Mexico (1520). Smallpox spreads to Peru (1524). Smallpox in Brazil (1555).
17th century		Severe smallpox outbreak in Massachusetts, USA (1617). Severe outbreak in Brazil (1665-1666).
18th century	Smallpox introduced into Cape Town and destroys Hottentots (1713 and 1755). Smallpox spreads in central Africa with slave traders.	Variolation introduced into North America (1721). Smallpox disrupts Colonial army at Quebec (1776). Washington orders variolation of Continental army (1777).
19th century	Further spread of smallpox in eastern and central Africa with caravans (1840s). Variola minor ("amaas") described in South Africa (1890s; 1904).	Pandemics among North American Indians (1801-1802 and 1836-1840). President Jefferson initiates vaccination of American Indians (1801). President Lincoln has smallpox (1863). Variola minor occurs in Florida and spreads throughout USA (1896-1900s).

Table 5.1. (continued)

Asia and Oceania	Europe
Epidemic spreads from Egypt to Hittites (~1350 bc) ?? smallpox.	
Compilation of <i>Suśruta Samhita</i> in India (~100 bc). Mentions <i>masūrikā</i> , which may be smallpox.	Plague of Athens, from Egypt and Libya, spreads to Persia (430 ac). Epidemic in Sicily, from Libya (395 ac) ?? smallpox.
Smallpox introduced into China from south-west (48-49).	Antonine Plague spread to Rome from Mesopotamia (165) ?? smallpox.
Ko Hung in China differentiates smallpox from measles (340).	Bishop Nicaise of Rheims recovers from smallpox (450); becomes patron saint of smallpox.
"Elephant War" in Mecca (568) ? smallpox decimates Ethiopian soldiers. Smallpox spreads from China to Korea (583) and from Korea to Japan (585).	Gregory of Tours describes ? smallpox in France and Italy (580). Bishop Marius uses term "variola".
Arabs carry smallpox with invading armies to North Africa and Spain.	
Al-Razi publishes descriptions of smallpox and measles (910). First use of modern Chinese character for smallpox. First use of variolation by intranasal route in China as secret rite. <i>Ishinho</i> published in Japan (982); describes "red treatment" and isolation hospitals.	Daughter of King Alfred of England has ? smallpox.
King of Burma dies of smallpox. Epidemic of smallpox in Siam.	Gilbertus Anglicus describes clinical types of smallpox in England (1240); recommends "red treatment". First introduction of smallpox to Iceland from Denmark (1241).
King of Siam dies of smallpox (1534).	Severe smallpox epidemic in Paris (1438). Records of deaths from smallpox maintained in Geneva (1580).
Severe epidemics in Siberia (1630). Variolation by nasal route popularized in China.	Severe smallpox in most of Europe. London Bills of Mortality record 10% of deaths due to smallpox (1629). First account of smallpox in Russia (1623). Sydenham describes clinical types of smallpox, and distinguishes measles from smallpox.
Chinese emperor sends variolation teams to control smallpox in Tartary (Siberia) (1724). Variolation introduced into Japan (1744). Smallpox epidemics among aborigines in Australia (1789 and 1829).	Variolation introduced into Great Britain and Bohemia (1721). London Small-Pox and Inoculation Hospital founded (1746). Heberden distinguishes smallpox from chickenpox (1768). Dimsdale variolates Catherine the Great of Russia (1768). Smallpox cripples Spanish-French fleet attacking England (1779). Jenner describes vaccination (1798).
Vaccination introduced into India (1802), Philippines (1803), Java (1805), China (1805). Vaccination introduced into Siam (1840). Vaccination introduced into Japan (1849).	Vaccination spreads throughout Europe (1800-1801). Compulsory vaccination in Bavaria (1807). Revaccination proposed in Württemberg (1829). National Vaccine Establishment founded in England (1808). Negri in Naples begins systematic production of vaccine in cow (1845). Production in cows introduced in France (1864). Last great epidemic in Europe, after Franco-Prussian War (1870-1871). Copeman demonstrates bactericidal effect of glycerol (1892).

to it as a trivial skin disease. The first extant description of *masūrikā* as a severe and sometimes fatal disease appears in the works of Vagbhata, a physician writing early in the 7th century AD. A century later the *Nidana* of Madhava-kara included an extensive and knowledgeable chapter on *masūrikā*, treating smallpox, chickenpox and measles together. Wise (1867) suggested that the failure of earlier Indian writings to identify *masūrikā* as a severe disease indicates that smallpox may have changed its characteristics not long before al-Razi, towards the end of the 1st millennium AD, in Baghdad, described the disease as we now know it (see below). However, Chinese descriptions identify smallpox as a serious disease that was imported from the west, apparently as early as the 1st century AD.

The only suggestion of the possibly earlier existence of smallpox in the Indian subcontinent was the epidemic that attacked Alexander's army in 327 BC, when it was camped on the lower Indus, but although "scabs" are mentioned the description is so incomplete that it is difficult to be at all certain of the diagnosis.

We can speculate that smallpox was brought to India by Egyptian traders during the 1st millennium BC, to become endemic in the large population of the Ganges valley. However, there is no reliable evidence of its existence there before the description in the *Sūsruta Samhita*, which appears to relate to a rather trivial skin disease rather than a generalized infection with a high mortality.

However, for the last 1500 years smallpox has been known to be endemic in India, especially in the densely populated agricultural settlements of the Ganges plain. Periodic epidemic episodes occurred then, as they continued to do until the disease was eradicated in the latter part of the 20th century.

South-western Asia

Apart from the problematic epidemic among the Hittites, already referred to, the earliest reference to an epidemic disease that may have been smallpox is the description of a plague that afflicted the Ethiopian invaders of Mecca in Arabia in AD 568, in what was called the "Elephant War" (Moore, 1815). The Ethiopian soldiers were afflicted by a severe illness characterized by a rash, which almost totally destroyed the invading army and ended Ethiopian rule in Arabia.

Scholars in south-western Asia and in Alexandria, on the Egyptian Mediterranean coast, produced notable works on smallpox long before European physicians did. Ahrun, a Christian priest who lived in Alexandria 30 years before the Arab conquest of Egypt, wrote clear descriptions of smallpox and measles in AD 622 (Moore, 1815):

"When the smallpox pustules are white and red, they are healthy; when green and black, malignant; and if, after a time, the eruption of smallpox and measles changes to a saffron colour, and the fever moderates, good hopes may be entertained; but if these eruptions appear during a frenzy fever, they are fatal."

The most notable of these writings, however, is that of al-Razi (Abu-Bakr Muhammad Ibn Zakariya, al-Razi (Rhazes)), the great Persian-born physician who was in charge of the hospital at Baghdad. Al-Razi's treatise on smallpox and measles was translated into Latin and Greek and influenced European physicians until the 17th century and even later (al-Razi, 910).

Besides clearly distinguishing between smallpox and measles, as Ko Hung in China had done 6 centuries earlier (see below), al-Razi made some astute epidemiological observations on smallpox, describing its seasonal incidence (most common in spring) and the fact that it was primarily a disease of children.

Another great Persian scholar, Avicenna (980-1037), also wrote on smallpox; translations of his works into Latin influenced medical practice in Europe in Renaissance times.

Europe

During the classical era Greece was the only densely populated part of Europe, with a population of about 3 million in 400 BC. By the beginning of the Christian era emigration had reduced the population to about 2 million and the centre of gravity of the population of Europe had shifted to Rome.

There are no unequivocal records of smallpox in Europe before the 6th century AD, but it has been suggested that it was a major component of the "Plague of Athens" that occurred in 430 BC, during the Peloponnesian Wars, and was described by Thucydides. This affliction was said to have originated in "Ethiopia" and spread to Egypt and Libya before crossing the Mediterranean to the port of Piraeus and thence reaching Athens.

From Epidemics to Endemicity

The earliest writers on smallpox whose descriptions are now universally accepted—Ko Hung in China, Vagbhata in India and al-Razi in Asia Minor—describe smallpox as primarily a disease of children. This is a mark of well-established endemicity and was the result primarily of demographic factors. Alivizatos (1950) noted that smallpox was repeatedly imported into Germany by the Crusaders towards the end of the 12th century. It began to cause extensive epidemics only by the 14th century, eventually becoming a disease in which the majority of cases occurred in children (it was given the name *Kinderblättern*) only at the end of the 17th century. The change occurred more rapidly than this in more densely populated countries (for example in Mexico, see below), but in most places it probably took several human generations. Thus the classical early descriptions of smallpox as a disease primarily affecting children argue for the presence of smallpox in the area concerned (for example in south-western Asia, following al-Razi's description) some centuries earlier.

Except for the absence of any reference to residual pockmarks in those who recovered, Thucydides' description has suggested to several medical historians (Zinsser, 1935; Alivizatos, 1950; Littman & Littman, 1969) that the epidemic may have been due to smallpox. It lasted for over 2 years and devastated the Athenian army.

According to some authorities (Alivizatos, 1950), an epidemic that prevented the Carthaginians from gaining control of Sicily, at the siege of Syracuse in 395 BC, may also have been smallpox. The next speculative suggestion of smallpox in Europe was its possible role in the Antonine Plague, which appeared to start in a Roman army fighting in Mesopotamia in AD 164. Returning soldiers brought an infectious disease to Syria and Italy, where it raged for 15 years and greatly weakened the Roman empire. The clinical features were described, rather inadequately, by Galen, and, more recently, in a critical analysis of the evidence Littman & Littman (1973) argue convincingly that the principal disease that occurred in the Antonine Plague was probably smallpox.

Apart from Rome, there were few centres of population in Europe large enough at that time to have supported endemic smallpox, but various epidemics from the 5th century onwards have been ascribed to the disease. St Nicaise, the Bishop of Rheims, who is said to have suffered from smallpox, was beheaded by the Huns in AD 452 and was later accepted as the patron saint of European victims of smallpox. During the 6th century smallpox may have occurred as an endemic disease with

epidemic episodes, one of which was described by Bishop Gregory of Tours, but Moore (1815) considers that this outbreak was due to bubonic plague. At about this time Bishop Marius of Avenches (near present-day Lausanne, in Switzerland) used the Latin word "variola" for the first time (from *varius* = mottled, or *varus* = a pimple) to describe the epidemic illness then present in Italy and France. It was not until 5 centuries later that Constantinus Africanus first explicitly limited the use of the word "variola" to the disease we call smallpox.

There is a dearth of information on smallpox, as on most subjects, for the remainder of the Middle Ages. However, it undoubtedly accompanied the armies of Islam across North Africa in the 7th century and spread into Spain and Portugal with their conquest in 710. The Germanic warriors crushed the Moors when invasion of France was attempted in 731, but smallpox and measles remained in France as legacies of the Moors. Smallpox may also have occurred from time to time in other parts of Europe following importations from endemic areas, and by the latter half of the 10th century it was a relatively common disease in most of the Arab-controlled areas of North Africa and Europe.

China and Japan

The earliest agricultural society of China comprised about 1 million peasants dependent on wheat-growing, in the valley of the Huang Ho river in 3000 BC. The population

grew steadily, until by 400 BC there were some 25 million people living in the northern half of China proper, mostly in the valleys of the Huang Ho and Yangtse rivers. After the political unification of China in 221 BC the population grew to about 50 million and fluctuated around that number until AD 1000, when there was a demographic explosion fostered in part by fuller exploitation of the rice-growing potential of the Yangtse valley.

In contrast to the speculations on the existence of smallpox from very early times in Egypt and India, there is general agreement that smallpox was introduced into China from outside the country. According to Needham & Lu (in press), the earliest description of smallpox and its origins in China occurs in the *Handbook of Medicines for Emergencies*, which was completed by the great physician Ko Hung in AD 340:

"Recently some people have suffered from seasonal epidemic sores which attack the head, face and trunk. In a short time they spread all over the body. They look like red boils, all containing some white matter. The pustules arise all together, and later dry up about the same time. If the severe cases are not treated immediately many will die. Patients who recover are left with dark purplish scars the colour of which takes more than a year to fade . . . People say that it first appeared from the West in the fourth year of the Yung-Hui reign-period, and passed eastwards, then spreading all over the country . . . Another saying is that in the Chien-Wu reign-period prisoners of war brought it back from Nan-yang, and for this reason one of its names is still 'prisoners' pox'."

Needham & Lu (in press) point out that there are difficulties in giving accurate dates for the periods mentioned in this text, but they conclude that the likely date for the introduction of smallpox was in the years between AD 25 and AD 49, when Ma Yuan was subduing the aboriginal tribal people of Hunan province. Following Hirsch (1883) and Macgowan (1884), Hopkins (1983a) suggests that there may have been an earlier introduction than this, from "Huns" in the north in about 250 BC. If so, as Macgowan suggests, it died out and had been forgotten. From about the 2nd century AD smallpox was established as an endemic disease in the densely populated river valleys; there are references from the latter part of the 6th century onwards to pockmarked persons and to various treatments for smallpox.

Japan consisted of a group of sparsely inhabited islands with a total population of

less than 5 million in AD 1000; most of the islands were too small and too thinly populated to support endemic smallpox. There were nevertheless repeated introductions from China and Korea. As early as the 6th century cultural and trading contacts were increasing between China and Japan, both directly and via Korea. Buddhism was first introduced into Japan from Korea in AD 552, and further contacts were made later that century. Smallpox was introduced at about the same time, and the Japanese were perplexed to know whether to ascribe the pestilence to their indigenous Shinto gods or to the new Buddha. There were repeated reintroductions during the 7th and 8th centuries. Nara, the first real city in Japan, was established in 710; in 735 smallpox, introduced by a shipwrecked sailor, devastated the city of half a million inhabitants and killed many of the nobles. Smallpox continued to be the focus of religious argument between the Shinto priests and the adherents of Buddhism, and in 748 the great bronze statue of Buddha, the *Nara Daibutsu*, was completed, having been commissioned by the Emperor to put an end to his troubles with smallpox. Endemic smallpox was established in Japan during the 10th century, but there were still recurrent severe epidemics that affected villages and towns in which the endemic disease did not occur.

