Chapter

Introductory Chapter: The Journey of Vaccines - The Past and the Present

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1. Introduction

The history of the process of vaccination and the concept to vaccinate is 1000 of year old (>3000 years) that originated in the ancient Indian peninsula (Northern and Eastern India) as a practice of variolation/inoculation (the immunization of individuals from the materials taken from the infected person) by "Woodiah" (Oriya) Brahmans since "time immemorial" due to its unidentifiable time of origin [1]. The evidence of protective measures of the process of variolation/inoculation is greatly described in the ancient Sanskrit text called Sacteya, mainly devoted to Dhanwantari, the physician [2]. Thereafter that technique may have spread to the China due to the transfer of education and knowledge as Chinese scholars were visiting the world's oldest Universities (Nalanda and Takshashila Vishwavidyalaya or University). Hence the technique of variolation moved from ancient India to the China around 1000 CE. Thereafter, the technique of variolation traveled to Africa and Turkey before its arrival to the European and American continents. Before the introduction of variolation there was no protective measure to counter the attack of smallpox and the observation was made by the Greek historian Thucydides (430 BC) that the attack of smallpox provides protection to the person surviving the attack of the smallpox. Evidence indicate the first existence of smallpox as a disease in ancient Egypt that reveled to ancient India through Egyptian traders visiting India during first millennia BC [3]. From India then it traveled to China in first century AD and reached in Japan in the sixth century AD [3]. It spread to Europe in the eleventh and twelfth centuries from there to North America (seventeenth century) and Australia (eighteenth century).

It is well established that smallpox is neither described in the Old and New Testaments nor in the classical Greek (including the Hippocratic and Galanus writings) and Roman literatures [2]. It was Abu Bakr Muhammad Ibn Zakariya al-Razi (864–930 CE), a Tehran (Iran) born Muslim physician who first differentiated between smallpox and the measles based on their symptoms and clinical examination of the patients [4]. However, the term smallpox is an English term for the disease, introduced first in India during the British rule and before it was known as the Masurika (For about 2000 years as mentioned in Charak and Sushruta Samhita before the Christian era) Basanta roga (*Paproga, Sitalika, Sitala, Gunri*, and *Guli*) or the spring disease in Eastern India. The concept of variolation or inoculation moved from India to the England in the early eighteenth century or 1721 by the British Lady Mary Wortley Montagu, who was living in Ottoman Empire (1716–1718) and communicated to her friend in Britain (Miss Sarah Chiswell, who died of smallpox 9 years later) about this technique by letters [2, 5]. Even in 1731 one British called Robert Coult in Bengal wrote a letter to Dr. Oliver Coult in England describing the

procedure of variolation used in India to protect the local population from smallpox [6]. Dr. Edward Ives (1773), a British naval surgeon, also observed the procedure of variolation as described by the Robert Coult on his visit to India (Bengal) in 1755 [6]. Before the introduction of variolation/inoculation in England in the sixteenth century the burden of infectious diseases including smallpox, measles, whooping cough, dysentery, scarlet fever, influenza, and pneumonia accounted for the death of more than 30% children of age below 15 years as the record. The concept of variolation/inoculation was introduced in North America in 1721. By 1777, George Washington, ordered that all the soldiers and recruits of his army should be inoculated/variolated. Thus introduction of the concept of variolation was the first step towards the development of Edward Jenner's cowpox/smallpox vaccine, modern day vaccines, and the introduction of the concept of vaccination to fight against infectious diseases.

Almost all text books of immunology and microbiology mention Edward Jenner as a father of immunology or vaccination due to his invention of the technique called vaccination as he injected the cowpox immunogenic material (pus) isolated from the hand of Sarah Nelmes (a female milkmaid, who got the cowpox from the infected cow called Blossom) to the both arms of James Phipps (a young boy of 8 years) on May 14, 1796 [7]. However, the process of vaccination was developed almost 22 years before Edward Jenner by a farmer called Benjamin Jesty [7]. No one knows Benjamin Jesty. Even the reports are available to indicate the existence of the concept/Sanskrit literature of cowpox vaccine to induce the immunity against smallpox in ancient India. It may be an injustice to the real discoverer of the concept of cowpox vaccination but the journey of vaccines and vaccination had started that never looked back. However the technique of variolation banned or made illegal in Britain in 1840 and the Jenner's vaccination was promote and offered free of cost [3].

