

# The Life and Death of Smallpox

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## ‘The most terrible of all the ministers of death’

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*Te Deum Laudamus!*

Little Wolfgang has got over the smallpox safely!

*Letter from Leopold Mozart, in Vienna, 10 November 1767*

Mozart was eleven when he became delirious with smallpox, and he was lucky to survive with only a few pockmarks; in England in 1700 the disease had killed Queen Anne’s eleven-year-old son, ending the Stuart line. It was a terrible century for smallpox all over the world, from the royal families of Austria, Spain and France to the isolated communities of Iceland and Greenland, from the long established centres of the disease in China and India to the newly colonised lands of the New World. The growing towns were particularly vulnerable – most children born in eighteenth-century London had smallpox before they were seven, and more than 6,000 people died in the epidemics in Rome in 1746 and 1754.

There was no effective treatment. It flourished for many centuries, bringing horrific death, disfigurement and blindness on a huge scale; armies were checked, populations decimated, economies ruined. It is only in the last few years that drugs able to attack the smallpox virus have begun to emerge. They should not be needed, for a generation ago smallpox was defeated by a vigorous world-wide campaign of

vaccination – the first (and so far the only) serious infectious disease to be totally eradicated. This book tells the story of smallpox and of the long battle to control and ultimately eliminate it. The new horror is that there has to be a postscript – the threat that bio-terrorists may try to exploit our unvaccinated state and use smallpox as a weapon.

Like most people over thirty-five we, the authors, both have pockmarks on our upper arms resulting from vaccination against smallpox when we were babies. But routine vaccination of civilians in the United Kingdom and North America stopped in the early 1970s, and world-wide by 1980; and so effective has the eradication of smallpox been, that most people alive now have never seen a case.

So what was it like? As children, we were told it was like chickenpox but worse. In fact it is not related to chickenpox, and it was unimaginably worse. In an unvaccinated population, something like 10–30 per cent of all patients with smallpox would be expected to die. And dying was not easy; smallpox was, as Macaulay wrote, ‘the most terrible of all the ministers of death’.

Smallpox is virtually restricted to humans; patients are highly infectious for only about two weeks, and those who recover from it are immune for the rest of their lives. In small isolated communities the disease was therefore likely to die out for lack of sufficient potential victims. In larger communities, even if they were isolated, there would always be sufficient susceptible children to keep the infection going, though the number infected might fluctuate wildly, with peaks (*epidemics*) only every few years, each followed by a trough until the birth of more children restored the supply. In such a community, smallpox was said to be *endemic*, and the majority of its victims were children. In communities never previously exposed, or where the disease had been absent for many decades, when it arrived the whole population was at risk.

Whether child or adult, about twelve days after infection the patient was struck with a sudden fever, splitting headache and often backache, and sometimes vomiting. Two to three days later, the rash appeared, the temperature fell, and the patient, who had been feeling extremely



1. A child with smallpox; the 'recognition card' used in the eradication campaign

ill, felt a little better. Over the next two weeks the fever returned, and the rash went through a characteristic series of changes. Starting flat, the spots gradually became raised above the skin surface and felt hard, like embedded lead shot. They then softened, becoming filled first with clear fluid and then with pus. In most cases the ‘pustules’ gradually flattened, dried up and scabbed, the fever went, and within three weeks of the appearance of the rash the scabs fell off, often leaving permanent, pitted scars – the pockmarks – particularly on the face.

Usually, the rash began in the lining of the mouth and throat and on the face, then spread to the upper parts of the limbs and to the trunk, and finally to the hands and feet. In mild cases the rash was sparse and the scarring very limited. Lady Mary Sidney, who had nursed Elizabeth I of England through a frightening but not too disfiguring attack, was less lucky herself. ‘I left her a full fair lady, in mine eyes at least the fairest,’ wrote her husband sadly, ‘and when I returned I found her as foul a lady as the smallpox could make her.’<sup>1</sup> In severe cases, the pustules could be so crowded that they fused together (‘confluent smallpox’), and the number dying rose to about 60 per cent; in the rare and most horrific form there was severe bleeding (‘haemorrhagic smallpox’) and over 90 per cent died. If the rash was extensive in the mouth and throat, eating and drinking could become intolerably painful, and if the eyes were affected the patient could be permanently blinded. At the end of the eighteenth century about a third of all cases of blindness in Europe are thought to have been the result of smallpox; and the death toll was terrible – about 400,000 a year in Europe, excluding Russia. It was children who suffered most – in English towns, nine out of ten of those dying from smallpox were children under five years old.<sup>2</sup>