Summary: the Spread of Smallpox from Antiquity until AD 1000

It is impossible to do more than guess about the original home of smallpox, which may have developed as a specifically human disease at any time after irrigated agriculture had allowed human populations to grow sufficiently large, perhaps some 6000 years ago. The major contenders for the doubtful honour are Egypt and India. It is reasonable to argue that smallpox was endemic in the densely populated Nile and Ganges river valleys at the beginning of the Christian era. From there it spread west to south-western Asia and made periodic incursions into Europe, but was not properly established around the Mediterranean littoral until the armies of Islam drove through North Africa into the Iberian Peninsula in the 8th century. As population size increased in various parts of Europe, endemic smallpox extended, so that it was probably known throughout south-western Asia and the Mediterranean

littoral of Africa and Europe by the end of the 10th century. Al-Razi published his detailed and percipient account of smallpox and measles about AD 910.

Early in the Christian era smallpox was carried to the east, first with warring armies and later with traders who moved along the Burma Road in the south and the Silk Road in the north. Smallpox was probably already established as an endemic disease in China by the 4th century, when Ko Hung differentiated between smallpox and measles, some 600 years before al-Razi. Subsequently, as contacts were developed between China and Korea and Japan, smallpox was repeatedly imported into the two latter countries, to become endemic there during about the 10th century.

By the end of the 10th century, therefore, smallpox was probably endemic in the more densely populated parts of the Eurasian land mass and along the Mediterranean littoral of Africa. There were still many uninfected localities, but the stage was set for endemicity with periodic explosive epidemics, a situation that characterized the 16th and 17th centuries in Europe, when this disease then spread to most of the inhabited world. Fig. 5.1 presents a possible scenario of the spread of smallpox throughout the Eurasian land mass and to adjacent countries up to the end of the 1st millennium AD.

SMALLPOX IN SOUTHERN ASIA BETWEEN 1000 AND 1900

The Indian Subcontinent

With a population of 25 million by 500 BC, already dense enough in the valley of the Ganges to support endemic smallpox, the population of the Indian subcontinent rose steadily over succeeding centuries to reach about 80 million by AD 1000 and 100 million by 1500. Thereafter it rose somewhat more rapidly, to 185 million by 1800, and then exploded, exceeding 280 million in 1900.

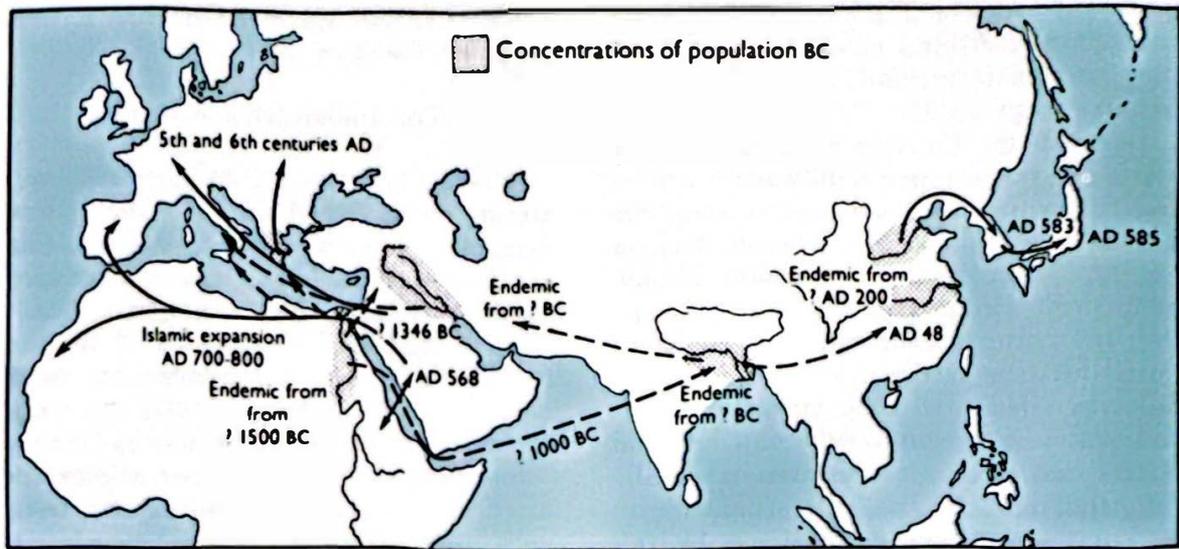
Smallpox was probably present in India for over 2000 years and remained endemic there until its final eradication from the subcontinent in 1975. Apart from the writings of Vagbhata and allusions to the Hindu goddess of smallpox, Śītalā (see Plate 5.2), there is little historical evidence of smallpox in India until after 1500, when European commentators began to report on various aspects of Indian life. The ecological and demographic conditions in India were such that the pattern of endemicity with seasonal (spring) epidemics that was observed after 1500 had probably prevailed for a millennium before that.

The earliest European accounts of smallpox came from the Portuguese enclave of Goa, where 8000 children are said to have

Inoculation, Variolation and Vaccination

When the practice of deliberately introducing material from smallpox patients into the skin of susceptible subjects was introduced into Great Britain early in the 18th century it was called "inoculating the smallpox" or "inoculation". With Jenner's replacement of material from smallpox patients with fluid from cowpox lesions in 1798, from cows or humans, it became necessary to distinguish inoculating the cowpox from inoculating the smallpox. At first the term "vaccine inoculation" was used; later, Jenner's practice came to be called "vaccination" and the inoculation of material from smallpox patients was called "variolaion". In this book we have used the terms inoculation and variolation as synonyms, reserving "vaccination" for procedures involving cowpox or vaccinia virus.

Variolation was always carried out with material from the pustules or scabs of patients. After animal vaccines were introduced during the latter part of the 19th century, vaccination was usually carried out with vaccine "lymph" from cows. However, before that time the virus was maintained by arm-to-arm vaccination of children, and was sometimes shipped over long distances as "vaccine scabs", as well as being dried on threads or ivory points (see Chapter 6).



"Plagues": ? smallpox

Hittites 1346 BC
Syracuse 595 BC
Athens 430 BC
Antonine AD 165
Mecca AD 568

Writers or books

Suśruta
Ko Hung
Ahrun
Vagbhata
Al-Razi
Ishinbo

Place

India
China
Alexandria
India
Baghdad
Japan

Date

? BC
AD 340
AD 622
AD 600-700
~ AD 910
AD 982

Fig. 5.1. Possible early sites of outbreaks and routes of spread of smallpox in the ancient world. "Plagues" are historical episodes of epidemic disease reported in ancient and classical literature, which may have been due to smallpox. "Writers" refer to physicians who wrote the principal descriptions of smallpox before the end of the 1st millennium AD.

died in an outbreak in 1545. Scattered references occur to outbreaks of smallpox accompanying military campaigns in Ceylon and on the Indian mainland, but more complete descriptions date from the 18th century, after the beginning of *de facto* British rule in India in 1757.

A decade later, Holwell (1767) described a situation in Bengal which remained characteristic of smallpox in many parts of India during the succeeding 2 centuries: endemic disease with spring (dry season) maxima, punctuated by outbreaks of epidemic intensity every 5-7 years. There were droughts, floods, famine and a particularly severe epidemic of smallpox in Bengal in 1769-1770.

Although variolation had been known for centuries in India, it was nowhere practised on a large enough scale to be of importance as a public health measure. It protected individuals, but its spread from inoculated persons contributed to outbreaks of smallpox. In 1802 the Swiss physician Jean de Carro, who then lived in Vienna and was an enthusiastic supporter of Jennerian vaccination, succeeded in sending viable vaccine to Bombay, via Baghdad. Although at first viewed with

suspicion as a British trick, vaccination spread, initially more rapidly in Ceylon than in India. However, during the first half of the 19th century smallpox continued to take its toll. For example, superimposed on the endemic background were 4 major epidemics in Calcutta during the first half of the 19th century: in 1832-1833, 1837-1838, 1843-1844 and 1849-1850.

During the second half of the 19th century, statistical reports of the occurrence of various infectious diseases were compiled which always ranked smallpox as one of the leading causes of death in India. For example, during the 10 epidemic years of 1868-1869, 1872-1874, 1877-1879 and 1883-1884 (Fig. 5.2), at least 2.5 million out of the estimated 180 million people in British India were reported to have died of smallpox, and experience in the 20th century suggests that there was gross underreporting of deaths as well as of cases. Even in a non-epidemic year, as many as 100 000 deaths from smallpox were reported. Many of the epidemics in India, up to the time of eradication, were intensified by crowding and poverty and the vast movements of people associated with religious festivals,

Gods, Goddesses and Saints Associated with Smallpox

A feature of human reactions to smallpox that demonstrates its impact was the association of specific gods, goddesses and saints with the disease (Plates 5.2–5.5). Hopkins (1983a) describes these deities and saints in some detail; the characteristics of the best known are briefly noted here.

In Europe, *St Nicaise*, the Bishop of Rheims, who was killed by the Huns in 452, shortly after he had recovered from an attack of smallpox, became the patron saint of smallpox and was revered during the Middle Ages. Subsequently, the Reformation and the greater menace of plague (which threatened all adults as well as children, whereas endemic smallpox was by then mainly a disease of children) led to the neglect of St Nicaise.

Śitalā (Sitala) mata appears to have been an Indian folk goddess from early times, whose association with smallpox dates from a later period (Nicholas, 1981). However, from about the 18th century onwards *Śitalā* was closely associated with smallpox and was a widely patronized goddess, with temples and shrines all over India. It will be interesting to see what changes occur in the worship of *Śitalā* now that smallpox has been eradicated from India.

T'ou-Shen Niang-Niang was a goddess of smallpox in China. Tradition traces her worship to an 11th century Buddhist nun who is credited with introducing variolation into China (see Chapter 6), and during the mid-19th century she was one of the most popular objects of worship among the people at large, irrespective of their religious affiliations. Temples were erected to her all over China.

In Japan, a red picture of *Tametomo*, a 12th century hero who was reputed to have thwarted a smallpox demon, was often hung in the rooms of smallpox victims to aid their recovery. The colour red had an ancient and persistent association with smallpox, and was supposed to promote recovery (see Hopkins, 1983a).

In Africa, worship of *Sopona*, a smallpox deity, existed among the Yorubas and some of their neighbours in south-west Nigeria, Benin and Togo, having been introduced from the north at the beginning of the 18th century. Formal worship of *Sopona* was controlled by *féticheurs*, who were in charge of the shrines and carried out variolation. Sometimes *féticheurs* were suspected of spreading smallpox. When they were transported to Brazil as slaves, some of the Yoruba-speaking people took *Sopona* with them, although he was more generally known by another of his names from western Africa, *Obaluaye* ("King of the Earth") or *Omolu*.

famines and wars. Although many adults were attacked, in the majority of cases and deaths the victims were infants and young children. In India at this time, as was the case a century earlier in Europe, there was a popular saying that children should not be regarded as permanent members of the family, for purposes of inheritance, until they had recovered from smallpox. Facial pockmarks were the rule among adults, and blindness, for which smallpox was often responsible, was common.

Against a background of endemic smallpox, a steady succession of major epidemics, peaking every 5–7 years, continued after the great epidemic of 1883–1884 but at a much lower level, because of the cumulative effect of steadily increasing vaccination (see Fig. 5.2). Nevertheless, in many parts of the subcontinent vaccination was not extensively

practised until the 1950s. India and countries adjacent to it remained the major focus of smallpox in the world until 1975, when eradication was achieved there.

Burma, Siam and Indochina

The population histories of the countries between India and China—Burma, Siam (Thailand) and Indochina (comprising present-day Democratic Kampuchea, Lao People's Democratic Republic and Viet Nam)—are rather similar, although until 1900 the population of Siam was only about half that of the other two. Two thousand years ago the populations of Burma and Indochina each numbered about 1 million (0.5 million for Siam). They had doubled by AD 1000 and doubled again by 1500. By 1800 the popula-

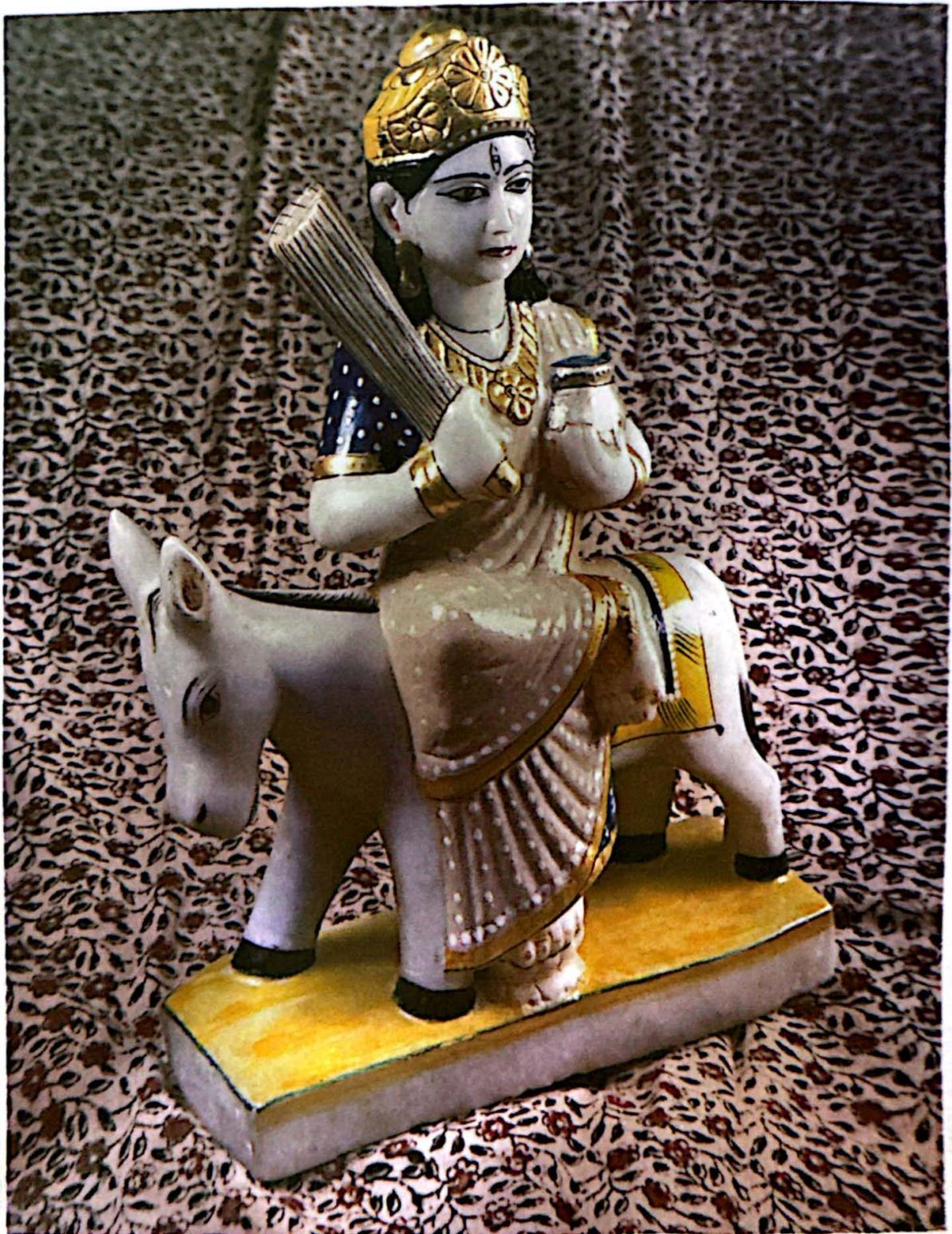


Plate 5.2. *Sitalā Mata*, the Hindu goddess of smallpox.

