

Vaccines and Vaccination in Historical Perspective

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INTRODUCTION

The history of immunization, from earliest attempts to modern genetically engineered vaccine candidates, represents a long road marked with many milestones. Extensive historical reviews document many of these cardinal achievements (1–4). A few of the most pivotal milestones are mentioned briefly in this chapter, such as variolation, Jenner’s experiments of inoculating subjects with cowpox to prevent smallpox, and the earliest live and inactivated bacterial and viral vaccines and toxoids. On the other hand, the main purpose of this chapter is to emphasize historical accounts of several aspects of vaccinology that are not generally well described. These include some early attempts at eliciting local immunity by means of oral vaccines, attempts over the centuries at grappling with the problem of how to assess the safety and efficacy of candidate vaccines before their widespread use, and the evolution of controlled field trial methodology.

THE DAWN OF IMMUNOPROPHYLAXIS

The first attempts to prevent an infectious disease by means of immunoprophylaxis involved the process of “inoculation of the smallpox” or “variolation,” wherein the contents of smallpox vesicles, pustules, or scabs were used to inoculate individuals who had not previously experienced the disease (4). Records of this procedure date to about AD 1000 in China (4). Scabs from mildly affected smallpox patients were stored for approximately one month (longer in winter), ground up in a ratio of 4:1 with the plant *Uvularia grandiflora*, and then inoculated intranasally. A slight fever was expected six days thereafter, which rose markedly on the seventh day, to be followed by the onset of the rash on the ninth or tenth day following inoculation. Fatalities were reportedly uncommon compared with victims of natural smallpox infection. It was stated, “Not one in 10, not one in 100 does not recover” (4).

Parenteral variolation was practiced in the Indian subcontinent, southwest Asia, and North Africa in the 16th and 17th centuries. Reports of variolation reached England as early as 1700 through letters to the Royal Society sent by Joseph

Lister, an Englishman working in China with the East India Company (5). Over the next 15 years, further reports came from many sources, and in 1713 the Greek physician Emmanuel Timonis published the first European article about variolation (6). Many references credit Lady Mary Wortley Montagu with having *introduced* the practice of variolation into Great Britain in 1721 (7). Lady Mary herself suffered from smallpox in 1715, leaving her pockmarked. While living in Constantinople as the wife of the British ambassador, she became aware of variolation, as it was practiced every autumn by skilled Turkish women. In 1718, Lady Montagu had her five-year-old son inoculated with smallpox under the supervision of Charles Maitland, the surgeon to the British Embassy (5,8).

Lady Montagu wrote to a friend in England, Sarah Criswell, extolling the practice of variolation and vowed to make the procedure fashionable in England upon her return. In 1721, three years after she returned to England, an epidemic of smallpox raged in London. Lady Mary contacted Maitland, who was also in Great Britain at this time, and convinced him to variolate her four-year-old daughter. Maitland agreed, but demanded that there be two witnesses, one of whom was Dr James Keith (8). Keith was so impressed with the outcome that he had his six-year-old son variolated. Because these first inoculations were done in the face of considerable attention by the College of Physicians as well as the Royal Court, Lady Mary, whose insistence led to the first inoculation, has been widely credited with having introduced the practice into Great Britain. However, Miller (8) argues that Lady Mary’s contribution to variolation becoming an accepted and widespread practice in England was, in fact, quite minimal and that the real driving force for the introduction of variolation into the British Isles was Hans Sloane, physician to the king of England and president of the Royal Society.

Zabdiel Boylston used variolation for the first time in the United States, during a smallpox epidemic in Boston in 1721. The new procedure was promoted by the clergyman Cotton Mather who, reportedly, learned it from Onesimus, one of his African slaves (9). In Latin America, variolation was probably first introduced in Chile in 1765 by another clergyman, Father Pedro Manuel Chaparro.