Since smallpox cannot be treated effectively, prevention is crucial. Inoculation, which was introduced to Europe at the beginning of the eighteenth century from far earlier origins in the East, first gave the idea that prevention might be possible. It involved the insertion of a small amount of matter from the pustule of a smallpox patient into the skin of a healthy subject. If it worked, as it generally did, it produced a very mild attack of the disease, and gave lasting immunity. But during this

mild attack the inoculated subjects were themselves infectious and so the disease could spread further; and occasionally the disease produced by inoculation was not mild, and might even be fatal.

Edward Jenner, at the end of the eighteenth century, took the vital next step. By introducing 'vaccination' (that is, inoculation with material not from smallpox pustules but from the pustules of cows suffering from the related disease cowpox), he usually produced a milder and uninfected reaction which gave immunity though, as it turned out, not quite permanent immunity. This drawback was easily tackled by later revaccination; and the idea of eradication changed from a utopian dream to a practical possibility – though it took nearly 200 years to achieve.

By 1967, when the World Health Organisation (WHO) started its final eradication campaign, smallpox had virtually disappeared from Europe and the Americas, but from figures reported to the WHO's Smallpox Eradication Unit it is now reckoned that the disease was still endemic in thirty-three countries, including the whole of the Indian subcontinent, and that there were 10 to 15 million cases and about 2 million deaths per year world-wide.<sup>3</sup> Twelve years later, after an amazing effort of organisation and co-operation the world was officially declared free of smallpox.



## From myths to mummies

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The scorching sands of Afric gave him birth

Thence sprang the Fiend and scourged the afflicted earth

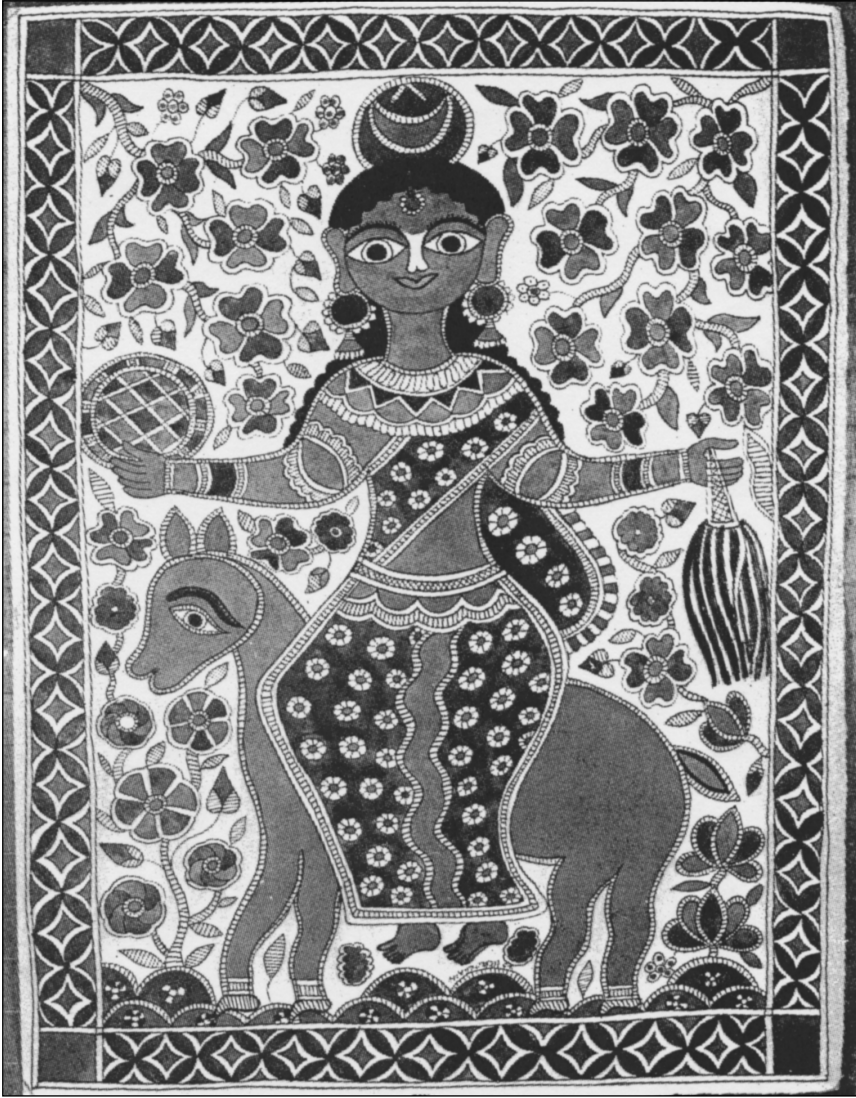
*William Lipscomb, 'The Beneficial Effects of Inoculation', the Chancellor's prize poem, Oxford, 1772*