White-bodied one, mounted on an ass, in your two hands a broom and a full pot,
To mitigate fever, you asperse, from the full pot, with the broom,
the water of immortality.
Naked, with a winnowing fan on the head, your body
adorned with gold and many gems, three-eyed,
You are the quencher of the fierce heat of pustules;
Sitalā, I worship you.
(Quoted in Nicholas, 1981.)

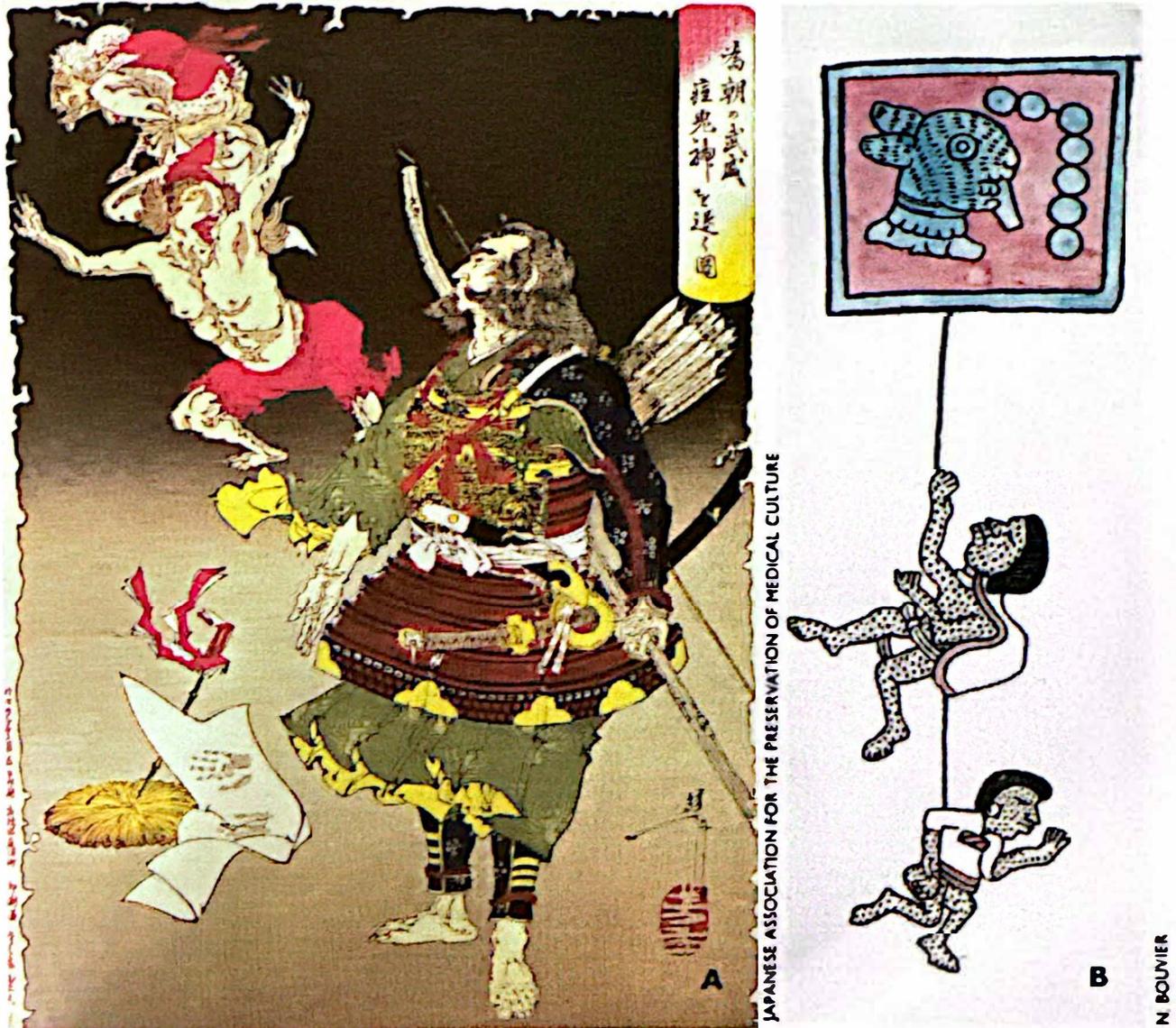


Plate 5.3. **A:** Chinzei Hachiro Tametomo (1139–1170), a skilful archer, was exiled to the island of Oshima. He is reputed to have prevented a smallpox demon from landing there. His image was hung on the walls of Japanese homes to help to protect them against smallpox. **B:** Drawing of patients with smallpox in Mexico in the year 1538. (Detail from *Codex telleriano-remensis*, in the Bibliothèque nationale, Paris.) **C:** K'ang Hsi, Emperor of China, 1661–1722. Although the third son, the pockmarked K'ang Hsi was chosen as emperor after his father died of smallpox in 1661. Unlike previous Manchus, he variolated his children and his troops. (Detail from a 19th century portrait.)



Plate 5.4. A: T'ou-Shen Niang-Niang, the Chinese goddess of smallpox. B: Ma-chen, the god who heals the scars of smallpox. C: Pan-chen, the god prayed to in black smallpox. (From Doré, 1915-1925.)



Plate 5.5 African gods of smallpox. **A:** Sozona, smallpox god among the Yorubas of western Africa. **B:** Yorubas who were taken to South America as slaves took their gods with them. Sozona was in time transformed into Omolu/Obaluaye.

The Significance of Epidemics

Devastating epidemics of smallpox created a deep impression on the population, and all histories of smallpox are punctuated with lists of the years of the major epidemics. It is important to distinguish two ecologically distinct situations in which such epidemics occurred. The first was when smallpox was introduced into a place in which it had not occurred previously, or at least not for many years, so that a large segment, perhaps all, of the population was susceptible. This led to epidemics that affected all age groups, and because of the great social disruption caused by the simultaneous illness of most of the bread-winners in a subsistence society, such epidemics were associated with very high death rates. In small populations, whether on islands such as Iceland or in the early colonial settlements in North America, the disease finally died out for lack of susceptible subjects. Further epidemics some years later would occur when fresh importations of smallpox encountered populations with adequate numbers of susceptible persons composed of hitherto unexposed children or immigrants.

The second situation in which "epidemic years" were recorded was in populous areas in which smallpox was always present as an endemic disease, as in Europe in the 18th century and the Indian subcontinent until 1975. For a variety of reasons—demographic, climatic and, in later years, the activity of vaccinators—the population of susceptible persons and optimum conditions for transmission fluctuated so that epidemic exacerbations occurred every few years, against a background of endemicity. In this latter situation disruption of the community was much less severe, because there were always many smallpox-immune bread-winners.

tions of the 3 countries were 6 million, 3 million, and 6.5 million respectively; population growth then took off, doubling during the next century.

There is only scanty information on smallpox in these countries prior to the late 19th century. A king of Burma died of smallpox during a military campaign in 1368, and variolation is said to have been introduced into Burma in 1785 from the recently annexed province of Arakan. From the mid-19th century Burma was administered as part of British India, and its smallpox statistics are included in the Indian records (Annual Reports of the Public Health Commissioners with the Government of India).

Siamese writings refer to epidemics of what was probably smallpox during the 14th century, and from the 16th century onwards there are repeated references to *thoraphit* and *ōk fī dāt* (the formal and familiar Siamese words for smallpox), with severe epidemics in 1563–1564, 1621–1623, 1749–1750 (Terweil, 1987). These Siamese writings were confirmed by the French writer de la Loubère in the late 17th century: "In a word, there are some contagious diseases but the real Plague of this Country is the Small Pox: it often makes dreadful ravages, and then they enter the bodies without burning them" (Loubère,

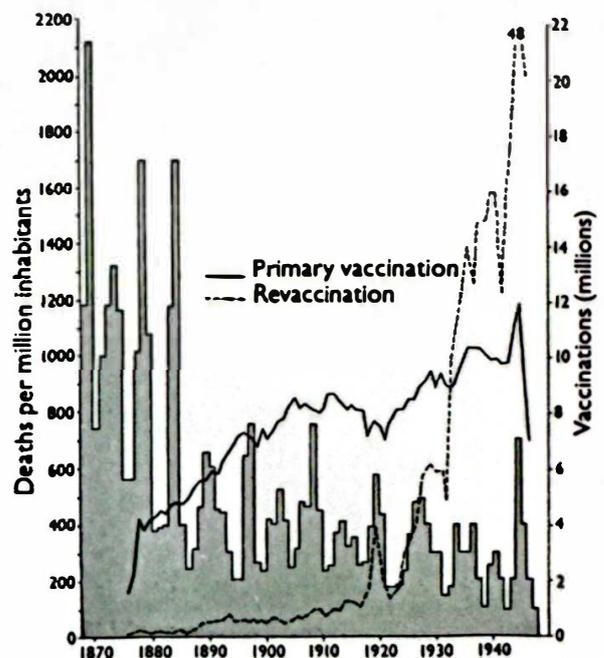


Fig. 5.2. Reported numbers of deaths from smallpox per million population in British India from 1868 to 1947, and the numbers of primary vaccinations and revaccinations from 1875 onwards. Epidemic peaks occurred about every 5 years throughout this period. (Data from Annual Reports of the Public Health Commissioners with the Government of India.)

reprinted 1969). Vaccination was introduced into Siam in 1840, shipments of vaccine scabs

being sent from Boston, USA, in 1840, 1844, 1846 and 1861, through Christian mission societies.

Severe epidemics continued to occur in Siam and Indochina during the latter part of the 19th century, the mortality among children in some epidemics being so great as to have a prolonged demographic effect because of the paucity of nubile women. As late as 1898, 95% of adolescent children in northern Viet Nam were pockmarked and nine-tenths of all blindness was ascribed to smallpox.

South-western Asia

Between the Indian subcontinent and Europe lies part of the Eurasian land mass that is variously described as south-western Asia, the Near East and the Middle East. It comprises present-day Afghanistan, Iraq and the Islamic Republic of Iran, the Arabian Peninsula, including its Mediterranean littoral, and Turkey-in-Asia. In 1800 none of these countries had a population of more than 9 million. However, Turkey, Arabia and Persia (Iran) had supported populations of some 4–5 million for the previous 2 millennia, and they were of major importance as centres of culture during the Dark Ages of Europe and as the corridor for trade, culture and conquest between Europe and the Indian subcontinent.

The work of Persian scholars, notably al-Razi and Avicenna, shows that smallpox was endemic in many parts of south-western Asia from at least the 6th century. Early in the 7th century, inspired and united by Mohammed's teachings, Arab armies began their war of conquest and took smallpox with them to Persia, across western Asia and northern Africa and into Spain, which was conquered in 710.

Although by the time they had reached adult life most persons would have been immune to the disease, smallpox affected several of the rulers of the Arabian empire, killing one caliph, leaving three with pockmarks and blinding two others. In the 10th and 11th centuries, as Arab traders extended their voyages to the east coast of Africa and across the Sahara to western Africa, their expeditions introduced smallpox into Africa south of the Sahara (see below).

Variolation by cutaneous inoculation was practised in various parts of south-western Asia from early times. It is said to have been introduced into Egypt by the Mamelukes in the 13th century, and it was in Constantino-

ple that Lady Mary Wortley Montagu and the physicians Emanuele Timoni and Jacob Pylarini learned of the procedure in the early 18th century (see Chapter 6). However, it does not appear to have been practised on a scale or in a way that mitigated the severity of smallpox in the community, although it was important in preserving the beauty of recruits to the imperial harems.

SMALLPOX IN EASTERN ASIA BETWEEN 1000 AND 1900

China and Korea

The population of China, which had remained at 50–60 million for the whole of the 1st millennium of the Christian era, doubled during the next 2 centuries as the rice-growing potential of the Yangtse valley was further exploited. Then in 1211 the Mongols began their conquest of China, a bloody war which killed some 35 million people. It was 1500 before the population reached the level (110 million) that it had attained 300 years earlier. Thereafter population growth surged ahead, apart from a set-back in the middle of the 17th century associated with the Manchu conquest, and by 1900 the total number of inhabitants had reached about 475 million.

Smallpox spread through the dense agricultural settlements of the Huang Ho valley and from about the 2nd century AD was established as a major endemic and epidemic disease in China and Korea. As early as the 4th century Ko Hung had written a good clinical description of smallpox (see above), and in the 11th century medical descriptions of smallpox were published by Ch'ien Chung-Yang (1040–1121), who popularized the modern Chinese character for smallpox (a combination of the characters for "lentil-bean" and "sickness"). At about this time worship of a goddess of smallpox, T'ou-Shen Niang-Niang (Plate 5.4A), began. Buddhist, Taoist and Confucian adherents paid tribute to the "Dame who controls smallpox", who was feared more than she was loved.

Although preventive inoculation (variolation) was probably introduced into China at about this time it appears to have been practised as a secret rite and on a small scale (see Chapter 6). It became a public practice during the first half of the 16th century (Needham, 1980), but was never widely used.

