Article: RT0480

Biotica Research Today

Vol 3:1 038/041

2021

Understanding Vaccine and Life-Saving Vaccination in the Era of Covid-19 Pandemic

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Open Access

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Keywords

Covid-19, Vaccination, Vaccine, Vaccine candidates

Article History

Received in 17th January 2021

Received in revised form 19th January 2021

Accepted in final form 20th January 2021

E-mail: *bioticapublications@gmail.com*

How to cite this article?

Samal *et al.*, 2021. Understanding Vaccine and Life-Saving Vaccination in the Era of Covid-19 Pandemic. Biotica Research Today 3(1): 038-041.

Abstract

As Covid-19 continues to spread around the world, people in all countries are being encouraged to take precautions to prevent transmission, including in many countries by staying at home and physical distancing. But a pandemic does not erase other diseases and their impact. While many services, including some health services, are being scaled back, the risk of further outbreaks of infectious diseases grows. The healthcare disruptions caused by Covid-19 could have a devastating impact on child mortality. So, it is essential to understand vaccine and life-saving vaccination in the era of Covid-19 pandemic. According to a report of WHO on 12th January 2021, 63 vaccine candidates are now in clinical development and 173 vaccine candidates are in pre-clinical development. Some authorized or approved vaccines are now under distribution for Covid-19 pandemic.

Introduction

A vaccine is a biological preparation that contains an agent that resembles like a disease-causing microorganism, and is often made from weakened or killed forms of this microorganism, its toxins or one of its surface proteins. These are disarmed micro-organisms which are either killed or weakened to the point that they don't make you sick. Some vaccines contain only a part or subunits of the disease-causing microorganism. Vaccine stimulates immune system of the human body to produce antibodies against a specific harmful agent exactly like it would if you were exposed to the disease. After getting vaccinated, the vaccinated person develops immunity against that disease which makes vaccines such powerful medicine. Unlike most medicines, which treat or cure diseases, vaccines prevent the occurrence of the disease in future. The vaccines are prepared in different forms such as live, attenuated or killed microorganisms, or their antigens or toxoids or their subunits. In killed vaccines the organisms are killed by heat, formalin, phenol and alcohol. Toxoids are prepared from bacterial exotoxins inactivated by formalin or by alum. Toxoids are immunogenic but not toxigenic.

What Does A Vaccine Contain?

Vaccine contains live, attenuated or killed microorganisms or their antigenic epitopes or subunits or toxoids along with other fluids (such as water or saline), additives or preservatives (to prevent contamination) and sometimes adjuvants (to increase immunogenicity of the vaccine). Vaccines formulation should be safe and immunogenic. After immunization vaccine should trigger immunogenicity and produce antibodies or memory cells (humoral immunity) or T-cells (Cell-mediated immunity) to fight against pathogens and keep the individual disease fee or mild disease. Vaccines

are available in different forms such as liquids or lyophilized.

Vaccination and Immunity

Vaccination triggers immune response and develops active artificial immunity. Active immunity is the stimulation of the immune system to produce antigen-specific humoral immunity (antibody) and cellular immunity (T-Cell). Following immunization B lymphocytes immediately produce antibodies to fight against invading pathogens. Many vaccines also produce immunologic memory cells (B cells) for future protection.

History of Vaccine and Vaccination

Long ago, the ancient people observed that people who were come in contact with smallpox once were immune to reinfection. They came up with the idea of preserving scabs from individuals who had suffered mild cases, drying them out, crushing them to a powder and blowing them up the nostril. In this way the people acquire ability to be less infected with the smallpox in future. British physician Edward Jenner, harvested bits of a cowpox pustule from a milkmaid named 'Sarah Nelmes' and scratched it into the arm of an 8-year-old boy named 'James Phipps', on May 14th, 1796. After, he attempted to infect Phipps with human smallpox, but the boy simply shook off the virus. Two year later, Jenner published his results and used the cowpox virus (vaccinia) to confer protection against smallpox, a related virus, in humans. So Edward Jenner is well known around the world for his innovative contribution to immunization and the ultimate eradication of smallpox for which he is known as "father of vaccination". In 1881, French microbiologist Louis Pasteur demonstrated immunization against anthrax by injecting sheep with a preparation containing attenuated forms of the bacillus that causes the disease. Four years later he developed a protective suspension against rabies.

