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Editorial

Vaccine, vaccination & personal decision making

The expanded programme on immunization (EPI) was launched by the World Health Organization (WHO) at the behest of its member States in 1974 and is completing its 50-year journey in 2024. The motto with which this programme was initiated was to make life-saving vaccines available to all. This initiative is estimated to have accounted for 40 per cent of the observed decline in infant mortality worldwide, and the increased survival probability extends well into late adulthood[1].

The seed of the aforementioned global feat was sown 250 years ago in the countryside of England. Benjamin Jesty (1736-1816), a hero who remained unsung until recent times, was an English farmer and cattle breeder who, by using his wife's knitting needle, inoculated his two sons and his wife with fluid material collected from the lesions on the udder of a cow infected with cowpox[2]. Benjamin intended to protect his family from the brunt of the smallpox epidemic, gaining a foothold in 1774 in the area close to where they lived (initially in Yetminster, North Dorset, and later, the family moved to Downshay)[2]. This innovative intervention, which was not in vogue then, worked! The family remained unharmed by the raging smallpox. Notably, Benjamin did not inoculate himself as he had cowpox some years ago and was certain he was already protected[2]. This conviction was grounded in the local wisdom and observations that milkmaids who contracted cowpox during their work somehow remained protected against smallpox[3] and were even called on occasions to nurse patients suffering from smallpox. Elizabeth Jesty, the wife of Benjamin Jesty, who lived until 1824 and was buried beside her husband[2], ensured the engraving of Benjamin's achievement on his tombstone.

Some 22 yr later, Dr Edward Jenner (1749-1823), a physician in Berkley, Gloucestershire (about 100 miles north of Yetminster), carried out similar experiments by vaccinating James Phipps, an 8-yr-old boy, on May 14, 1796. He inoculated James with cowpox material collected from Sarah Nelmes, the milkmaid with cowpox lesions on her hand, followed by deliberate challenge with smallpox infection, which did not lead to disease development, thus proving protection against smallpox[4]. Dr Jenner also conducted a nationwide survey in England and obtained proof of resistance to smallpox among those who had cowpox. Furthermore, he advocated relentlessly for the smallpox vaccine among physicians and academicians and even sent vaccine materials to them across England and the US and whoever requested it[4]. Notwithstanding, he had his share of ridicule and rejection during this journey, including the rejection of a short communication he submitted to the Royal Society in 1797 describing his experiment and observations. He was forced to publish his findings at his own expense in 1798[4,5].

The approach of Jesty and Jenner was a significant departure from variolation – a practice of inoculation of susceptible individuals through scarification with infective pox material collected from patients, preferably with milder disease (or insufflation of water or wine solution of dried scabs of a smallpox patient by administering it in the nose of a healthy individual)[6]. The acceptance of variolation, due to its ability to offer protection (immunity) against smallpox, was increasing globally. However, variolation (Edward Jenner as a child received it in 1757) had its associated safety concerns, including pain, complications akin to natural infection and even the risk of spreading the disease to the community, and required isolation following variolation. Vaccination (*Vacca* meaning cow in Latin), practiced in the post-Jennerian era, surmounted such problems to a great extent. The work of Benjamin Jesty and Edward Jenner prepared the ground for the development of other vaccines, such as the first attenuated prophylactic vaccine against rabies by Louis Pasteur in France[7].

The following century witnessed the development of vaccines against various diseases, initially against bacterial infections such as cholera, which appeared in multiple waves as a pandemic and later against viruses, autoimmune diseases and tumours. Advances in immunology in human health and diseases[8-10], polysaccharide and conjugate vaccine revolution (against *Hemophilus influenzae,* meningococcal, and pneumococcal infections)[11], genomics, and next-generation antigen design contributed to these achievements[12]. The growing body of knowledge and technology around vaccine development over the last three decades, in particular, has been breathtaking. When the saga of the COVID-19 pandemic unfolded recently, all these incremental accumulations paid dividends. Today's vaccines have traversed a long distance from drawing upon killed or attenuated offender microorganisms to a wide range of technological developments, including synthetic biology, the usage of viral vectors, reverse vaccinology and mRNA-based approach[12,13]. Targeted research around adjuvants to go with the vaccines to elicit immune responses in a desired direction and with durability has further contributed significantly to these success stories[14].