At the beginning of the 13th century China had a population of about 100 million, and

smallpox was established in the densely populated areas as an endemic disease, affecting mainly children. It was seen as a threat by the tribal peoples to the north. The Mongols, for example, who began their invasion of China at this time, regarded contacts with the Chinese as a grave danger, whether at horse fairs or in border raids. Four centuries later the leaders of the Manchus dreaded smallpox. In planning raids through weak spots in the Great Wall in 1633, the Manchu Khan insisted that only officers who had had smallpox should be sent on these expeditions, since they would have to go through populations in which smallpox was endemic. When the Manchu dynasty was later established, care was taken to exempt both Manchus and Mongols from otherwise mandatory appearances in Peking (see box). Perhaps, as Manchus, they did not trust variolation; at all events, in 1661, the Shun-Chih Emperor, Aihsin-Chueh-lo Fu-lin, died of smallpox. The third son, the pockmarked K'ang-Hsi (Plate 5.3C), was chosen to be his successor precisely because he had already had smallpox; he reigned as Emperor of China from 1661 to 1722 (Spence, 1974). Unlike earlier Manchus, K'ang-Hsi had his regular troops inoculated against smallpox "as I did my own children".

Late in the 18th century the Tibetan leaders, the Dalai and Panchen Lamas, for a long time declined invitations to come to the court in Peking because of their fear of smallpox. In 1780 the Panchen Lama acceded to the invitation of Emperor Ch'ien-Lung, only to die of smallpox within a few weeks of his arrival. From this time onwards, variolation and, later, vaccination played increasing roles in the epidemiology of smallpox in China, but towards the end of the 19th century European visitors noted that it was difficult to find an adult Chinese entirely free from pockmarks and that persons blinded by smallpox were still very common.

Vaccination was first introduced into Canton and Macao in 1805 by the famous Balmis-Salvany Expedition organized by King Carlos IV of Spain (see Chapter 6). However, the practice was not readily adopted and only spread at all widely in China during the latter half of the 19th century. Indeed, vaccination in China was totally inadequate until the campaign mounted in 1950.

Epidemics of smallpox of great severity ravaged Tibet until 1940, when vaccination was first introduced. Smallpox is thought to

have contributed significantly to the declining population of Tibet in the early 20th century.

Japan

The Japanese state came into being in about AD 650, when the population of the islands had reached approximately 3 million. Thereafter the population grew steadily—to 4.5 million in 1000, 9.75 million in 1300, 22 million in 1600 and about 30 million in 1700. There was then a check in population growth for a century and a half, with an explosion after 1850, when Japan was opened up to Western shipping and Western ideas, so that by 1900 the population had reached 45 million.

Smallpox had been repeatedly introduced into Japan from China and Korea ever since AD 585. At first it died out after each introduction but by the 10th century the disease was endemic. Numerous outbreaks occurred throughout the 10th century, with major epidemics recorded in the years 915, 925, 947, 974, 993 and 998. In 982 the "red treatment" (see box) was first described in *Ishinho*, a Japanese medical book. This practice later spread around the world and persisted in Europe and the USA down to the 20th century, as described by Hopkins (1983a). *Ishinho* also makes mention of special isolation hospitals for smallpox patients, several hundred years before the London Small-Pox and Inoculation Hospital was established in 1746.

During the 13th, 14th and 15th centuries Japan recorded 7 widely spaced epidemics of smallpox (1209, 1277, 1311, 1361, 1424, 1452 and 1454). Only 2 epidemics were recorded in the 16th century (1522 and 1550), but in the 17th century the country was more severely afflicted by outbreaks, during which the Japanese royal family was affected. The northern island of Hokkaido recorded an average of 1 epidemic of smallpox every 14 or 15 years during the 17th and 18th centuries.

At the end of the 17th century the Japanese distinguished 4 types of pox-like illnesses: *sooso* (variola), *fasukea* (measles), *kare* (chickenpox) and the "Portuguese disease" (syphilis) (Kaempfer, 1906). Strangely, the Japanese remained ignorant of the value of variolation until it was introduced from China in the mid-18th century, and as its population density increased Japan continued to suffer heavily from smallpox. Eventually, after

Customs of Mongols, as Affected by Smallpox

“From hereon, Mongols from the Inner Administration [i.e., Inner Mongolia] and from the Qalqas who are to inherit a rank, and have reached (legal) age [18 years], if they have once contracted smallpox, shall come to the capital to be installed, presented at court, and receive their succession. Those who have not yet contracted smallpox, shall proceed to Jeho [= Jehol, north of the Great Wall] to be installed, appear at court, and receive their succession.” (Edict, 1784, quoted by Serruys, 1980.)

several unsuccessful attempts, vaccination was introduced into Japan in 1849, using crusts from vaccination lesions imported from the Netherlands East Indies. Between 1850 and 1860, smallpox vaccination clinics were opened all over Japan, and their success helped to erode the Japanese inhibition about Western learning. Smallpox epidemics continued, however, and there were several severe outbreaks in 1870. A new vaccine institute was established in Tokyo in 1874, and a compulsory vaccination act was promulgated in 1876.

Most accounts of the mortality associated with smallpox in the days before vaccination was available relate to statistics gathered in large cities. Suda & Soekawa (1983) have now provided a fascinating account of the impact of smallpox in rural Japan in the 18th and early 19th centuries. In 1795 a “virgin-soil” epidemic occurred in the village of Mine, on Hachijo-Jima, a small island south of Honshu. There were 1200 cases in a population of 1400 persons (85.7% morbidity) with 460 deaths (a case-fatality rate of 38.3%).

Using temple records, Suda & Soekawa were able to compute the smallpox mortality in the mountainous Hida district on Honshu Island, between the years 1771 and 1851. Smallpox was endemic in the district and neither variolation nor vaccination was practised. The smallpox mortality, as a percentage of total mortality in the whole population and in children under 5 years of age, is shown in Fig 5.3. Although the data relate to mortality, it is reasonable to assume that this reflects the morbidity. The periodicity of outbreaks is obvious, due presumably to the decrease and subsequent increase in the number of susceptible persons, with the periodic disappearance and reintroduction of smallpox. The brunt of the mortality was borne by children under 5 years of age, who constituted about 11% of the population but suffered well over 50% of the deaths from smallpox in epidemic years. In spite of the mortality due to smallpox, the population rose slowly from 2677 (calculated) in 1771 to 3127 (calculated) in 1851.

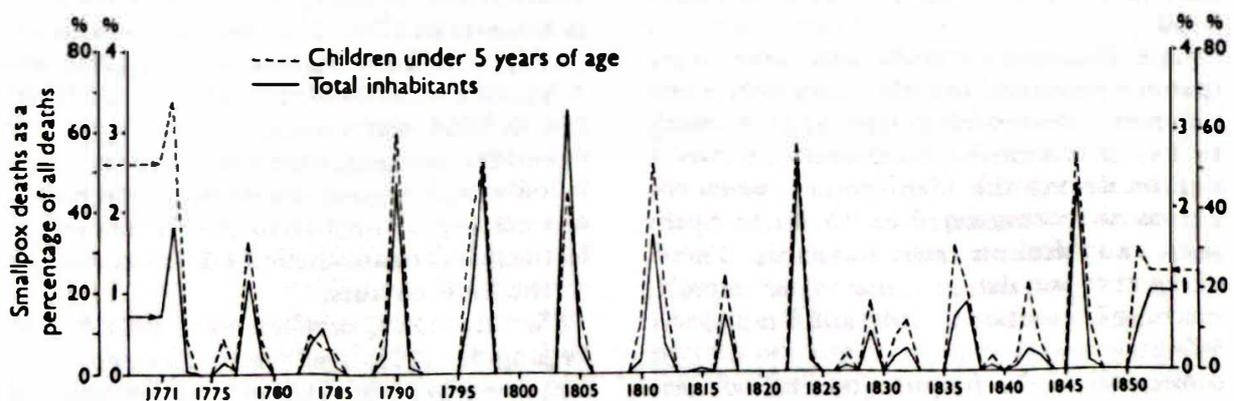


Fig. 5.3. The mortality from smallpox in the Hida district on Honshu Island, Japan, from 1771 to 1851. The population of the district rose from 2677 in 1771 to 3127 in 1851 (lowest 2535 in 1786; highest 3132 in 1834). The solid line indicates deaths due to smallpox as a percentage of all deaths. The broken line (and higher percentage figures) indicates deaths due to smallpox as a percentage of all deaths in children under 5 years of age. The total number in this age group rose from 310 in 1771 to 439 in 1851 (lowest 234 in 1838; highest 444 in 1850). (Data from Suda & Soekawa, 1983.)

The Red Treatment

Ishinbo was probably the first book to mention the existence of red cloth hangings in the rooms of smallpox patients. The practice persisted and in the 17th century a European doctor reported that Japanese physicians "... think it very material in the cure of smallpox to wrap up the patient in red cloth. When one of the Emperor's children falls sick of this Distemper, not only the room and bed are furnished with red; but all persons that come near the patient must be clad in gowns of the same colour" (Kaempfer, 1906). Red paper and red cloth were also hung around the beds of children with smallpox in China, India, Turkey and Asian Georgia; even in western Africa, the Yoruba god of smallpox, Sopona, was associated with the colour red.

In European countries the red treatment was practised from the 12th century onwards, and when he caught smallpox, King Charles V of France (reigned 1364–1380) was dressed in a red shirt, red stockings and a red veil. Queen Elizabeth I of England was likewise wrapped in a red blanket when she fell ill with smallpox in 1562, and similar treatments were applied to other European monarchs.

The red treatment was given scientific authority by Finsen, who claimed that the treatment of smallpox patients with red light reduced the severity of scarring, and later developed rules governing erythrotherapy (Finsen, 1901). It lingered on into the 1930s, although Ricketts & Byles (1904), Schamberg (1904) and others had declared it to be useless.

Indonesia and the Philippines

Two thousand years ago rice-growing Malay peasants were concentrated on the island of Java and the total population of the Malay Archipelago was about 2 million. Wet rice cultivation was introduced from India in about the 4th century and the population rose to 4 million by 1000 and 8 million by 1500. It continued to increase slowly until the European domination of the islands early in the 19th century, when the population soared from about 12 million in 1800 to 38 million in 1900.

The Philippine islands were even more sparsely populated initially, with only a few hundred thousand inhabitants by 1000, rising to half a million by 1500 and just over a million during the 17th century, when the islands were conquered by Christian Spaniards and Muslims from Indonesia. Thereafter, the population grew more rapidly, reaching 2.5 million by 1800 and 8 million by 1900.

Because of the frequent trading contacts between India and the larger islands of the Malay Archipelago from the 4th century onwards, there were repeated opportunities for the introduction of smallpox, but initially population concentrations were too small for the disease to become endemic. The Philip-

pinas were in frequent contact with China, but their population was even more sparse.

No written accounts of smallpox in the Philippines and Indonesia are available until the explorations of the Portuguese and Dutch seafarers in the 16th century, who reported that the disease was then known in both the archipelagos, but was endemic only on the larger islands. Elsewhere, importations of smallpox caused greatly feared epidemics, which occasionally originated from far away, as, for example, when a ship from Mexico carried smallpox to the Philippines late in the 16th century. Severe epidemics were reported in Sumatra in 1780–1783 and in Sarawak, on the island of Borneo, in the following century.

Vaccine virus arrived in Java from Mauritius in 1804, and vaccination was employed from 1816 onwards. However, supplies often failed because regular arm-to-arm vaccination was not begun until 1856. A central vaccine institute was established in Jakarta at the end of the 19th century.

Further north, smallpox was recorded in Penang in 1805, and was introduced into Singapore shortly after it was founded in 1819. Because of commercial traffic with India and China, Singapore, while too small to maintain endemic smallpox, was subject to repeated epidemics due to importations, with notable outbreaks in 1838, 1849–1850, 1859–1860, 1899–1900, 1902–1903 and 1910–1911.

SMALLPOX IN EUROPE BETWEEN 1000 AND 1900

Smallpox had occurred in Europe as an occasional epidemic following importations before the end of the 1st millennium of the Christian era, by which time it was established as an endemic disease on the southern and western fringes of the continent, but not in central and northern Europe. The movement of European Christians to and from southwestern Asia in the course of the Crusades during the 11th and 12th centuries helped to spread smallpox in Europe, and "entirely unambiguous" statements about the prevalence of smallpox in Europe date from that time (Hirsch, 1883). Some dramatic episodes were recorded shortly after this; for example, in 1241 the first epidemic among the "virgin-soil" inhabitants of Iceland killed some 20 000 of its total population of about 70 000, to be followed by other severe epidemics in 1257 and 1291.

The steady growth of population in Europe, particularly in the north-west, from a low figure of about 26 million in the 8th century to some 80 million by the beginning of the 14th century, was interrupted by the Black Death, which reduced the population by more than 25%. Thereafter, it began to increase steadily again—from 80 million in 1500 to 100 million by 1600—but there was a set-back in 1620–1650 associated with the Thirty Years War and several severe outbreaks of plague. The 18th and early 19th centuries saw very rapid population growth—from 140 million in 1750 to 250 million by 1845.

By the 15th century smallpox had become endemic in many parts of Europe and was recorded as a disease of children in Paris. However, it does not appear to have been quite as severe as it became in the 17th and 18th centuries. Reasonably good mortality records are available for Italy and Spain at this time, but they give little prominence to smallpox (Carmichael, 1983). Perhaps the strains of virus then circulating, although not as mild as variola minor as seen in the 20th century, were somewhat less virulent than classical variola major. Endemicity was not established in the outlying islands and both Iceland and Greenland occasionally suffered epidemics that caused numerous deaths in all age groups (Steffensen, 1977).

At the end of the 15th century venereal syphilis was recognized as a "new" exanthematous

disease, which the French called "*la grosse vérole*" to distinguish it from variola, which became "*la petite vérole*". The English followed suit; "pox" becoming the "small pox" and syphilis the "great pox"—the epithet "great" denoting the larger size of the primary and tertiary lesions and, in addition, conveying the notion that it affected adults whereas smallpox was largely a disease of children.