William Lipscomb, Oxford undergraduate and son of a Winchester surgeon, may well have been right when he claimed that smallpox originated in Africa – though it is more likely that it emerged in a populous river valley than in the scorching sands. Myths and theories abound. Some tried to link smallpox with biblical diseases; Philo of Alexandria, the Jewish emissary to Caligula's Rome in the first century AD, confidently described the sixth Egyptian plague ('boils') as a red eruption in which 'the pustules, confluent into a mass, were spread over the body and limbs' – a good description of confluent smallpox, but a creative interpretation of the biblical verses, and one which ignores the inconvenient point that the biblical plague affected beasts as well as people.<sup>1</sup> The Revd Edmund Massey, preaching against inoculation in eighteenth-century London, saw smallpox as a trial or punishment sent by God, as in Job's boils.<sup>2</sup> In the eighteenth century too, Father Pierre Cibot, a Jesuit missionary studying ancient medical texts in Peking, claimed that a disease resembling smallpox had existed in China for 3,000 years – a claim often repeated but not now widely accepted.<sup>3</sup> Another suggestion was that smallpox entered China with

the Huns, arriving from the north about 250 BC, before the Great Wall was built.<sup>4</sup>

A disease referred to as *masurika* is mentioned in two Indian medical texts thought to be about 2,000 years old. The word is derived from the name of an orange lentil whose shape and colour are supposed to resemble the pustules of smallpox, and the same word is used much later to refer to what was almost certainly smallpox.<sup>5</sup> So it might seem that smallpox existed in India 2,000 years ago. But in 1981 Ralph Nicholas, an anthropologist from Chicago, pointed out that neither of the two early texts appears to take *masurika* very seriously.<sup>6</sup> One does not include it in an enumeration of diseases, and mentions it only briefly in a section on treatment; the other gives a short description that fits smallpox well enough except that there is no mention of its life-threatening quality or epidemic tendency, and the description is included in a section on minor ailments, sandwiched between a discussion of premature greying of the hair and the treatment of congenital moles and freckles.<sup>7</sup> It is not until the seventh century AD that Indian medical texts describe a fatal disease with the features of smallpox. So either the disease changed, or, more probably, the early disease was not smallpox.<sup>8</sup>

There is, though, a long-held assumption that Indians have worshipped a goddess of smallpox for two or three thousand years. In 1767 John Zephaniah Holwell<sup>9</sup> gave a talk to the College of Physicians in London. He had spent nearly thirty years of his life in India and he had been a surgeon in the East India Company, a member of the council running the company's affairs, the man called on to take charge when the Nawab of Bengal attacked the British settlement in Calcutta (and the governor and many of the senior officers skedaddled down the Hooghly), and one of the few survivors of the subsequent incarceration in the Black Hole – the infamous jail of Calcutta's Fort St William. For a short time, too, he had been deputy governor of Bengal. But Holwell did not talk to the physicians about his life story. In an address mainly concerned with the manner of inoculating for the smallpox in the East Indies, he told them that the *Atharva Veda* – the fourth book



