



Mini Review

Copy Right@ Sarbani Chattopadhyay

Vaccinations, The Journey So Far and The Road Ahead

Dr Sarbani Chattopadhyay*

University of Gottingen, Germany

*Corresponding author: Sarbani Chattopadhyay, University of Gottingen, Bonn, Germany.

To Cite This Article: Sarbani Chattopadhyay. Vaccinations, The Journey So Far and The Road Ahead. *Am J Biomed Sci & Res.* 2021 - 13(4). AJBSR. MS.ID.001884. DOI: [10.34297/AJBSR.2021.13.001884](https://doi.org/10.34297/AJBSR.2021.13.001884).

Received: ☒ June 06, 2021; **Published:** ☒ July 12, 2021

Abstract

The advancement of science has led to the development of vaccines that arm the human beings against infectious diseases, reducing morbidity and mortality. Vaccines are the monetarily convenient mass scale preventive measure against deadly diseases and pandemics. The constant scientific efforts in this area has led to new and better ways of conferring immunity to mankind to the disease that have created havoc in the past. This is review of the different types of vaccination techniques that have developed over time and how these have been utilised to address the SARS-CoV-2 virus. The future for immunization is promising with vaccinations being developed for diseases like cancer.

Keywords: Vaccinations; Infectious Diseases; SARS-Cov-2 Virus; Cancer; Antibody Production.

Abbreviations: OPV: Oral Poilo Vaccine; HIV: human immunodeficiency virus; SARS: severe acute respiratory syndrome; HPV: Human papillomavirus; Hib: Haemophilus influenzae type b; PD-1: Programmed cell death protein 1; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease

Introduction

Vaccination treatment empowers the body's immune system against the harmful foreign intruding elements, the pathogens. When the body is introduced, on purpose, to the weakened version or any kind of blueprint of the specific antigen in the pathogen, it produces antibodies against the antigen. The primary response being antigen specific antibody production, the body also produces memory cells that remain alive even after the antigen is defeated. In the event of infection by the real antigen, the body responds quickly with the memory cells producing the antibodies effectively [1]. The doses of vaccines required, are case specific and depend on what is required to ensure long term development of memory cells and antibodies.

The agents that can be introduced to activate body's immune response have developed historically. The earliest vaccine developed by Edward Jenner against smallpox was the first live attenuated vaccine [2]. These kinds of vaccines have been further developed against other diseases like measles, mumps, rubella etc. Live viruses that have been attenuated such that they can't cause the disease but still can replicate, even if not properly, in the human host, can be recognized by the human immune system. Their effect

being very similar to the actual natural infection, these vaccines incite long term immune response, even conferring lifetime immunity. However, there always remains the risk that weakened virus can gain back the virulence through mutations while being inside the human body, which was reported in case of the oral polio vaccine (OPV). This is the main reason OPV was banned in the USA in 2000 [3]. Caution also needs to be exercised with such vaccines for people with weak immune system such HIV patients. These live vaccines need to be stored at low temperatures and thus easy and ample access to refrigeration process is essential for widescale vaccination program using attenuated vaccines. These factors affect the potential of any live attenuated vaccine to be able to address the current SARS-CoV-2 virus, which itself has undergone numerous mutations for its survival gaining further lethality and contagiousness with each mutation.

Inactivated form of harmful foreign elements, when introduced into the body can still incite immune response. Virus or bacteria killed using heat or chemicals e.g. formaldehyde or other means like Ultraviolet rays are the candidates for inactivated vaccines. These can be conveniently stored and the risk of the introduced antigen gaining back pathogenicity is also avoided. However, these



are not as efficacious as the live attenuated vaccines and multiple doses may be required to confer immunity. Currently the Sinovac vaccine developed against the Covid-19 virus in China by Sinovac Biotech is based on inactive particles of SARS-CoV-2 virus [4]. Covaxin developed by Bharat Biotech in India is also inactivated vaccine against SARS-CoV-2 [5].