By the 16th century smallpox was well established over most of Europe, except possibly Russia, and as the population increased and became urbanized epidemics occurred more and more frequently, and were better recorded, especially when they affected the royal houses of England, France and Spain. For the first time, important scientific works on infectious disease emerged from Europe, and Girolamo Fracastoro's classic treatise on communicable diseases, *De Contagione et Contagiosis Morbis*, was published in 1546. He noted that diseases such as smallpox were specific contagions that could spread from person to person directly or via fomites, or even through the air. He also commented on the fact that smallpox was primarily a disease of children, as had al-Razi 600 years earlier. In Spain, the presence of smallpox at this time was of particular importance because it provided the source of the shipboard infections that the conquistadors were to spread to the New World.

The 17th century was a period of turmoil in Europe, with constant military activity, the rapid growth of cities and the burgeoning of intellectual activities in the urban class. Academies were established and scientific journals published. Smallpox succeeded plague, leprosy and syphilis as the continent's foremost pestilence. The great English physician Thomas Sydenham (1624–1689), like Ko Hung and al-Razi long before him, clearly distinguished smallpox from measles and observed the different prognoses of patients with confluent and discrete smallpox rashes. A pandemic of smallpox that swept much of Europe and the Near East in 1614 was important because it was probably responsible for the first importation of smallpox into the English and French colonies in North America. At this time also smallpox was established in Russia and was soon carried from Moscow to Siberia, where devastating epidemics occurred in previously unexposed populations.

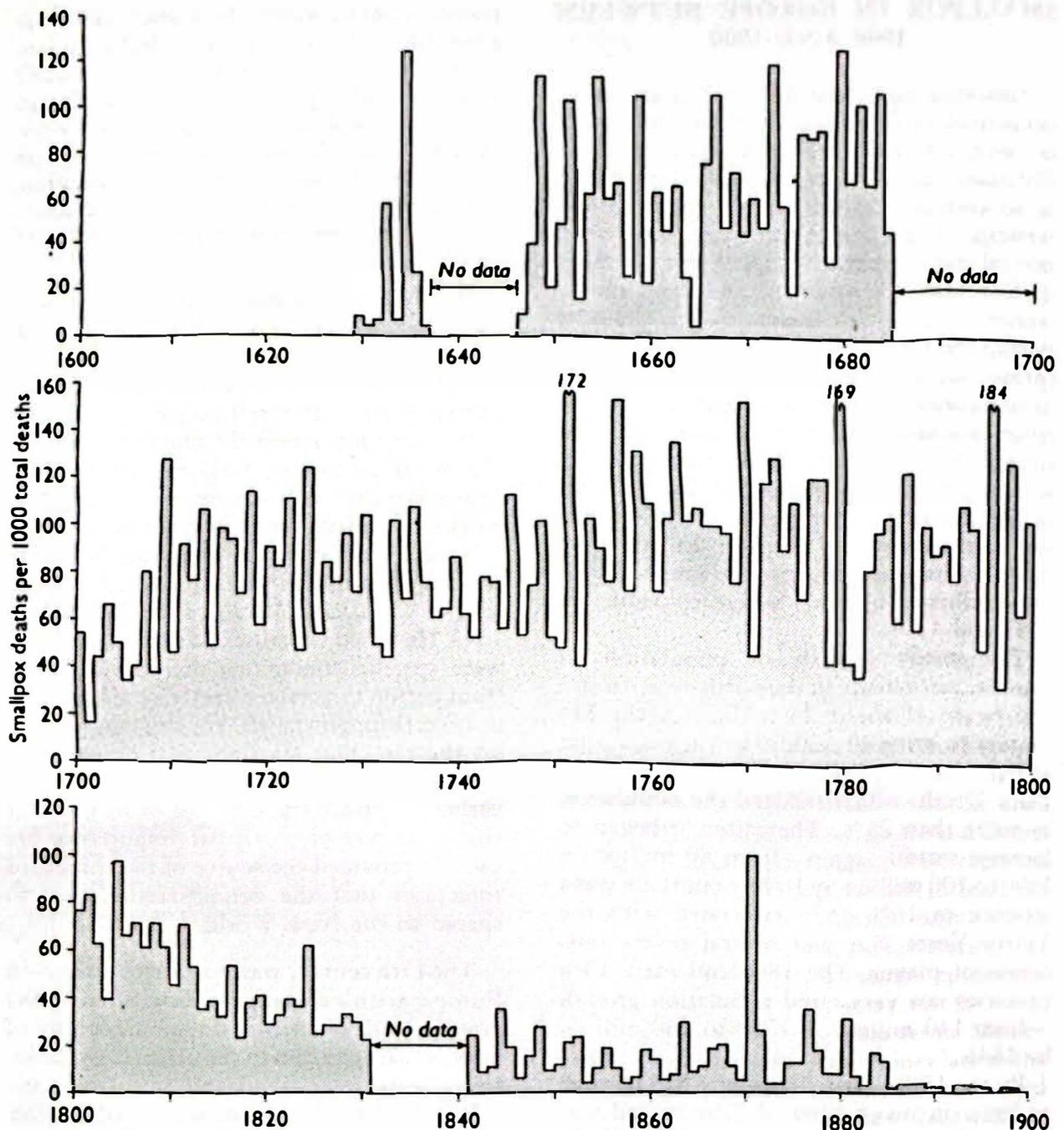


Fig. 5.4. Deaths from smallpox per 1000 deaths from all causes in London, from 1629 to 1900. (Data from Guy (1882) and the Registrar General's Statistical Review of England and Wales.)

An important innovation at this time was the introduction of statistical records. Parishes in London began registering church burials by cause of death, and from 1629 onwards "Bills of Mortality" were published in London (Fig. 5.4).

The authorities in Geneva had started keeping records of deaths from smallpox by age groups from 1580 (Perrenoud, 1980), and in 1680 the Tsar initiated a reporting system in Moscow. From this time onwards, also, the infection of members of Europe's royal houses

had dramatic effects on the succession in several countries, a feature of smallpox in history that is well described by Hopkins (1983a).

Even greater devastation occurred during the 18th century, affecting the general population and royalty alike. The London Bills of Mortality, incomplete though they were, record the increasing impact of smallpox in England (Fig. 5.4). Severe epidemics occurred in Paris in 1719 and 1723, and in the 80 years before 1775 smallpox killed Queen Mary II of England, Emperor Joseph I of Austria, King

Luis I of Spain, Tsar Peter II of Russia, Queen Ulrika Eleonora of Sweden and King Louis XV of France; this doubtless influenced royalty in several countries to promote the practice of protective inoculation (variola-tion). By the middle of the 18th century variolation was having an ameliorating effect on the mortality of smallpox among the well-to-do in Great Britain, the Netherlands and Switzerland. As with vaccination in later centuries, its popularity waned when smallpox was less common and was revived by epidemics, such as the large epidemic in Great Britain in 1752. Variolation remained unpopular in France, Italy, Spain and Sweden, all of which experienced severe outbreaks. In Russia, however, Catherine II, affected no doubt by the experience of smallpox in her own household and by the tragedies in the Hapsburg families, commissioned an Englishman, Thomas Dimsdale, to inoculate her and thus popularized variolation in Russia, which was still suffering from recurrent severe epidemics of smallpox, especially in Siberia and Poland.

The effects of smallpox during the latter part of the 18th century can be appreciated by an examination of the data assembled by Hopkins (1983a). During the last 2 decades of the 18th century, smallpox killed over 36 000 persons in London, and an equal number in Glasgow. This constituted almost 1 out of every 10 deaths in London, and nearly a fifth of all the deaths in Glasgow in that period. In British towns, 9 out of every 10 persons who died of smallpox were under 5 years old.

Smallpox was always present in Great Britain's densely populated large cities, even between epidemics, whereas in the more sparsely populated countryside it commonly appeared only in epidemics, separated by smallpox-free intervals of several years. For young adults from these rural areas who had previously escaped infection, smallpox was one of the most serious risks they faced in the big cities.

In continental Europe also, smallpox was still very destructive. In Sweden, major epidemics in 1779 and 1784 killed over 27 000 persons in those two years alone. Rosen von Rosenstein, a Swedish physician, reported that smallpox killed 10% of all Swedish infants each year. In Russia, Sir Alexander Crichton, the Tsar's British physician, reported that one-seventh of all Russian infants died of smallpox each year. And in France also, de La Condamine claimed that 1 out of every 10

persons born in that country died of smallpox. Berlin recorded 6 smallpox epidemics between 1766 and 1795, each of which carried off about 1000 inhabitants. The Berlin epidemic of 1795 was thought to have been initiated by spread from freshly inoculated persons, and epidemics in Weimar (1788) and Hamburg (1794) were attributed to the same cause. In Vienna, over 16 000 persons were infected during an outbreak in 1790, of whom about 1500 died. Iceland had epidemics in 1707 and 1786.

In 1796, the year of Jenner's discovery of the protective value of cowpox, smallpox killed over 3500 persons in an epidemic in London. Throughout Great Britain and Ireland, the disease claimed an estimated 35 000 more lives that year. In the German states, over 65 000 deaths were attributed to it. Europe (excluding Russia) was losing over 400 000 citizens each year through deaths from smallpox, which also was responsible for more than a third of all the cases of blindness in Europe.

With Jenner's publication of his discovery of the protective effect of inoculation with cowpox virus (see Chapter 6), vaccination spread with remarkable speed, in sharp contrast to the slow adoption of variolation in most European countries. It was soon practised on such a large scale that it altered the pattern of smallpox, the incidence of which declined and remained at relatively low levels for the first few decades of the 19th century (Fig 5.4). Such epidemics as did occur were less severe. In Sweden extensive vaccination reduced the number of reported deaths from smallpox from about 12 000 in 1800 to 11 in 1822 (see Chapter 6, Fig. 6.1), and in Denmark not a single case was recorded between 1811 and 1818. Nevertheless, an estimated 8 million Russians suffered from smallpox between 1804 and 1810, of whom 827 000 died. In addition to epidemics in various European cities, smallpox pandemics occurred in 1824-1829 and 1837-1840 which affected nearly all of Europe. The reasons for this resurgence were complex. At that time vaccination was a cumbersome procedure involving arm-to-arm inoculation, and, with the lower incidence of smallpox, enthusiasm for vaccination declined. Another reason was probably the failure to appreciate the fact that a single vaccination did not give lifelong protection. This problem was overcome when revaccination was introduced in Germany in 1829, although it was not adopted by the

British army until 1858 and by the civilian population much later than that.

The Franco-Prussian War of 1870–1871 was associated with severe outbreaks among the poorly vaccinated civilians of France and Prussia (Prinzinger, 1916). The Prussian army of 800 000 men, revaccinated every 7 years, suffered only 8463 cases of smallpox, with a case-fatality rate of 5.4%, whereas in the unvaccinated French army there were 125 000 cases, with a case-fatality rate of 18.7%. As expected, smallpox spread beyond the belligerent states to the rest of Europe, and it was estimated that at least half a million Europeans died of smallpox in the pandemic triggered by the Franco-Prussian War (Rolleston, 1933). One consequence was legislation to enforce vaccination and revaccination in many countries of Europe, but in some countries these efforts were countered by violent antivaccination movements—notably in Great Britain—based primarily on the principle that compulsory vaccination was an infringement of personal liberty. The century closed with smallpox still endemic in every country of Europe, but with more hope for the future because of improvements in vaccine quality and production methods and in the public health infrastructure.

THE SPREAD OF SMALLPOX BY EUROPEAN EXPLORERS AND COLONISTS

Up to about the 15th century smallpox appears to have been confined to the Eurasian land mass and a few adjacent countries: those of northern and western Africa and the Horn of Africa, Japan, and Ceylon and the Malay and Philippine archipelagos. Arab traders and slave-traders had introduced it into the coastal areas of eastern and western Africa, but most of central and southern Africa was probably free of the disease. The great explorations and subsequent migrations of Europeans to the Americas, Africa and Australia in the 15th–18th centuries opened up those entire continents to the fatal impact of the advanced technologies and infectious diseases of Europe. Some European conquests owed a good deal of their success to the effects of disease on the indigenous peoples, especially smallpox in the Americas. Fig. 5.5 illustrates the pattern of introductions of smallpox to continents outside the Eurasian land mass. Subsequent sections of this chapter elaborate on the history of smallpox in these newly invaded continents—Africa, the Americas and Australia.

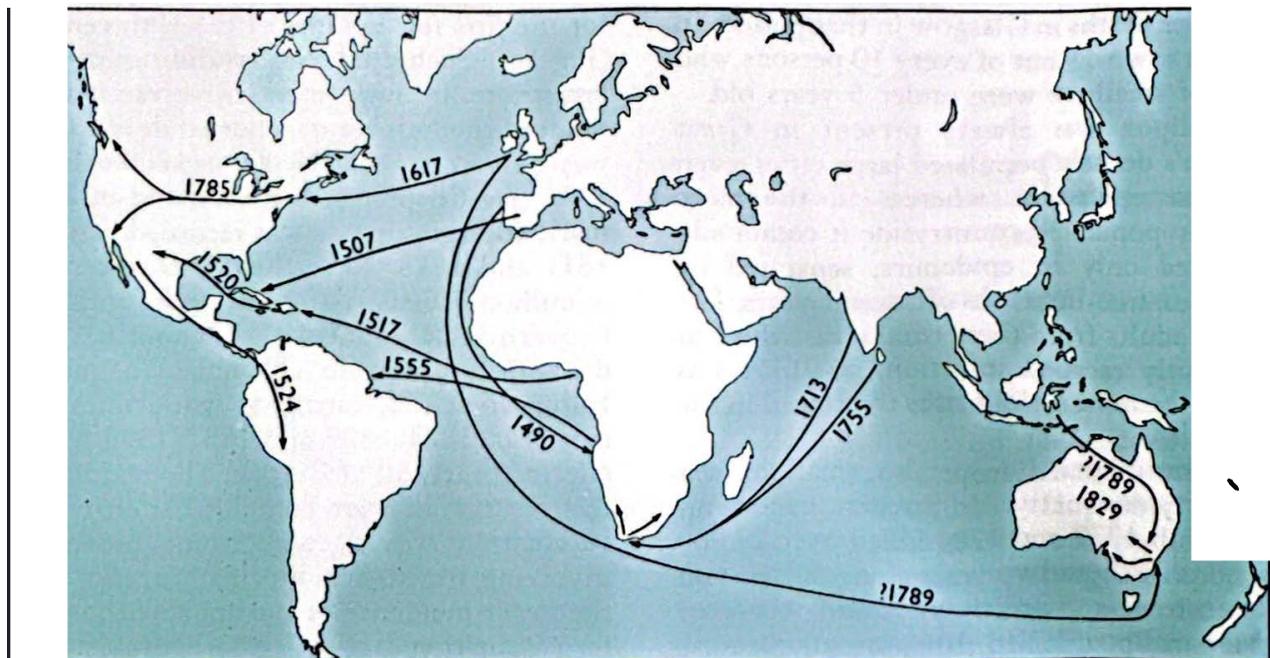


Fig. 5.5. The spread of smallpox to the Americas, South Africa and Australia with European exploration and colonization. It is not known whether the outbreaks among Australian aborigines in 1789 were caused by the transmission of the disease by ship from Great Britain or spread from islands of the East Indies to northern Australia.