2. *Sitala, Hindu goddess of smallpox*

of the ancient Hindu scriptures, written according to the Brahmins more than 3,000 years ago – ‘instituted a form of divine worship, with Poojahs or offerings, to a female divinity, stiled by the common people ... the goddess of spots ...’ This story was often repeated and widely believed, until it lost credibility at the beginning of the twentieth cen-

tury when Sanskrit scholars said that they could not find any such reference in the ancient scriptures.<sup>10</sup>

It is true, though, that for a long time a Hindu goddess of smallpox has been worshipped with much enthusiasm throughout India, and that over the whole of northern and central India and Nepal she is known by a single name, Sitala – literally ‘the cool one’.<sup>11</sup> She is believed to be able both to bring smallpox and to help those suffering from it, and she is represented in different forms. She may appear deceptively charming, sitting decorously side-saddle on a donkey, carrying a water pot and a broom, with a winnowing fan on her head, and dressed in red with polka dots. Or she may stand threateningly with crooked daggers in both hands raised to strike. But does she provide evidence for the existence of smallpox in ancient India? References to her are not found earlier than the beginning of the sixteenth century and, though sculptures with variations on the same theme have been found in the thirteenth, twelfth and ninth centuries, there is no solid evidence that she existed at still earlier times; nor is it certain that she has always been connected exclusively with smallpox – measles and chickenpox probably came into the picture too.<sup>12</sup> Smallpox gods or goddesses have also been found in China, Japan, West Africa and Brazil, but though they too are often assumed to go back to ancient times it is not clear that they do.

More convincing, though still uncertain, evidence that smallpox flourished in the first millennium BC is the plague of Athens described by Thucydides in lurid detail in his *History of the Peloponnesian War*.<sup>13</sup> The epidemic started in 430 BC and by its end had killed a quarter of the Athenian army, as well as Pericles and all his legitimate children. Whatever it was, it began in Ethiopia

*and then descended into Egypt and Libya and spread over the greater part of the King's territory. Then it suddenly fell upon the city of Athens, and attacked first the inhabitants of the Peiraeus, so that the people there even said that the Peloponnesians had put poison into their cisterns; for there were as yet no fountains there. But afterwards it*

*reached the upper city also, and from that time the mortality became much greater ...*<sup>14</sup>

And Thucydides continues:

*... I shall describe its actual course, explaining the symptoms, from the study of which a person should be best able ... to recognize it if it should ever break out again. For I had the disease myself and saw others sick of it.*

What is striking about Thucydides' account is that it includes most of the features characteristic of smallpox – the infectiousness, the immunity conferred by an attack, the sudden onset, headache, 'inflammation of the eyes and the parts inside the mouth', the skin 'livid and breaking out in small blisters and ulcers', the eruption starting with the head and moving to the extremities where it 'attacked the privates and fingers and toes', restlessness, vomiting, and in some patients diarrhoea, convulsions or blindness. But it fails to mention residual pockmarks, and it also includes features not usually associated with smallpox, such as the loss of fingers or toes, and the loss of memory or of the ability to recognise people and objects. The loss of fingers and toes could be the result of gangrene, which though not common in smallpox is not unknown. Alternatively, the Greek words can refer not only to 'loss' but also to 'loss of the use of', and such loss might be caused by pustules crowded on the digits, with or without secondary infection. Loss of memory and of the powers of recognition could be signs of the encephalitis that is occasionally a complication of smallpox. And there is, of course, no reason to assume that every feature described by Thucydides was the result of whatever it was that caused the epidemic. Epidemics have no monopoly, and in any epidemic there will be many patients suffering from the epidemic disease who also have other diseases with their associated symptoms. Physicians who have wondered about the cause of the plague of Athens have generally regarded measles, plague, typhus and smallpox as the candidates, with smallpox the favourite and typhus

the runner-up. Hans Zinsser, who in his classic *Rats, Lice and History*<sup>15</sup> argued strongly for smallpox, pointed out that less than forty years after the plague in Athens a similarly smallpox-like epidemic attacked the Carthaginian army besieging Syracuse – as described by Diodorus Siculus, though he was writing more than 300 years after the event. (A result of this epidemic was that the Carthaginians failed to gain complete control of Sicily – a failure which, Zinsser likes to think, tipped the balance against Carthage in the First Punic War that was to follow more than a century later.)