Vaccines are also developed based on a part of the pathogen: a protein or carbohydrate or the antigen itself, which when injected into the body trigger immune response. These are referred to as Subunit vaccines [6]. These are more safe as only a part of the whole germ is introduced and are expectedly easy to produce. However, detailed research is required to study the kind of antigenic properties the parts of the pathogen have and the best combination to incite the desired immunogenic response needs to be determined. These subunits do not actually infect the cells; the immune response is through action of antibodies against the antigenic parts. Thus, the immune response can be weak compared to other vaccines, which is why these are sometime combined with adjuvants that act as boosters. Furthermore, questions regarding the longevity of the immunity based on memory cells also need to be addressed. The viruses in the Coronaviridae family: SARS-CoV-2 virus, SARS and MERS virus have membranes with glycoprotein spikes which are responsible for their 'crown' like or 'corona' like appearance under the microscope. These spike proteins anchor the virus onto the host human cell. There are a number of vaccines that have been developed on the subunits of the SARS-COV-2 virus, some with adjuvants. Sanofi in collaboration with GSK is developing a vaccine against Covid-19 virus, comprising the spike protein with the adjuvant provided by GSK [7]. Novavax has developed a vaccine based on the Spike protein carried by nanoparticles, along with its own proprietary adjuvant Matrix-M to fight against the SARS-CoV-2 virus [8].

Conjugate vaccines are developed against those foreign elements whose antigens can't be recognized by the body's immune system as they remain encapsulated in polysaccharide capsule [9]. Strategically an antigen from another identifiable pathogen is coated in the same polysaccharide capsule to enable the immune system to recognize the polysaccharide coating as threatening and to attack the same. Haemophilus influenzae type b (Hib) was successfully eradicated using conjugate vaccine technique [10]. Conjugate vaccine against SARS-CoV-2 is being developed in Cuba. It comprises two doses: The Spike protein of the SARS-COV-2 virus and tetanus toxoid conjugated to it [11].

Toxoid vaccines are also widely used to induce immunity against the toxin that is released by the foreign element i.e. the germ. The body acts against the toxin and not the entire germ and thus chances of single dose leading to lifelong immunity is low [12]. Toxoid vaccines are used against Tetanus [13] etc.

Methods by which the antigen instead of being externally administered into the body are produced within the body, have been developed, to induce immunity. The antigens are delivered into the body a 'vector', which is generally a virus that has either been engineered to be incapable of replicating inside the body and causing any disease and capable of undergoing degradation or is capable of replicating but is weakened to be able to cause any disease [14]. One such virus that qualifies for acting like a vector is the Adenovirus belonging to the family Adenoviridae [15]. There are different genera in the family that infect mammalian species, birds, reptiles, amphibians and fishes. These are naked, viruses with double stranded DNA genome. Adenovirus generally causes common cold in humans but can be dangerous for human beings with decreased inherent immunity.

The commonly occurring adenovirus infections in humans make the body already immune to these as antibodies against the virus are expected to be already present in the body. This can affect the potential of this virus to act as a vector for carrying DNA of specific antigen. This issue is overcome by using adenovirus from other species that the human body has not likely encountered. There are numerous vaccines that have been developed against the SARS-CoV-2 by this method. The adenovirus vector is designed to encode for the spike protein inside the body to elicit immune response against the Covid-19 virus. The AstraZeneca- University of Oxford vaccine uses the engineered version of Chimpanzee Adenovirus ChADOx1 as vector [16]. Johnson & Johnson uses its proprietary recombinant adenovirus that was being developed against the Ebola virus as the vector [17]. Sputnik V from Russia uses recombinant human adenovirus [18], so does CanSino [19] from China.

The most recent approach in vaccine development is that based on nucleic acids. Similar to the viral vector process, the mRNA with the genetic code to make the antigen, can be directly injected into the human body, leading to the production of the antigens using the body's own proteins, thus triggering an immune response [20]. The process is advantageous because the antigen is produced inside the body and thus these can be produced in large quantities inducing strong response. In case of fight against SARS-CoV-2, mRNA-based vaccines mostly encoding for the spike protein have been developed. The Pfizer-BioNTech COVID-19 vaccine is mRNA in lipid nanoparticle that codes for spike protein [21]. The Moderna vaccine is also an mRNA encapsulated in lipid nanoparticle, coding for the spike protein [22]. These are landmark cases in themselves where for the first time mRNA-based vaccines have been successfully produced, administered and have been found to be effective.