SMALLPOX IN AFRICA BETWEEN 1000 AND 1900

The vast continent of Africa is relatively sparsely inhabited now, and its population was far smaller a thousand years ago. The desert area of the Sahara, then as now, separated the countries of the Mediterranean littoral and the Nile valley state of Egypt from sub-Saharan Africa, in which the great rain forests of the Niger and Zaire basins and the Kalahari desert in the south were largely uninhabited (Fig. 5.6).

Africa is racially and culturally complex. By AD 1000 the Bantu-speaking Negroes, who originated in western Africa, had spread throughout central and eastern Africa and were probing southwards. The aboriginal inhabitants of central and western Africa were reduced to a minority living in the dense tropical forests, and the Bushmen were confined to southern Africa and the Kalahari desert. The population south of the Sahara probably numbered about 30 million, mostly Negroes.

In the north the earliest presumptive evidence of smallpox anywhere in the world is in Egyptian mummies, over 3000 years old. Later, smallpox swept along the North African coast at the time of the great expansion of Islam in the 8th century, and from that time onwards remained endemic in these Mediterranean lands.

Apart from areas of western Africa near the Gulf of Guinea, the mediaeval African countries developed in the interior of the continent, in the grasslands south of the Sahara, the central uplands of the Rift Valley and south to Zimbabwe. Commerce between Egypt and the north-eastern countries (present-day Ethiopia, Somalia and the coastal part of Kenya) and the countries of south-western Asia to the north was active from ancient times. One of the earliest records of a pestilence that may have been smallpox was, as already noted in this chapter, associated with the "Elephant War" in AD 568, when Ethiopian troops besieged Mecca and were decimated by disease, which they carried back to Africa.

Since there were Arab colonies in the port towns along the eastern African coast as far south as Mombasa, and Arabs traded as far afield as India and China, it is likely that smallpox was periodically imported into these coastal towns, perhaps as early as the 13th or 14th century. But no written records are available earlier than those of the 16th

century, when Portuguese traders replaced Arab merchants. The coastal towns were sometimes raided by tribes from the interior, and in 1589, after one such raid along the coast of Kilwa and Mombasa, a severe epidemic of smallpox affected all age groups among the African inhabitants but spared all the Portuguese except the young children.

The populous countries of western Africa were connected by caravan routes to Nubia and Ethiopia in the east and the countries of the Mediterranean littoral to the north. After the arrival of Islam in the 11th century, trading relationships were strengthened and pilgrims travelled to Mecca. It is likely that smallpox was introduced into some of these relatively densely populated western African kingdoms from the 11th century onwards, but there are no European records about smallpox in western Africa until the 17th century, when the disease was apparently widespread, variolation appears to have been practised, and a god of smallpox was an established member of the indigenous pantheon of some tribes (Plate 5.5). Smallpox had probably been endemic there for some centuries, many years before the slave trade to the Americas was established in the 16th century.

The slave trade provided excellent conditions for spreading smallpox, and since raiders penetrated deep into the interior the overland caravans carried the disease far and wide in central Africa. No contemporary records exist of these incursions, but later European explorers recorded the devastating effects of smallpox that they found along every caravan route. Those who failed to contract smallpox on the trek to the coast were liable to be infected while awaiting shipment or on board ship, and there are numerous records of smallpox at the coastal camps and in the slave ships during the 17th and 18th centuries. Indeed, such shipments were a perceived threat to the colonists in the Americas. On the east coast, also, slave ships carried smallpox, as recorded in 1729 in a ship travelling from Madagascar to Réunion.

The Portuguese established a settlement at Luanda, Angola, in 1484, and probably introduced smallpox into the area shortly after that. Over the next 2 centuries smallpox and the slave trade combined to take a terrible toll of the population.

Southern Africa was free of smallpox when the Dutch settled in Cape Town in 1652. At this time the only indigenous inhabitants were Bushmen and Hottentots, but the Ban-

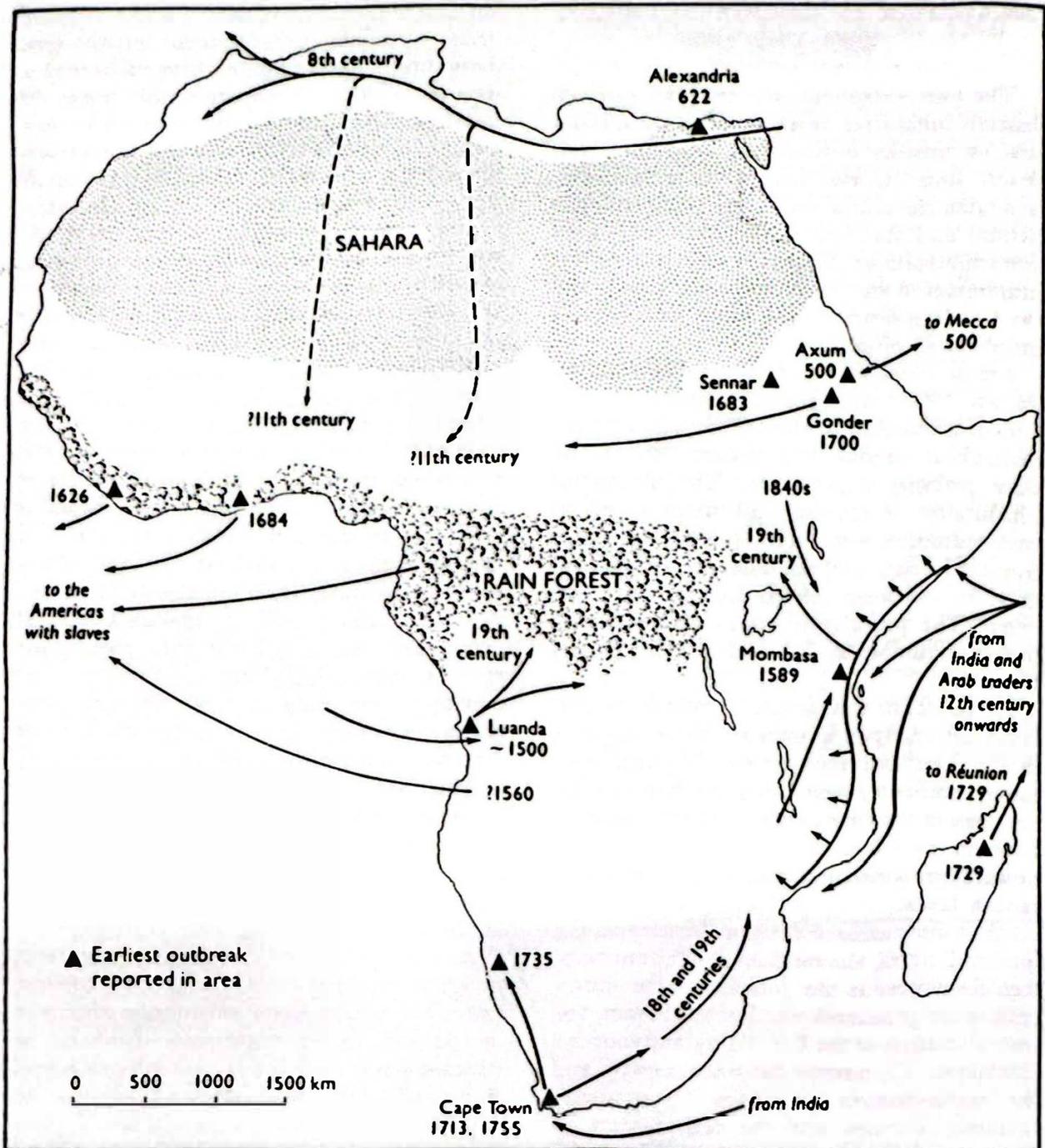


Fig 5.6. Spread of smallpox to Africa and within the African continent. Endemic smallpox was established in the Maghreb during the Islamic conquests in the 8th century and probably spread from there along the trade routes across the Sahara to the dense populations of western Africa during the 11th and 12th centuries. Further south in western Africa smallpox was not imported until the Portuguese occupation in the 15th and 16th centuries. Thereafter it was exported from western Africa to the Americas. On the eastern coast, smallpox was imported periodically from India via Arab and Indian traders. Another focus was established in southern Africa after importations in 1713 from India and 1755 from Ceylon. The interior of the continent was probably smallpox-free until the 19th century. (Based on Hopkins, 1983a.)

tus were already migrating southward from Zimbabwe. In 1713 smallpox was imported into South Africa with a ship that was returning from India and docked at Cape Town. Although there were no active cases aboard, the virus was taken ashore in laundry.

In the ensuing outbreak the white population suffered severely, nearly every family being affected. Many of the Dutch adults were immune because of smallpox contracted during their childhood, but the Hottentots were totally susceptible, and very large numbers of

them died, whole clans being wiped out. Smallpox did not become endemic, however, and a second outbreak followed an importation into Cape Town from Ceylon in 1755. Again, although the whites suffered severely, with over 1000 deaths between May and October, the Hottentots were even more severely devastated. The disease spread among the Hottentots and Bushmen as far as the Kalahari desert, and wiped out several Hottentot tribes. Yet a third outbreak occurred in 1767, introduced on this occasion by a Danish ship from Europe. The European settlers had by this time learned of the value of variolation and suffered only 179 deaths among some 2000 cases, but the remnants of the Hottentots and the Bantu tribesmen, who were by then in the vicinity, suffered much more severely.

Although the Atlantic slave trade was curtailed from the early 19th century onwards, Arab slavers continued to operate in eastern Africa and carried smallpox from Mozambique to Cape Town in 1812, and to Mauritius in 1840. Slave ships intercepted by the British navy sometimes brought smallpox into African ports then free of the disease—as occurred in 1840, when a captured slave ship brought smallpox again to the Cape Colony, starting another outbreak, which killed over 2500 of the inhabitants.

In the 19th century the Arab slave trade expanded from the east coast ports into central Africa. Smallpox was brought into Uganda by slave caravans in the 1840s. Although there may have been earlier introductions by ivory hunters, the populations were too sparse to support endemic smallpox. The increased commerce and population movements of the 19th century thus brought smallpox to hitherto unaffected populations, on which it wrought extreme havoc. Mortality rates of 80% were reported among the Griqua people in 1831, and as late as 1899 smallpox almost exterminated some tribes in northern Kenya. A similar pattern was observed as central Africa was opened up to European trading from the west, and some parts of the eastern Zaire river basin were completely depopulated.

In the meantime smallpox continued to be a severe endemic disease in coastal towns and in northern Africa. In addition, 6 epidemics were recorded in Ethiopia and the Sudan in the 19th century—in 1811–1813, 1838–1839, 1865–1866, 1878–1879, 1885–1887 and 1889–1890. In western Africa, also, smallpox

continued to take a toll of lives and to affect military campaigns, as in the Ashanti Wars in the 19th century. In Angola, an epidemic that started in 1864 affected about one-third of the Angolan population, killing over 25 000 persons, and helped to shift the balance of population towards the south.

“The variola epidemic by mid-1864 was on the rampage. It spread inland to the east with many caravans of trade, and spread south along the coast by contact with vessels in the ports. Two of the most famous explorers of Central Africa residing in Angola died as a result of this epidemic in 1864 . . . The negroes fled in all directions to avoid the epidemic . . . entire populations would migrate from their villages . . . Luanda was on the verge of anarchy as people died in great number . . . Great quantities of wax, ivory, gum, and copper, indeed the sinews of trade, stayed in piles along the roads and paths or abandoned in heaps at such inland stations as Malanje.” (Wheeler, 1964.)

Variolation antedated European colonization of western Africa. It was practised in southern Africa from the mid-18th century and was known in all regions of Africa from the early 19th century (see Chapter 6), but nowhere was it used as a method of protecting communities—only individuals. In some parts it was feared as a mechanism for the spread of smallpox, especially in western Africa, where the *féticheurs*, who by tradition carried out the inoculations, stood to profit from the practice.

Finally, the earliest accounts of a mild form of smallpox, now called variola minor, are those describing “kaffir-pox”, or “amaas”, in South Africa (see Chapter 6).

SMALLPOX IN THE AMERICAS BETWEEN 1507 AND 1900

The Americas were first colonized by migrants from Asia who crossed the northern land (ice) bridge over the Bering Strait some 20 000 years ago. Before Columbus “discovered” America in 1492 these people had spread throughout both North and South America, to the very southernmost tip of the continent in Tierra del Fuego. Two thousand years ago the total population of the Americas was probably about 5 million; it had doubled by AD 1000 and reached approximately 25 million by 1500. In Mexico the Aztec empire embraced an estimated 8 million subjects, somewhat more than did the Inca empire in Peru. Tenochtitlán and Cuzco were great cities, with large populations. Along the

eastern seaboard of North America, in the Caribbean, in southern Mexico and Central America, Venezuela, Colombia and northern and eastern Brazil, there were semi-agricultural tribes who added another 5 or 6 million to the continental total. In addition, there were about 3 million hunters and food-gatherers roaming the immense and empty lands of central and western North America, the tropical jungles of Brazil and the desolate wastes of southern Argentina (Fig. 5.7).

These large populations, city-dwellers and agriculturists alike, were free of the familiar communicable diseases of Europe. When smallpox was introduced into Mexico and Brazil by the Spanish and Portuguese invaders and into North America by the British and French, its impact was catastrophic. Since these episodes differed in many respects it is convenient to consider them separately.