Despite initial excitement about the possibility of intercepting the chain of transmission of infection by vaccinating a critical number of individuals in a population, public health experts soon realized that such programmes come with their respective challenges. Besides logistic issues (supply, cold chain and delivery), nuances related to population-level uptake of vaccines play critical roles. In this context, the following observations merit due attention: 'It's often said that vaccines save lives, but this is not strictly true; it is vaccination that saves lives. A vaccine that remains in the vial is zero per cent effective even if it is the best vaccine in the world. Thus, it is imperative that we all work together to assure that a high level of coverage is obtained among populations for whom vaccines are recommended'[15].

Notably, benefits from vaccination are not restricted to only those who receive vaccines but reach much beyond. Such indirect beneficiaries comprise unvaccinated individuals belonging to different groups, such as those who fail to mount a protective immune response following vaccination or those for whom vaccines are contraindicated[16]. They benefit because their probability of getting exposed to vaccine-preventable pathogens is reduced (herd effect), resulting from the reduced number of susceptible individuals following immunization in a population and the breach of the human-to-human chain of transmission of infection. An updated systematic review and meta-analysis based on data from 60 million individuals and up to eight years of post-vaccination follow up highlighted the compelling evidence of the substantial impact of HPV vaccination programmes (among those vaccinated and beyond) on HPV infections and cervical intraepithelial neoplasia grade 2+ among girls and women and anogenital warts diagnoses among girls, women, boys, and men[17].

However, vaccination programmes faced vociferous opposition during smallpox time[5]. Since then, anti-vaccine sentiments based on misinformation and disinformation, religious considerations, ethical grounds, confidence in the natural ability to resist infection, safety, perceived risk-benefit balance, fear of side effects, trust in the health system, assumed genocidal plot and even wrong scientific interpretation have surfaced and re-surfaced: against pertussis in the 1970s and 1980s and measles, mumps and rubella (MMR) in the 1990s in Britain[18]. Mass refusal of oral polio vaccination in northern Nigeria in 2003-2004[19] and hesitancy to take the COVID-19 vaccine in 2021 in India[20] and other countries further exemplify such nuances. In the United States, policy interventions, such as immunization requirements for school entry, have been put in place to address issues around vaccine refusal and outbreaks of vaccine-preventable infections (VPIs) in schools and communities[21]. Despite this different States have witnessed a rise and fall in number of appeals for exemption of this requirement on religious reasons, medical grounds, or philosophical or personal beliefs[21].

The susceptibility of vaccination programmes to community resistance of different types, as mentioned above, underlines the necessity of understanding these with the associated political issues of the places and the day, and within the specificity of their social contexts[22]. Community engagement in health system decisions beyond 'immunization coverage and fulfilment of programme targets' constitutes an essential component of such discourses. Other issues, such as a pandemic or a conflict between countries, have also negatively affected vaccination programmes. For example, the estimates of the national immunization coverage released by the WHO and UNICEF on July 15, 2024 revealed that the global childhood immunization coverage halted in 2023, leaving 2.7 million additional children unvaccinated or under-vaccinated compared to the pre-pandemic levels in 2019[23]. Specifically, the number of children receiving three doses of vaccine against diphtheria, tetanus and pertussis (DTP) in 2023 stalled at 108 million. The number of children who did not receive a single dose of DTP increased from 13.9 million in 2022 to 14.5 million in 2023[23]. Therefore, the path ahead is arduous and checkered, with a pattern that is probably a few steps forward and two steps back.

In addition to the factors mentioned above, the personal decision 'to take or not to take' a vaccine is further influenced by the fallacy of thinking that if anything goes wrong after vaccination, it must be due to vaccination. In modern times, such discussions on social media without critical considerations, essential to arriving at a cause-and-effect inference, amplifies vaccine refusal. 'To take or not to take a vaccine' also remains predisposed to one's mental calculation about the possibility of an event happening (occurrence of an infection or its severity) shortly versus in the far future. A particular vaccine like COVID-19 or a vaccine to avert comorbidities such as influenza or pneumococcal vaccines in the elderly that may seem 'urgent and acceptable' during the pandemic time may seem 'not so' when the pandemic becomes a thing of the past and not perceived as imminent in future (despite a contrary stance taken by the scientists). The vivid detail of the near future makes it much more palpable than the far future[24]. It may influence decisions out of anxiety or excitement as human brains imagine the near and far futures with different textures and clarity[25].

This special issue on 'Vaccine & Vaccination', conceived through a prestigious collaboration between the Indian Journal of Medical Research (IJMR), the flagship monthly publication of the Indian Council of Medical Research (ICMR) and the World Health Organization - Regional Office for South-East Asia (WHO SEARO), presents many such thought-provoking articles submitted from within India and outside.

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