The scope of immunotherapy and immunization is not only

restricted to foreign pathogens but has also advanced to the field of treatment of cancer [23]. The process to stimulate body's own immune system to act against the cancer cells is being developed. Therapeutic vaccines are based on personalized precision therapy whereby patient's own white blood cells are taken from the body and engineered upon e.g. in case of prostate cancer, the white blood cells are mixed with prostatic acid phosphatase (PAP) and then reintroduced into the patient through infusion [24]. This has allowed patients to live longer. Drugs that inhibit the various check point inhibitors e.g. Keytruda acting against PD-1 inhibitor, boosts the body's own immune response against prostate cancer cells [25,26]. The vaccine against the Human papillomavirus (HPV) helps prevent cervical cancer and other types of cancer linked to it [27].

Biographical Notes

Dr Sarbani Chattopadhyay PhD, LL.M., is a computational biologist with a PhD in Biochemistry from the University of Calcutta (India) and a LL.M. in European IP and IT Law from the Georg-August-University of Göttingen (Germany). She assists her clients in searching and analysing patents to gain insights about patent portfolios and technologies.

Acknowledgement

None.

Conflict of interest

No conflict of interest.

References

- Maurice JM, Davey S (2009) State of the world's vaccines and immunization (3rd ed). Geneva: World Health Organization.
- Baxby D (1999) Edward Jenner's Inquiry after 200 years. *BMJ* 318(7180): 390.
- (2021) Polio vaccination: what everyone should know | cdc.
- The Sinovac COVID-19 vaccine: What you need to know.
- Vaccine information, icmr new delhi - covid-19 vaccine.
- Skwarczynski M, Tóth I (2017) Micro-and nanotechnology in vaccine development.
- Anon (2020) Sanofi joins forces with U.S. Department of Health and Human Services to advance a novel coronavirus vaccine.
- Pinho AC (2021) EMA starts rolling review of Novavax's COVID-19 vaccine (Nvx-cov2373), European Medicines Agency.
- Rappuoli R, De Gregorio E, Costantino P (2019) On the mechanisms of conjugate vaccines. *Proc Natl Acad Sci U S A* 116(1): 14-16.
- (2021) About hib vaccine (Haemophilus influenzae type b vaccine) | cdc.
- Mega ER (2021) Can Cuba beat COVID with its homegrown vaccines?. *Nature*.
- Module 2-toxoid vaccines - who vaccine safety basics.
- Tetanus toxoid vaccine example - who vaccine safety basics.
- Ura T, Okuda K, Shimada M (2014) Developments in viral vector-based vaccines. *Vaccines* 2(3): 624-641.
- Tatsis N, Ertl HCJ (2004) Adenoviruses as vaccine vectors. *Mol Ther* 10(4): 616-629.
- Folegatti PM, Katie J Ewer, Parvinder K Aley, Brian Angus, Stephan Becker, et al. (2020) Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *The Lancet* 396(10249): 467-478.
- Shay DK (2021) Safety monitoring of the janssen (Johnson&johnson) covid-19 vaccine-united states, march-april 2021, MMWR. *Morbidity and Mortality Weekly Report*, pp: 70.
- Jones I, Roy P (2021) Sputnik V COVID-19 vaccine candidate appears safe and effective. *The Lancet* 397(10275): 642-643.
- Zhu FC, Xu Hua Guan, Yu Hua Li, Jian Ying Huang, Tao Jiang, et al. (2020) Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. *The Lancet* 396(10249): 479-488.
- Pardi N, Michael J Hogan, Frederick W Porter, Drew Weissman (2018) mRNA vaccines-a new era in vaccinology. *Nat Rev Drug Discov* 17(4): 261-279.
- Haas EJ, Frederick J Angulo, John M McLaughlin, Emilia Anis, Shepherd R Singer, et al. (2021) Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *The Lancet* 397(10287): 1819-1829.
- Cao Y, Gao GF (2021) mRNA vaccines: a matter of delivery. *EClinicalMedicine* 32: 100746.
- Saxena M, Sjoerd H van der Burg, Cornelis J M Melief, Nina Bhardwaj (2021) Therapeutic cancer vaccines. *Nat Rev Cancer* 21(6): 360-378.
- Doehn C, Torsten Böhmer, Ingo Kausch, Martin Sommerauer, Dieter Jocham (2008) Prostate cancer vaccines: current status and future potential. *BioDrugs*: 22(2): 71-84.
- Immunotherapy for prostate cancer.
- Ye Z, Qiming Qian, HuaJun Jin, Qijun Qian (2018) Cancer vaccine: learning lessons from immune checkpoint inhibitors. *J Cancer* 9(2): 263-268.
- CDC (2020) Vaccinating boys and girls against hpv, Centers for Disease Control and Prevention.