Vaccine Types

1. Traditional Methods of Vaccine Production

The first human vaccine against the smallpox is a cowpox virus, a poxvirus that was similar enough to smallpox to protect against it but usually didn't cause serious illness. Rabies was the first virus attenuated vaccine for humans.

a) Egg-Based Vaccines: Over the last six decades, seasonal flu vaccines have been prepared using fertilized embryonic eggs. It takes about four months to produce a batch of vaccines for a new strain of influenza virus; from the moment the new influenza virus' culture becomes available for vaccine manufacturing. In this method seasonal flu vaccines are prepared and which are found to be safe.

b) Cell-Based Vaccines: In the late 1990, newer cell-based vaccine manufacturing process are developed which uses cells from mammals to culture the influenza virus for vaccine production. Many pharmaceutical companies use different sources of mammalian cell cultures (cells extracted from the kidney of the African Green Monkey or kidney cells from canines) for the vaccine manufacturing process of seasonal flu vaccines.

c) Production of DPT Vaccine: DPT is a class of combination vaccines against three infectious diseases in humans: diphtheria, pertussis (whooping cough), and tetanus. The vaccine components include diphtheria and tetanus toxoids and killed whole cells of the bacterium that causes pertussis.

2. Production of Modern Vaccines

a) Inactivated Vaccines: Inactivated vaccines are produced by growing the micro-organisms in culture media, then inactivating it with heat and/or chemicals (usually formalin). In the case of fractional vaccines, the organism is further treated to separate fractional units (for example the polysaccharide capsule of pneumococcus.) These inactivated vaccines are very safe as they are not alive and cannot replicate.

b) Live Attenuated Vaccines: Live vaccines are derived from "wild," or disease-causing, viruses or bacteria by repeated sub-culturing for a long period of time. For example, the measles virus used as a vaccine today was isolated from a child with measles disease in 1954. Almost 10 years of serial sub-culturing in a tissue culture media the wild measles virus are transformed into attenuated vaccine virus. These live attenuated vaccines replicates (grow) in the vaccinated person but they usually do not cause disease on the other hand they stimulate an immune response and protect the person for future natural disease infection.

c) Toxoid and Subunit Vaccine: Toxoid vaccines are made from inactivated toxic compounds extracted from the disease causing micro-organism (tetanus and diphtheria). Toxoid vaccines are prepared by the formalin treatment of the toxin extracted from disease causing micro-organism. The subunit vaccine uses a fragment of an inactivated or attenuated micro-organism rather than injecting whole micro-organism. After immunization the human body elicits immune response against subunit vaccine. An example of the subunit vaccine is hepatitis B virus vaccine that is composed of only the surface proteins of the virus. Other examples are influenza virus vaccine and plague vaccine.

d) Conjugate Vaccine: The polysaccharide outer coats of several bacteria are found to be poorly immunogenic. By linking these outer coats to proteins (*e.g.*, toxins), the conjugate vaccine is prepared and when it is administered, the immune system recognizes the polysaccharide as if it were a protein antigen and immediately elicit immune response. The example of conjugate vaccine is the *Haemophilus influenzae* type B vaccine.

e) Heterologous Vaccine: Heterologous vaccines use pathogens of other animals that either do not cause disease or cause mild disease in the human being. The classic example is the smallpox vaccine. In this case cowpox virus (causing pox in cattle) is administered in humans to protect against smallpox. This is also known as "Jennerian vaccines". Another example, Heterologous vaccine is the BCG vaccines which are made from *Mycobacterium bovis* to protect against tuberculosis.

f) Recombinant Vaccines and RNA Vaccine: The antigens or antigenic epitopes can be prepared by employing genetic engineering technology. These preparations are known as recombinant vaccines. In these techniques modern Hepatitis B and human papilloma virus (HPV) vaccines are prepared which are very much effective and safe. In these cases vaccine are prepared by insertion of a segment of the respective viral gene (DNA) into the gene of a yeast cell or virus. The modified yeast cell produces pure hepatitis B surface antigen or HPV capsid protein when it grows. Another example of recombinant vaccines is typhoid vaccine (Ty21a) against *Salmonella typhi* bacteria. An RNA vaccine or mRNA (messenger RNA) vaccine is a novel type of vaccine which is composed of the nucleic acid RNA, packaged within a vector such as lipid nanoparticles. When administered, mRNA vaccine transfects into immunity cells and triggers the cells to build the foreign protein that would normally be produced by a pathogen (such as a virus). These protein molecules stimulate an adaptive immune response which helps the body how to identify and destroy the corresponding pathogen. The mRNA vaccines have effective and desirable immunological properties and are very safe. As mRNA vaccine is capable of producing immunogenic proteins in situ the vaccine provides a balanced immune response comprising both cellular and humoral immunity. Among the COVID-19 vaccines there are a number of RNA vaccines under development to combat the Cocid-19 pandemic and some have received emergency use authorization.

Common Vaccines Used for Universal Immunization and Adverse Reactions of Vaccination

The common pediatric vaccines used are Polio, Measles, mumps, rubella (MMR); Chickenpox (Varivax); Hepatitis B; diphtheria, tetanus, and whooping cough (pertussis) (DTaP); Rotavirus (infant gastroenteritis, RotaTeq); Invasive pneumococcal disease (Prevnar), The Adolescents and Adult vaccines are HPV (cervical cancer, Gardasil); Meningitis (Menactra); Influenza; Invasive pneumococcal disease; Herpes zoster (shingles, Zostavax).