The Spanish and Portuguese Colonies

The first occurrence of smallpox in the Western Hemisphere was on the island of Hispaniola in 1507, following an importation from Spain. The epidemic which followed exterminated whole tribes, but eventually died out. Most subsequent importations into the Caribbean islands, Mexico and Brazil were associated with the African slave trade, which began in about 1503. In 1517 an outbreak occurred among African slaves in the mines of Hispaniola and spread rapidly to the Amerindian population of that island, killing about one-third of them. Smallpox spread to Cuba in 1518 and Puerto Rico in 1519, where over half the native population succumbed to the disease.

In 1519 Cortés and his followers sailed from Cuba to Mexico and arrived in November in Tenochtitlán, whose size and splendour amazed them. Jealous of Cortés' good fortune, the Governor of Cuba sent another expedition under Narváez to replace Cortés. Narváez landed near present-day Vera Cruz in April 1520, and his entourage included an African slave who had smallpox. The result (Plate 5.3B) was described by a Spanish friar, who arrived in Mexico in 1525:

"... at the time that Captain Pánfilo de Narváez landed in this country, there was in one of his ships a negro stricken with smallpox, a disease which had never been seen here. At this time New Spain was extremely full of people, and when the smallpox began to attack the Indians it became so great a pestilence among them throughout the

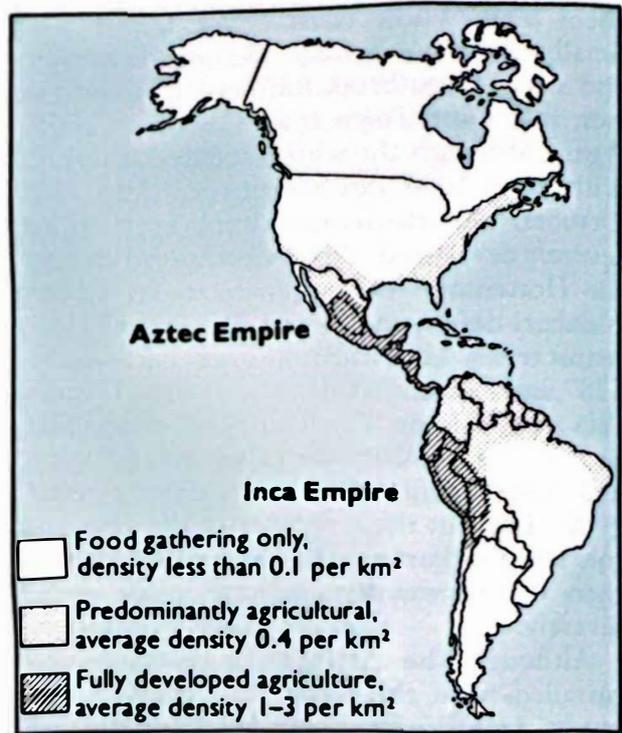


Fig. 5.7. Agricultural development and population densities in the Americas at the time of the European invasions. (Based on McEvedy & Jones, 1978.)

land that in most provinces more than half the population died; in others the proportion was little less. For as the Indians did not know the remedy for the disease and were very much in the habit of bathing frequently, whether well or ill, and continued to do so even when suffering from smallpox, they died in heaps, like bedbugs. Many others died of starvation, because, as they were all taken sick at once, they could not care for each other, nor was there anyone to give them bread or anything else. In many places it happened that everyone in a house died, and, as it was impossible to bury the great number of dead, they pulled down the houses over them in order to check the stench that rose from the dead bodies so that their homes became their tombs. This disease was called by the Indians 'the great leprosy' because the victims were so covered with pustules that they looked like lepers. Even today one can see obvious evidences of it in some individuals who escaped death, for they were left covered with pockmarks." (Foster, 1950.)

From the coast the disease spread inland, reaching the Valley of Mexico in September and shortly after that the capital, Tenochtitlán. The epidemic which followed was catastrophic for the Amerindians and assured the military success of Cortés and his conquistadors. The Aztecs' loss of chiefs and fighting men was serious enough, but the observation

that the Spaniards were immune (from childhood infection in Spain, into which country the Moors had introduced the disease in the 8th century) completed their demoralization. Estimates of the number of deaths vary. Some say that half the population of Mexico died within 6 months; other estimates put the population at 25 million before the conquest and 16.8 million 10 years later. At least half of the Aztecs who caught smallpox died of it. From Mexico, the disease spread south into Guatemala and Yucatán, which may have been ravaged by an earlier outbreak in 1515, and greatly decreased the formerly dense population of the Yucatán Peninsula.

Hearing of the riches of the Inca empire far to the south, the Spaniards decided on further expeditions. Before these could be mounted, smallpox reached the land of the Incas in about 1524–1527, killing some 200 000 of the 6 million inhabitants. Just as important as this widespread devastation, from the point of view of the subsequent Spanish conquest, was the fact that the Inca emperor and his designated heir also died of smallpox, and a disastrous civil war broke out for the succession. These events so weakened the Incas that Pizarro and his small band entered Cuzco in triumph in 1533, to be followed by further epidemics of smallpox.

From then on the history of the Amerindians in the Caribbean islands, Mexico, Central America and Peru is punctuated with epidemics of smallpox that were said to kill "hundreds of thousands"; in 1576, as many as 2 million Mexican Indians were alleged to have died. Colombia and Venezuela were invaded, with the same disastrous consequences for the natives, and Spanish soldiers introduced smallpox into Chile for the first time in 1554, and again in 1561 and 1591. By this time there were many locally born "Spaniards" who had not been exposed to smallpox and some 300 died, as well as countless Indians.

In 1506, by Papal decree, the New World had been divided between the Spanish and the Portuguese. What is now Brazil was the principal Portuguese colony, and it was soon struck by smallpox. The first introduction, in 1555, followed the establishment of a French Huguenot settlement, to be followed by fresh introductions by African slaves in 1560, and from Portugal in 1562 and 1563. The last epidemic spread along the coast and along the rivers into the Indian populations of the forested interior and was said to have killed

more than half the natives of the state of Bahia.

By 1588, epidemics of smallpox erupted over the whole South American continent, and subsequently wave after wave of epidemic smallpox decimated the native populations. The resulting depopulation had as important an influence on the history of South America as the supportive role of smallpox in the conquest of Mexico and Peru. No part of the continent was spared—not even the interior of Brazil, whose inhabitants were exposed through the enthusiasm of Jesuit missionaries for converts. As late as 1660, after the Jesuits had established missions along the banks of some of the great rivers, where some 100 000 Indians had been assembled, a smallpox epidemic killed 44 000 of them, to be followed by another 9 years later, which claimed 20 000 victims.

Variolation was introduced into the colonies in 1728 by missionaries from Portugal, but it was not extensively practised. Smallpox continued almost uncontrolled throughout the 18th century, occurring as an endemic disease with epidemics every few years. The last and best-described epidemic, before vaccination became available, occurred in Mexico in 1797. It was notable in that over 60 000 inoculations with variola virus were performed during the epidemic. While protecting most of those inoculated, the practice may have contributed to the spread of smallpox. The changed nature of the population was evidenced by the fact that three-quarters of the estimated 100 000–150 000 cases were in persons less than 20 years old. The case-fatality rate among 3300 variolated individuals was 3.5%, compared with 18.5% among 58 000 naturally acquired cases of smallpox.

The early years of the 19th century were marked by successful struggles for independence throughout South America. Brazil proclaimed its independence from Portugal in 1822, and in 1824 Spanish rule was ended in Peru, the last Spanish colony. From as early as 1798 attempts were made to introduce Jenner's vaccine, of which the most dramatic was the Balmis-Salvany Expedition of 1803–1806, ordered by King Carlos IV of Spain (Smith, 1974), in which 20 orphans were used for successive arm-to-arm transfer of the vaccine during the voyage. However, smallpox continued in all parts of the continent throughout the 19th century, as an endemic disease punctuated periodically by epidemics, especially in the densely populated port cities.

The most profound demographic effect of European conquest, achieved in large part by smallpox, was on the native populations of the islands of the Caribbean, where the population was virtually wiped out, to be replaced by African slaves and Spanish conquerors and their descendants. On the mainland the size of the Amerindian populations of the Aztec and Inca empires ensured their survival; over half the present populations of Mexico, the countries of Central America, Bolivia, Colombia, Ecuador, Paraguay, Peru and Venezuela are of Amerindian stock; elsewhere in North and South America they constitute a small minority.

North America

In contrast to the urban civilizations of Mexico and Peru, the vast area of America to the north of Mexico was occupied by an estimated 3 million Amerindians, living as hunter-gatherers, and practising a primitive type of agriculture along the eastern seaboard. It was almost a century after the invasion of the Caribbean, Mexico and South America by the Spanish and Portuguese that the east coast of North America was colonized by settlers from France, Great Britain and the Netherlands. Smallpox followed the settlers, the first epidemic in 1617-1619 killing many of the Indians on the Massachusetts coast, thus clearing a place for the settlers who arrived from Plymouth in 1620.

Further outbreaks of smallpox followed, with devastating effect as they spread inland, for the Indians were without immunity and their way of life was disrupted by the epidemics, which affected persons of all ages. Some colonists, being themselves immune from childhood infection, actively fostered the spread of smallpox among the native North Americans (Stearn & Stearn, 1945). The severity of the disease and its spread were exacerbated by the reaction of the Indians to the disease. Terror-stricken relatives of victims fled, carrying the infection with them.

As Crosby (1976) points out: "... the British tended to drive the Indians away, rather than ensnaring them as slaves and peons, as the Spaniards did, with the result that many of the most important events of aboriginal history in British America occurred beyond the range of direct observation by literate witnesses... Even so, the surviving records for North America do contain references—brief, vague, but plentiful—to deadly epidemics among the Indians, of which

we shall cite a few of the allegedly worst. During the 1630s and into the next decade, smallpox, the most fatal of all the recurrent Indian killers, whipsawed back and forth through the St Lawrence-Great Lakes region, eliminating half the people of the Huron and Iroquois confederations. In 1738 smallpox destroyed half the Cherokees, and in 1759 nearly half the Catawbas. During the American Revolution it attacked the Piegan tribe and killed half its members. It ravaged the plains tribes shortly before they were taken under United States jurisdiction by the Louisiana Purchase, killing two-thirds of the Omahas and perhaps half the population between the Missouri River and New Mexico. In the 1820s fever devastated the people of the Columbia River area, erasing perhaps four-fifths of them. In 1837 smallpox returned to the plains and destroyed about half of the aborigines there."

Not all the settlers were immune, so that smallpox was not, for them, an unmixed blessing. At this time smallpox was endemic in all the larger European cities, with epidemics occurring at intervals of a decade or so. The towns in North America were still too small to support endemic smallpox, so that epidemics occurred whenever the disease was imported at a sufficiently long interval after the last outbreak for enough susceptible persons to have accumulated within the population. The disease usually arrived by ship at the ports on the eastern seaboard, either with settlers from Great Britain or, later, with slaves from Africa. Boston suffered major epidemics in 1636, 1659, 1666, 1677-1678, 1689-1690 and 1697-1698, and there were outbreaks in New York, Jamestown (Virginia), Charleston (South Carolina), and elsewhere. As well as causing substantial numbers of deaths among the settlers, especially those born in the colonies, it disrupted life in the fledgling cities.

One consequence of the obvious association of smallpox outbreaks with cases on ships was the imposition of quarantine measures on ships with infected persons aboard. This was initiated in Boston in 1647, probably for yellow fever, and was later extended to other parts of the colonies. It proved useful in preventing the importation of smallpox. On land, also, attempts were made at various times from about 1670 onwards to prevent smallpox from spreading from Indians to the colonists, and among the colonists, by local quarantine and isolation. Another consequence of the difference in the endemicity of smallpox in the colonies and in Great Britain

Smallpox and Educational Institutions

"When a French visitor . . . visited William and Mary College in 1702, he was surprised to find as many as forty students there . . . he learned that wealthy parents who formerly had sent their sons to England now preferred the intellectual crudities of a colonial education to the perils of the English smallpox. The Rev. Hugh Jones, in 1724, observed that more Virginians would have been given an English education 'were they not afraid of the Small-Pox, which most commonly proves fatal to them'." (Boorstin, 1958.)

was that many young colonials, who had been brought up in smallpox-free areas, contracted the disease when they went to Great Britain for further studies, or else refused to take the risk and remained on their side of the Atlantic. Indeed, the risk of contracting smallpox in Great Britain was one of the reasons for founding colleges and universities in the colonies.

In the latter part of the 17th century smallpox and military activity interacted in the wars between Great Britain and France, each with Indian allies, in what was to become Canada. With the growth of populations in the port cities on the Atlantic coast and on the banks of the St Lawrence river during the 18th century, smallpox became more frequent and the outbreaks more intense; for example, an epidemic in Quebec City in 1702–1703 was said to have killed nearly a quarter of the inhabitants (Heagerty, 1928). Severe outbreaks occurred in Boston, New York, Philadelphia, and the State of New Jersey, and at the approach of such epidemics many of the townspeople fled to the country. In both New England and the South, smallpox broke the resistance of the Indians to the white invaders, and as white settlement moved westwards it was accompanied by smallpox, to which the local Indians had no resistance. A few of these 18th century epidemics among the Indians were probably initiated, or at least fostered, by whites. The most notorious record is contained in correspondence between Sir Jeffery Amherst, Commander-in-Chief of the British forces in North America, and Colonel Henry Bouquet in 1763, at the time of the Pontiac rebellion:

AMHERST: "Could it not be contrived to send smallpox among these disaffected tribes of Indians? We must on this occasion use every strategem in our power to reduce them."

BOUQUET: "I will try to inoculate the— with some blankets that may fall in their hands, and take care not to get the disease myself." (Heagerty, 1928.)

By 1785 smallpox had occurred among the Sioux Indians of the Great Plains and crossed the Rocky Mountains with them, and was reported in Alaska and California. Further south, Catholic missions in New Mexico had been invaded by smallpox much earlier, because of their contacts with New Spain.