The belief that smallpox existed more than 2,000 years ago does not, though, depend solely on historical accounts such as those of Thucydides or Diodorus, or on doubtful interpretations of ancient Chinese or Indian medical texts; it is also supported by the study of Egyptian mummies.

Marc Armand Ruffer, son of Baron Alphonse Jacques de Ruffer, a banker of Lyons, was educated at Oxford, and then took a medical degree in London.<sup>16</sup> Returning to France, he became a pupil of Pasteur and Metchnikoff at the Institut Pasteur, and then, in 1891, came back to London as the first director of the British Institute of Preventive Medicine – the body that would eventually become the Lister Institute. While testing new antisera to diphtheria, he was so severely paralysed by the diphtheria toxin that he felt he must resign the directorship. He went to Egypt to recuperate, settled in Ramleh, became Professor of Bacteriology at the Cairo School of Medicine, and played a crucial part in ridding Egypt of cholera by rigorous enforcement of quarantine stations along the routes of pilgrimage. But his interests were not limited to current problems; he was fascinated by ancient Egypt, writing on topics ranging from the way shepherds made bread from millet seed to the way the Ptolemies monopolised the (vegetable) oil trade – forbidding imports, registering oil presses, searching for concealed presses and imposing heavy fines when they were found.<sup>17</sup> Linking his medical and antiquarian interests, he was among the first to look at mummies for signs of disease.

In 1911, in collaboration with the Professor of Pathology at Cairo,



3. *Mummified pockmarked head of Ramses V*

A. R. Ferguson, he published a short account of a mummy of the twentieth dynasty (1200–1100 BC) whose ‘body was the seat of a peculiar vesicular ... eruption which in form and general distribution bore a striking resemblance to that of small-pox’.<sup>18</sup> They had been allowed to remove a bit of skin, which when examined under the microscope showed that the vesicles ‘must have originated and developed in the prickle layer, i.e. the situation in which the small-pox eruption is first seen’. Ruffer mentions finding a very similar skin eruption in a mummy of the eighteenth dynasty (1580–1350 BC), but the most convincing example is that of Ramses V, who died in 1157 BC.<sup>19</sup> His mummy, which was photographed in 1912 by the anthropologist Grafton Elliott Smith, has what looks like a pustular eruption on the lower neck, face and shoulders, and also on the lower abdomen and scrotum.<sup>20</sup> Elliott

Smith, Ruffer and Ferguson all thought this eruption looked like smallpox. In 1979, the physician–epidemiologist Donald Hopkins got permission from the then President of Egypt, Anwar Sadat, to examine Ramses V’s partially unwrapped mummy,<sup>21</sup> but he found that it ‘was not possible to examine the palms or soles where the presence of pustules would be highly characteristic of smallpox, because [the mummy’s] arms were folded across his chest with the palms down, and the shroud was stuck to his soles’.

Hopkins wanted to excise one of the pustules so that it could be looked at with an electron-microscope to see whether it contained the now well-known, characteristic, brick-shaped particles of smallpox virus, but that was not allowed; and examination of tiny pieces of tissue that had fallen on the shroud was unsuccessful. He does though provide interesting indirect support for the smallpox theory. Pharaohs were usually buried after sixty days of mummification; Ramses V was not buried until the second year of his successor’s reign. Why the delay? Hopkins has a plausible answer. If Ramses V really did die of smallpox, his embalmers ‘would likely have suffered a fearsome epidemic about two weeks after starting to prepare his body, and the source of such a local outbreak would surely have been suspected ... Fear of the infection (if not an acute shortage of embalmers) could then have postponed the remaining preparation and burial’.