Landscape of Novel Corona Virus Candidate Vaccine Development Worldwide

According to a report of WHO on 12th January 2021, 63 vaccine candidates are now in clinical development and 173 vaccine candidates are in pre-clinical development (Figure 1) worldwide. Among the 63 candidates in clinical phase (Table 1), the shares of the different types of vaccines are indexed in Figure 2. Authorized or approved vaccines worldwide for Covid-19 pandemic are indexed in Table 2.

Table 1: Vaccine candidates for Covid-19 in clinical phase (https://www.who.int/) as on 12th January, 2021

Types	Numbers
Protein Subunit	19
Viral Vector (Non-Replicating) - VVnr	10
DNA	8
Inactivated Virus	9
RNA	7
Viral Vector (Replicating) - VVr	4
Virus like particle	2
VVr + Antigen presenting cell	2
Live attinuated virus	1
VVnr + Antigen presenting cell	1
Total (In clinical phase)	63

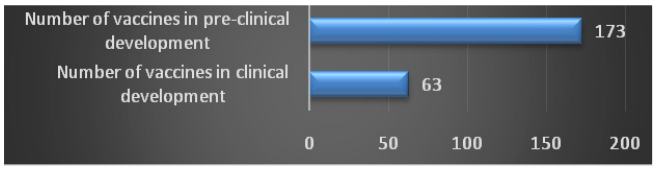

Figure 1: Summary of Covid-19 vaccine products in clinical and preclinical development (https://www.who.int/) - 12th January, 2021

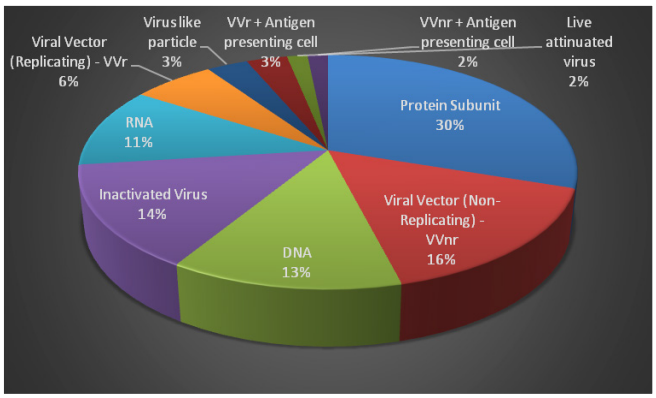

Figure 2: Vaccine candidates for Covid-19 in clinical phase (https://www.who.int/) - 12th January 2021

Covid Vaccine Drive in India

AIIMS Director Dr. Randeep Guleria (left side) and a sanitation worker from Delhi (right side) are became the first Indians to receive the Covid-19 vaccine on Saturday, January 16 in a move aimed at inspiring confidence among the public about the safety and efficacy of the vaccines being rollout out in the country (Figure 4).

Table 2: Authorized/ approved vaccines for Covid-19 (https://www.raps.org/) as on 15th January, 2021

Vaccine Name	Vaccine Type	Developers	Origin	Authorized/ Approval
Covaxin	Inactivated vaccine	Bharat Biotech, ICMR	India	India
Comirnaty (BNT162b2)	mRNA-based vaccine	Pfizer, BioNTech; Fosun Pharma	Multi-national	UK, Bahrain, Canada, Mexico, US, Singapore, Costa Rica, Ecuador, Jordan, Panama, Chile, Oman, Saudi Arabia, Argentina, Switzerland, Kuwait, EU, WHO (emergency use validation)
Moderna COVID 19 Vaccine (mRNA-1273)	mRNA-based vaccine	Moderna, BARDA, NIAID	USA	USA, Canada, EU, Israel, UK, France, Switzerland
CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac	China	China, Turkey
COVID-19 Vaccine AstraZeneca (AZD1222)	Adenovirus vaccine	BARDA, OWS	UK	UK, India, Argentina, Dominican Republic, El Salvador, Mexico, Morocco
Sputnik V	Non-replicating viral vector	Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	China, United Arab Emirates, Bahrain, Egypt
EpiVacCorona	Peptide vaccine	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology	Russia	Russia

Figure 3: Covid Vaccine Drive in India

Conclusion

The current COVID-19 outbreak is applying pressure on global manufacturer production capacities, supply availability and logistics. And it is putting at risk the continuation of immunization programmes in countries due to lockdowns and other measures to contain the spread of the virus, which also has an impact on supply. The international organizations as well as our country India, is in ongoing dialogue with governments, vaccine manufacturers, partners and freight forwarders to assess the risk to vaccine availability and accessibility and which mitigating measures can be undertaken.

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