Quarantine and isolation measures were strengthened, but often proved inadequate. A new element, variolation, entered the struggle against smallpox in 1721, which changed the situation among the whites but not the Indians. That year saw Boston's worst epidemic of smallpox in the 18th century. The epidemic in 1752 was less disastrous only because variolation was practised on a large scale (see Chapter 6, Table 6.2). In this latter outbreak, 1843 of Boston's 15 684 residents fled to the country; 5545 of the remainder caught smallpox, of whom 539 died; 2124 were inoculated, with 30 deaths, and 5998 persons had already had smallpox when the outbreak began. Only 174 susceptible persons who stayed in the city escaped infection (Blake, 1959). When smallpox broke out again in Boston, in 1792, practically the whole town was inoculated within a few days and only 69 deaths from naturally acquired smallpox occurred in the now much larger population.

Smallpox played a part in the Revolutionary Wars, General Washington being particularly anxious about the dangers of smallpox to the Continental army. Indeed, the long duration of the siege of Boston—from June 1775 to March 1776—is considered to have been due in large degree to the existence of smallpox in the city and Washington's fear of attacking it and exposing his army to the

disease. When the British finally left, on 17 March, Washington ordered "one thousand men who had had the smallpox" to take possession of the city. Further north, smallpox in the Northern army was so severe as to decide the course of the war in that region and thus the continued adherence of what is now Canada to the British Crown. In 1777 Washington ordered the compulsory variolation of all new recruits to his armies, an act which prompted a historian (Thursfield, 1940) to write "... I think it is fair to claim that an intelligent and properly controlled application of the only method then known of defeating the ravages of smallpox, which in the years 1775-76 threatened to ruin the American cause, was a factor of considerable importance in the eventual outcome of the War of Independence".

A few years later Jenner published his discovery of vaccination. This was taken up soon after by Dr Benjamin Waterhouse, the first Professor of Medicine at Harvard University, who received news of Jenner's discovery in 1799 and was immediately excited by it. Despite imperfect vaccine, widespread vaccination of the white population reduced smallpox during the early 19th century, although epidemics still occurred in the cities; between 1800 and 1850 Philadelphia had 8 epidemics, Boston 6 and Baltimore 3. Complacency and a failure to maintain supplies of the virus, as well as lack of recognition of the need for revaccination, contributed to the continued presence of smallpox among the white population, but their suffering paled before that of the Indians. Massive and devastating pandemics which occurred in 1801-1802 and in 1836-1840 led to the virtual extinction of many tribes of indigenous North Americans. The second outbreak affected the Indian population over the whole of the North American continent west of the Mississippi river, from Texas to Alaska and from St Louis to California.

One result of these terrible epidemics was the Federal decision to vaccinate the survivors, so that by the second half of the 19th century the Indians were better vaccinated than the white and black inhabitants of North America, many of whom refused vaccination. In the late 19th century smallpox was more severe in the non-Indian population, among whom there were 3 widespread epidemics, in 1865-1866, 1871-1875, and 1881-1883.

In spite of the adoption of vaccination by the United States army in 1812, this precau-

tion was neglected when regiments were raised for the Civil War in the 1860s. In the Union army, there were 6716 cases of smallpox with 2341 deaths among the Negro troops and 12 236 cases with 4717 deaths among the 431 237 white troops. The disease spread among the Confederate army, as well as among civilians on both sides. Indeed, President Lincoln was probably febrile with the prodrome of smallpox when he gave the Gettysburg address on 19 November 1863; his rash appeared on 21 November.

The slave trade, with its threat of smallpox importations, had been made illegal in the British West Indies in 1807 and in the USA in 1808, but after the Civil War migration from Europe increased greatly, and with it the risk of further importations of smallpox from that continent. Between 1871 and 1873 there were widespread outbreaks in Philadelphia, Baltimore, Washington, Cincinnati, New York, Boston and Chicago. A smaller series of outbreaks occurred in the early 1880s, by which time the railway network helped to spread the disease rapidly throughout the continent.

The closing years of the 19th century were marked by the appearance and spread of variola minor in Canada and the USA, a phenomenon described later in this chapter and in Chapter 8 (see Chapter 8, Fig. 8.4).

SMALLPOX IN OCEANIA BETWEEN 1789 AND 1900

Oceania is a term used to embrace Australia and the islands of the Western Pacific, including New Zealand and Papua New Guinea.

Australia

The existence of a "Great South Land", to "balance" the continents of the Northern Hemisphere, had long been suspected, and from the mid-16th century onwards several European explorers had made contact with parts of it. The prelude to European colonization was the first voyage of James Cook in 1768-1771, in which he charted the east coast of Australia. The loss of its American colonies shortly after this led Great Britain to seek some other distant place for the disposal of the victims of its repressive laws, and the new continent looked ideal. The First Fleet, comprising 11 ships carrying about 1500

persons—convicts and their guards and keepers—sailed from England on 6 January 1787, called at Rio de Janeiro on 4 August and at Cape Town on 13 October, and arrived in Botany Bay, just south of the present city of Sydney, on 20 January 1788. No addition was made to the infant colony until the arrival of the Second Fleet in 1790.

The early navigators had already reported that the country was inhabited by primitive dark-skinned people, and recent archaeological studies show that aborigines had been in Australia for at least 40 000 years. The late 18th century was a period of severe smallpox in Great Britain, mitigated somewhat by the increasing adoption of variolation. Knowing that the natives of other distant lands, such as South Africa and the East Indies, were infected with smallpox, the surgeons of the First Fleet brought with them "variola matter in bottles" for inoculation if it proved to be necessary. In fact they found a sparse population of hunter-gatherers who, like the aboriginal Americans, were free of smallpox, measles and most other of the common infectious diseases of Europeans.

However, in 1789, only a year after the landing, an outbreak of what was probably smallpox was recognized among the aborigines near the new European settlement, Sydney town, and appears to have spread far and wide among the aboriginal population of south-eastern Australia, as determined by explorers and by later commentators (Cumpston, 1914; Butlin, 1983, 1985; Campbell, 1983, 1985). None of the white settlers was affected, but one coloured seaman suffered from the disease. The origin of this outbreak has never been determined, but two possibilities have been canvassed. Although there is no record of the variola matter brought by the surgeons of the First Fleet ever having been used, lost or stolen, it was a potential source of infection. On the other hand, the newly arrived Europeans may, by chance, have witnessed the passage through the Sydney area of a very rare epidemic of smallpox that had been introduced along the north coast of the continent and spread southwards.

There was little contact between aborigines and whites, except near Sydney, for many years after this, and smallpox appears to have been absent until 1829–1831, when it spread extensively through the indigenous population of south-eastern Australia, affecting a few Europeans as well. Once again, its origin was never determined. Two other outbreaks

of smallpox occurred among the aborigines in the 1860s, the first extending from the north coast across central Australia to the southern coast between about 1861 and 1866, and the second extending along the north-west coast in 1865–1869 (Fenner, 1985). Both probably originated from the voyages of trepang traders coming from the islands to the north of Australia. Butlin (1983) has recently analysed the demographic effects of the 1789 and 1829 outbreaks and suggests that they played an important role in the great decline of the aboriginal population of south-eastern Australia in the first half of the 19th century.

The subsequent history of smallpox in Australia has been documented in great detail by Cumpston (1914). The first outbreak among Europeans occurred in Melbourne in 1857, originating from a ship hailing from Liverpool, England. There were 4 deaths among the 16 persons affected. Six other outbreaks of smallpox occurred in 3 of the colonies before the end of the 19th century, due to importations by passengers on ships; in addition, there were another 16 episodes in which one or two cases occurred, but their source could not be traced. The largest outbreak during the 19th century took place in 1881–1882 in New South Wales, with 154 recognized cases, occurring over a period of 6 months.

But for strict quarantine regulations there would have been many more outbreaks; Cumpston (1914) lists 145 ships quarantined for smallpox in Australian ports between 1828 and 1900, in which smallpox occurred but did not spread to persons on land. The passengers and crew on these vessels had acquired smallpox in many different ports; Cumpston lists 19 countries, located in every continent, as the sources of smallpox.

New Zealand

New Zealand was settled by Polynesian seafarers about a thousand years ago and by Europeans in 1840. During that year an immigrant ship arrived with cases of smallpox on board, but quarantine prevented spread to the colonists. No further mention of smallpox occurred until 1872, when 2 ships arrived with smallpox on board and 6 local cases occurred in Auckland. Between then and 1904 several other ships arrived with cases on board, but extension to the colonial popula-

tion occurred only in 1874 and 1903–1904 (Maclean, 1964).

Papua New Guinea

Smallpox was never endemic in Papua New Guinea, but occasional outbreaks occurred before and shortly after European settlement. Mikloucho-Maclay (1975), the first white man to live in the Astrolabe Bay area, noted pockmarked natives in 1872, and records that “the illness came from the north-west and many died of it”.

The German colonists of northern New Guinea (Kaiser Wilhelmsland) recorded outbreaks in June 1893, introduced by a Malay seaman on a German ship, and again in 1895. They obtained vaccine from Batavia and treated “thousands of natives”, but reconnaissance a year later showed that they did not entirely prevent the disease:

“The great villages, whose armed men had previously by a show of arms prevented us from entering, now contained only the wretched remnants of their former population. The survivors greeted us with lamentations and showed us the mass graves of those claimed by the epidemic. Thanks to the vaccination program which had been carried out, it did not spread any further northward along the coast. Nor did it advance to any extent inland, as the profound hostility between the coastal and mountain inhabitants cut both parties off from all contact.” (Sack & Clark, 1980.)

Other Pacific Islands

Although measles was brought to Fiji in 1875 and killed about 25% of the indigenous population, smallpox never occurred there, which was surprising in view of the large introductions of labourers and their families from India. Nevertheless, it was the fear of the introduction of smallpox that led in the 1880s to the training of young Fijians as vaccinators, and ultimately to the establishment of the Fiji Medical School.

None of the smaller Pacific islands had a population large enough to support endemic smallpox. However, smallpox is said to have reached the Palau Islands in 1783, and in 1854 an epidemic occurred in the Carolines in which 2000 of the 5000 inhabitants died. A severe epidemic in Guam in 1856 killed some 5000 persons out of the total population of 15 000 (Mumford & Mohr, 1943). In 1853 a ship from San Francisco brought smallpox to

Hawaii for the first time, and the disease killed 8% of the indigenous inhabitants within 8 months. Smallpox was introduced into Easter Island in 1863–1864, when islanders who had been forcibly removed to Peru were returned to their home, following intense international pressure. The combined effects of smallpox and tuberculosis reduced the population of the island to an all-time low of 110 persons.

THE APPEARANCE AND SPREAD OF VARIOLA MINOR

As mentioned in Chapter 1, the occurrence of a distinctive very mild variety of smallpox was reported by Korté (1904) in South Africa as a disease that had been common there for some years, and it was recognized at about the same time (1896) in the USA (Chapin, 1913). The disease that Korté described as “amaas or kaffir-pox” is clearly identifiable as variola minor. Since it appeared to have been endemic in southern Africa for a few years before it was first described there (Brown, 1896), Chapin & Smith (1932) suggested that the disease first observed in Florida in 1896 may have originated in southern Africa. However, recent investigations of the biological characteristics of the viruses that caused variola minor in Brazil in the 1960s and in Botswana, Ethiopia and Somalia in the 1970s (see Chapter 2) suggest that there may have been at least two separate origins of variola minor viruses—one in North America and one or possibly two in Africa.

The descriptions of variola minor in South Africa are unequivocal (Brown, 1896; Korté, 1904), but it is difficult to visualize how the virus spread from there to countries in eastern and central Africa. Burton (1860) provides a clue to a possible independent origin of variola minor in eastern Africa. In his description of the lake regions of central Africa, he refers to smallpox as “the most dangerous epidemic” in eastern Africa, but goes on to state: “There is a milder form of the malady, called *Shúruá*, resembling the chickenpox of Europe.”

From the time of recognition of this disease entity at the end of the 19th century, southern and eastern Africa, the USA and to a lesser extent Europe appear to have been the centres of distribution of variola minor viruses. The appearance and behaviour of variola minor in different countries will be traced in greater

earliest credible evidence is to be found in the Egyptian mummies of persons who died some 3000 years ago. It is not unreasonable to suggest that it was transferred from Egypt by land or water to India, where it remained as an endemic human disease for some 2000 years and perhaps longer. In the 1st century AD it was introduced into China from the southwest and became established in the local population, and in the 6th century it was carried from China to Japan. In the west, smallpox made periodic incursions into Europe but did not become established there until the population increased and population movement became more active during the time of the Crusades.

As populations grew in India, China and Europe, smallpox became established in the cities and more populous areas as an endemic disease affecting mainly children, with periodic epidemics that killed up to 30% of those infected. Its impact steadily increased, and by the 16th century it was an important cause of morbidity and mortality in Europe, southwestern Asia, India and China. The occurrence of the disease in Europe was of special importance, for this served as the focus from which smallpox spread to other parts of the world, as an accompaniment of successive waves of European exploration and colonization.

In 1507 smallpox was introduced into the Caribbean island of Hispaniola and in 1520 into the mainland of the Americas, in Mexico. It struck the native Amerindians with great severity and was an important factor in the

conquest of the Aztecs and the Incas by the Spaniards. Settlement of the east coast of North America occurred about a century later and was also accompanied by devastating outbreaks of smallpox among the Amerindians, and subsequently among the native-born colonists.

By the mid-18th century smallpox was a major endemic disease everywhere in the world except in Australia and in several small islands. It was introduced into Australia in 1789 and again in 1829 and caused devastation among the aborigines, but quickly died out on both occasions.

The widespread use of variolation in a few countries, notably Great Britain and its North American colonies, somewhat mitigated the impact of smallpox among the wealthy classes during the latter part of the 18th century, but a real reduction in its incidence did not occur until vaccination was widely used during the 19th century. Improved vaccines and the practice of revaccination led to a substantial lessening of the ravages of smallpox in Europe and North America, but at the end of the 19th century it remained almost unchecked elsewhere.

Just before the close of the 19th century a much milder form of smallpox, *variola minor*, was recognized in the State of Florida, USA, and in South Africa. From Florida it spread all over the USA and then into Canada, the South American countries and Great Britain. By the mid-20th century *variola minor* occurred along with *variola major*, in varying proportions, in many parts of Africa.