2. The development of vaccines from early nineteenth to twenty-first century

The early eighteenth century saw development of the vaccination procedure against small pox and its promotion in England by offering free vaccination there. Its spread all over the world revolutionized the field of vaccination against several other infectious diseases. However, the scientific origin of vaccines took at least a century following the discoveries made by Robert Koch and Louis Pasteur generating the concept there are pathogenic microbes/microorganisms causing infectious. Pasteur initiated attenuation of these pathogens in his laboratory by different methods including drying, heating, and exposing them to oxygen or passaging them in different animal hosts. The first live attenuated vaccine was developed for Rabies in 1885 and was used to immunize a boy named Josef Meister bitten by a rabid dog [8]. Thereafter killed whole organisms were used to develop vaccine against cholera (1896), typhoid (1896), and plague (1897) [9]. In second half of the twentieth century oral polio vaccine (OPV, 1963), measles (1963). Mumps (1967), and rubella (1969), all live attenuated vaccine came out along with several other vaccines (polio (injected, 1955), a killed whole organism vaccine, Anthrax vaccine (a protein-based vaccine, 1970), Hepatitis B surface antigen recombinant (a genetically engineered vaccine in 1986), and hepatitis A (a whole killed organism-based vaccine in 1996) were developed [9].

In twenty-first century, human papillomavirus (HPV) recombinant (quadrivalent in 2006), live attenuated vaccine Zoster in 2006, HPV recombinant (bivalent in 2009), pneumococcal conjugates (capsular polysaccharide conjugated with the career protein) (13-valent in 2010) are developed. Furthermore the live attenuated vaccine for the dengue virus infection is also developed by Sanofi Pasteur in 2016 and is called CYD-TDV that is sold under the brand name Dengvaxia [10, 11]. This

live attenuated tetravalent chimeric vaccine is developed through the use of recombinant DNA technology by replacing the PrM (pre-membrane) and E (envelope) structural genes of the yellow fever attenuated 17D strain vaccine with those from four of the five dengue serotypes [11]. However this dengue vaccine is recommended to the patients previously infected with dengue virus infection otherwise it may exert adverse effects during subsequent infections as their manufacture, Sanofi Pasteur. The vaccine is approved to use 11 countries including Mexico, Philippines, Brazil, El Salvador, Costa Rica, Paraguay, Guatemala, Peru, Indonesia, Thailand and Singapore [12–15]. The dengue vaccine has shown consistence efficacy in healthy adults of Australia and ready to go in clinics [16]. The vaccine has shown immunogenicity and safety during a 5-year study [17] A most recent development in the field of vaccinology is the clinical trial for the live attenuated vaccine for Zika virus vaccine at the Johns Hopkins Bloomberg School of Public Health Centre for Immunization Research in Baltimore, Maryland, and at the Vaccine Testing Centre at the Larner College of Medicine at the University of Vermont in Burlington. The clinical trial for Zika virus is sponsored by National institute of allergy and infectious disease (NIAID), USA. In addition to the development of vaccines for infectious diseases these are also to develop against different cancers through targeting cancer-associated neoantigens.

The major aim of the book is to provide the readers an updated information on the field. For example, the first chapter of the book written by Dr. Raw Isaias has updated the progress of regarding the innovation and development of new vaccines and their candidates in developing countries like Brazil. In the second chapter, Dr. Dai has provided a great information regarding the different types of vaccines that will be informative for undergraduate and graduate students along with researchers. The third chapter of the book provides the regulatory journeys of applications with genetically modified viral vectors and novel vaccine candidates already reviewed by GMO (Genetically modified organisms) national competent authorities in Belgium and in Europe. This chapter will be crucial for the readers interested in regulatory affairs for the vaccines developed via GMOs. In fourth chapter, author (Leunda Amaya) has given an emphasis to target the vaccination strategies wildlife reservoirs including bats, boars, rodents, and other carnivorous animals serving as reservoirs for zoonotic viral infections (Rabies, Hanta virus infection, and Hepatitis E virus) in humans. The fifth and last chapter of the book written by Dr. Dulcilene describes the development of vaccinia virus vector to develop the vaccines against leishmaniasis that is major problem for developing countries of Asia, Africa and South America. Thus the book starts with the introductory chapter regarding the history and present status of the vaccines along with the other chapters contributed by the authors known in their field. Thus book is intended to provide the current and updated knowledge in the field of vaccinology.

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