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Vaccine Quality Control and Cancer Vaccines

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ABSTRACT

Vaccine refers to an agent which is produced from an antigen or pathogen by deactivating its mechanism of protein synthesis or denaturing or killing them which allows it to be introduced into the host in order to induce an immune reaction which provides protection on re-infection. The first inoculation of vaccine was done against smallpox in China and India about 2000 years ago. However, credit for the first successful inoculation is given to Edward Jenner, a British physician who in 1976, used matter from cowpox pustules to inoculate humans successfully against smallpox, which is caused by a similar virus. By the year 1900, there were 2 human virus vaccines, against smallpox and rabies and 3 bacterial vaccines against cholera, plague and typhoid. By 20th century there were several other vaccines that were developed against different diseases such as measles, diphtheria, tetanus and many other communicable diseases. As the vaccine production increased and it became readily available, many developed countries began routine vaccination drives for the children of their countries. Vaccine is crucial in an organism's life be it be human or a dog. Each year vaccines prevent 2-3 crore lives around the globe. If global vaccination drives get better an additional 1 to 1.5 crore people can be saved every year. Mostly the vaccines used in national immunization drives are effective and safe, but many a times different side effects can occur which includes minor problems such as soreness on injecting site and severe problems such as seizures etc. but these are seen in very few percentages of the vaccinated population. Accordingly, it is very essential to look upon the quality and effectiveness of the vaccines.In the past decades, there have been developed a range of vaccines that could help treat cancer also known as cancer vaccines or treatment vaccines which are given to persons suffering from cancer. They are given as a part of immunotherapy. These vaccines enhance the body's immune system to fight cancer and many other diseases and also preventing them from coming back.

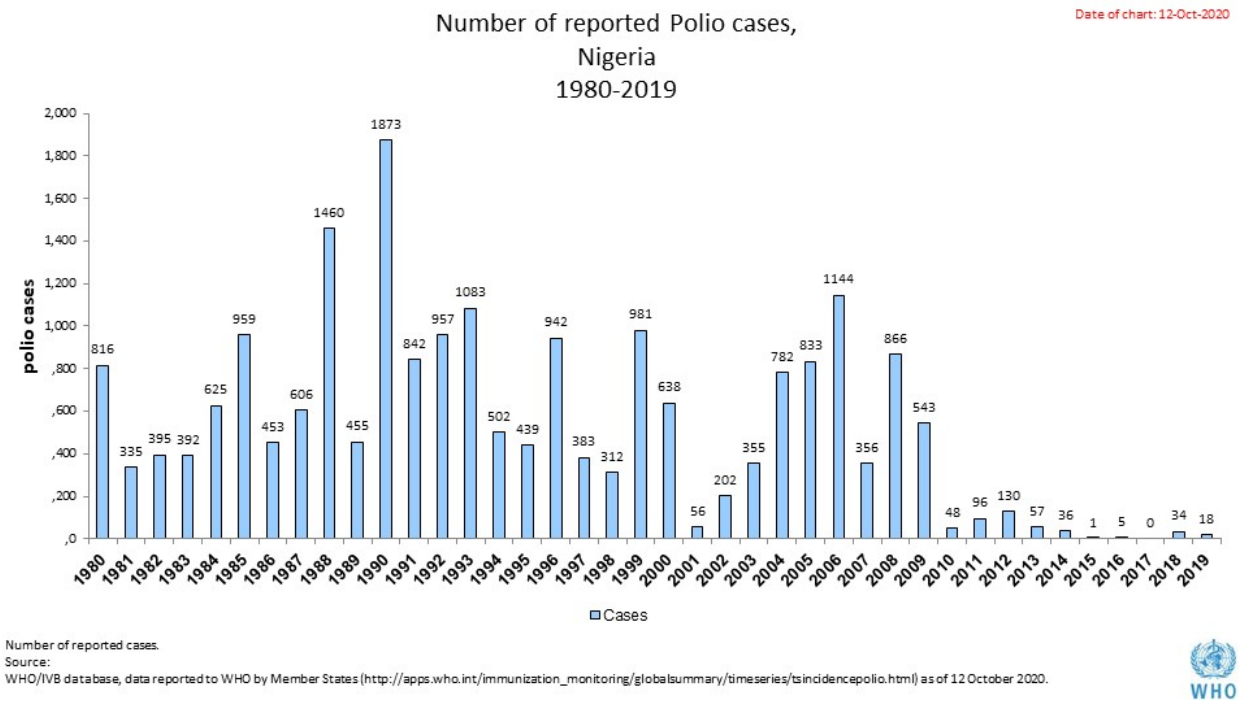
Introduction

The immune system of a body is its natural defense against foreign antigens. When an antigen enters the body, the immune system sends special cells such as killer T Cells which kills or fight the antigen. However, sometimes, the immune system can't naturally prevent a disease from potentially harming someone or even killing them. However, the immune response can be enhanced by injecting a vaccine. Vaccines are mostly given through mouth or in form of nasal sprays and by injecting through needles. Before vaccines, numerable children around the world suffered from different fatal diseases such as measles, smallpox, diphtheria etc. If a person got simple scratch and if it got infected by any of these diseases, it could lead to death of the person. After the increasing awareness about vaccines, smallpox is eradicated from the world and polio is also about to come to an end.

When a vaccine is injected in our body, it prepares antibodies against the weakened antigen and protects us when and if the body comes in contact with the real virus or bacteria. When any unknown antigen enters our body, the immune system takes a few days to prepare antibodies against it. After which it may make many copies of itself. Thus, getting vaccinated gives better protection against the disease. When a foreign antigen enters the body, the immune system generates innate immune response which is the primary response elicited upon the first encounter with the antigen. This response is usually slow hence the body will show symptoms of the disease before the immune system generates a reaction to kill the antigen, and therefore the body develops an adaptive immune response also known as the secondary response through specialized immune cells which kill the antigen and forms a long lasting memory. Thus, vaccination introduction of vaccine into the body will have an identical kind of immune response which is the secondary response and helps to overcome the slow initial response but enables the body to acquire immunity Vaccination is the safest way to gain immunity against a fatal bacteria or viruses that the body could encounter.

