

# The *Mayo Clinic Proceedings* Thematic Review on Vaccines



Edward Jenner, the creator of the smallpox vaccine, is widely accepted as being the father of modern vaccinology. Smallpox, a highly contagious viral infection, has changed the course of human history, caused the fall of monarchies, and resulted in untold suffering and death through the ages. Early on, it was realized that recovery from smallpox resulted in lifelong immunity, although infections often left people scarred for life. This led to the practice of “variola” or transfer of material from smallpox scabs of infected people to healthy individuals to induce immunity. Variolation was used as far back as 1500 BC in China and India; this practice spread to Europe in the early 18th century. However, variolation was unpredictable and resulted in smallpox infection and death in some recipients.

Jenner, an English physician, observed that milkmaids generally had perfect complexions and were free of smallpox scars. He hypothesized that infection with cowpox protected them from smallpox. Cowpox was a disease similar to smallpox, but much milder and limited to the forearms of milkmaids who came in contact with infected lesions on cow udders.<sup>1</sup> In 1796, Jenner tested his hypothesis by inoculating his gardener’s son, 8-year-old James Phipps, with pus scraped from cowpox blisters on the hands of a Gloucestershire milkmaid. The boy developed fever and malaise but no other signs of infection and recovered fully in a few days. Three months later, Jenner injected the boy with material from a smallpox victim and James remained healthy. James was challenged with smallpox several times over the next few years and remained protected. This formed the basis for the origin of “vaccination” from the term for the cowpox virus, “vaccinia,” which in turn comes from the Latin term for cow “vacca.”<sup>2</sup>

Over the next few years, this method of smallpox inoculation became widespread in England. The smallpox vaccine was first used in the United States in 1800 by Benjamin Waterhouse, a Harvard physician who vaccinated his children. Thomas Jefferson, who was then the vice president, became a strong vaccine advocate. In a letter to Waterhouse discussing the smallpox vaccine, Jefferson wrote, “Every friend of humanity must look with pleasure on this discovery, by which one more evil is withdrawn from the condition of man; and must contemplate the possibility that future improvements and discoveries may still more and more lessen the catalogue of evils.”<sup>3</sup> Those were prophetic words, although it was several years before additional vaccines were developed. Louis Pasteur developed a rabies vaccine in 1885. The second half of the 20<sup>th</sup> century heralded the golden age of vaccines, a number of vaccines against bacterial and viral infections became available, and previously widespread infections were drastically reduced. The last case of smallpox occurred in 1977, and the world was finally declared smallpox-free on May 8, 1980. Polio, a viral infection that routinely afflicted children and adults, was officially eliminated from the Western Hemisphere in 1991. Today, only two countries (Afghanistan and Pakistan) still report wild-type polio illness, and fewer than 30 cases occurred in 2018. The World Health Organization (WHO) estimates that vaccination prevents the deaths of roughly 2.5 million children per year or roughly 285 deaths per hour.<sup>4</sup> In the United States, routine childhood vaccinations of just the children born in a single year has been estimated to prevent approximately 42,000 early deaths and 20 million cases of disease, with net savings of \$13.5 billion in direct costs and \$68.8 billion in total societal costs, respectively.<sup>5</sup> We now have vaccines that

See also page 2127

prevent cancer — hepatitis B and human papilloma virus vaccines. Childhood diseases such as diphtheria, neonatal tetanus, and hemophilus B meningitis have disappeared in the United States.

It is no wonder that the Centers for Disease Control lists vaccinations as the top public health achievement of the 20<sup>th</sup> century. Vaccines have saved millions of lives, and prevented disabilities in countless more. However, there is a growing anti-vaccine movement that has resulted in the inclusion of vaccines in another top 10 list. Despite the remarkable and enduring benefits of vaccination, “vaccine hesitancy” is now labeled as a top-10 global health risk by the WHO.<sup>4</sup> Anti-vaccine sentiments are not new. In fact, they are as old as the history of vaccines. The United Kingdom Vaccination Act of 1853 was the first vaccination-related mandate. It mandated smallpox vaccination of infants in England and Wales, and noncompliant parents were subject to fines or imprisonment. The first US vaccine legislation was enacted in Massachusetts in 1855 and mandated smallpox vaccination of school children. These laws were met with immediate and vocal resistance from citizens who demanded the right to control their bodies and those of their children.<sup>6</sup> In 1903, a Minnesota activist Lora Little, who believed that the smallpox vaccine had resulted in the death of her child from diphtheria, persuaded the Minnesota legislature to rule against making the smallpox vaccination a requirement to attend school in the state.<sup>7</sup> In 1906, American Medical Association president William J. Mayo blamed this legislation “all due to a small but vociferous band of antivaccination agitators” for a smallpox epidemic that infected 28,000 people in his home state.<sup>8</sup>

These same kind of anti-vaccine sentiments persist today. Additionally, vaccines have been so successful that most individuals living today have never encountered previously widespread vaccine-preventable diseases such as diphtheria and tetanus. This has led to inaccurate assessments of risk versus benefits of vaccines. This phenomenon is not

limited to the United States. A WHO report found that 74% of 194 surveyed countries reported encountering resistance to vaccination with “concerns related to the risk and benefit of vaccines” being the most commonly cited reason.<sup>9</sup> Worldwide, this has resulted in a resurgence of vaccine preventable diseases. In 2018, more than 80,000 cases of measles were reported in Europe. There are ongoing large measles outbreaks in Israel, Venezuela, Philippines, and France. There were 17 outbreaks of measles in the United States in 2018, and more than 200 cases of measles have been reported in the first 3 months of 2019.

Vaccines protect not only the recipient of vaccination but also those around them, including infants who are too young to be vaccinated and those who are unable to respond adequately to vaccines, ie, the elderly and the immunosuppressed. To maintain the societal benefit from vaccines, we need to ensure that vaccine uptake remains high. Clinicians, who are knowledgeable about vaccines and recommend vaccines strongly, are the first line of defense against misinformation about vaccines and anti-vaccination rhetoric.

The Thematic Review on Vaccines aims to provide *Mayo Clinic Proceedings* readers with an understanding of the rationale for vaccine recommendations across the lifespan, including vaccines for special groups such as travelers,<sup>10</sup> health care workers,<sup>11</sup> and immunocompromised individuals.<sup>12</sup> It also provides an overview on new vaccines in the pipeline for emerging infectious diseases, ie, Zika and Ebola viruses.<sup>13</sup> Readers are also referred to prior articles in *Mayo Clinic Proceedings* that have addressed vaccine hesitancy.<sup>14</sup>

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