Vaccines are proven to provide a higher degree of protection against the disease. However, if vaccines were still not available then the survival of an organism against the fatal disease would be based on their body's immune system.

Below given is a table enlisting the data about Polio in Nigeria that led to many deaths and how vaccines, over the last few years have helped to combat this disease thereby reducing the death rates.



As new and effective vaccines were being developed, it became a global objective to eradicate Polio. The WHO, in 1998, proposed a worldwide poliomyelitis eradication to its member states which involves several developed and developing countries. A strategy, The Global Polio Eradication Initiative (GPEI) was established which involved activities required for polio eradication, certification for regions, OPV (oral polio vaccine) taxation and post-OPV phase. Initially, the plan aimed at maintaining a high vaccination coverage of > 80% among children, mopping up vaccination and establishing effective PV (polio virus) infection surveillance system. The presence of vulnerable subgroups with time gap in immunization favors the establishment of wild PV strains in an immunized populace. The OPV strains became the major instrument for the wild-type PV eradication program because it induces both a systemic and mucosal immune response. Various countries switched their objective of vaccination against polio by using Inactivated Polio Vaccine (IPV) instead of OPV[1.] The advantage of using IPV is that it has no side effects. Major disadvantages of IPV are its cost, its inability to produce optimal intestinal immunity and the intramuscular administration. In 2011, 23 years after the decision of global eradication of polio by the WHO, the wild PV (type 1 and 3) is still endemic in only four countries: Afghanistan, India, Nigeria and Pakistan. The type 2 wild PV strain has been eradicated globally since 1999, while a kind 2 circulating vaccine-derived PV (cVDPV) has persisted in northern Nigeria since 2006[2.]

Types of vaccines

There are various types of vaccines. They are designed in such a way that they boost our immune system and prevent life-threatening and severe diseases. There are four types of vaccines currently available[3]

I) **Live attenuated vaccines:** Live attenuated vaccines were first developed in 1950s. They contain a replica of the virus, with weakened pathogenicity so that they cannot cause disease but can induce an immune response, hence it is referred as attenuated. The most common method of their production is passing them through a series of cell cultures or animal embryos such as chick embryos. The virus is often attenuated or grown in cells in which they are not supposed to grow, thus, after each passing generation the virus adapts to the new surrounding cells and replicates itself rapidly and loses its ability to replicate in human cells. This method is also helpful in selecting mutants that can grow under artificial cell cultures thus they won't replicate in natural hosts. These vaccines provide lifelong immunity after 1 or 2 doses as it resembles the real disease-causing virus. To maintain their potency, live attenuated vaccines require freezing temperatures and protection from direct light. Some examples of live attenuated vaccines are Measles/Mumps/Rubella (MMR) and Influenza Vaccine Live, Polio (Sabin vaccine), Tuberculosis, Yellow fever.

II) **Inactivated vaccines:** These vaccines are produced by the use of heat and chemical treatment which can destroy the pathogen's ability to replicate but also keeps it intact so that the immune system can recognize it. Inactivation of pathogen using heat can lead to severe denaturation of proteins thus it often leads to unsatisfying results. However, chemical treatment using formaldehyde or formalin for inactivation is a quite successful approach. Salk poliomyelitis vaccine which involves inactivation of formaldehyde. As these vaccines have inactivated or killed pathogens, it prevents the pathogens to turning them into a severe form capable of causing the disease. These vaccines, unlike live attenuated vaccines provide short term immunity and often requires booster doses. These vaccines are successfully used to prevent diseases like hepatitis-B, Polio and rabies.

III) **Subunit, recombinant and conjugate vaccines:** These are vaccines that contains man made substances which completely resembles the virus or bacteria, thus, recognized by the immune cells. These vaccines use very specific parts of the pathogen which results in a vigorous immune response. They are also known as biosynthetic vaccines. Hepatitis-B vaccine is one of the biosynthetic vaccines. The advantage of these vaccines is that they can be injected into hosts with weak immune systems and long-term health problems. Subunit vaccines use a part of the pathogen such as isolating a certain protein and presenting it as an antigen. Some influenza vaccines and acellular pertussis vaccines are some examples of subunit vaccines. Recombinant vaccines make use of attenuated viruses or bacteria. A gene encoding a major antigen of a certain pathogen can be introduced into an attenuated virus or bacterium to produce vaccines. The attenuated organism acts as a vector that replicates and expresses the gene in the host. Conjugate vaccines are quite similar to recombinant vaccines. They are produced by combining 2 different components. These components are fragments of bacterial coats These fragments are then linked to a carrier protein. The carrier protein causes the immune response and the not the bacterial fragments.

IV) **Toxoid vaccines:** These vaccines are prepared using a mixture of toxins which is treated with formalin, a solution of formaldehyde and sterilized water. The toxins used are sufficiently attenuated and are capable of inducing a humoral immune response. These toxins produce identical symptoms as that of the original disease. For example, diphtheria and tetanus vaccines can be prepared by extracting and purifying bacterial toxins and then inactivating them with formaldehyde to form a toxoid.

Preservatives and stabilizers

A preservative is any compound that increases the shelf life of a product, here, vaccine. These compounds help prevent or kill any microbial growth. They are mostly used in multi dose vial vaccines which involves injected needles in a single vial more than one time. Multiple pricking can lead to contamination; thus, preservatives help to prevent contamination by killing unwanted microbes. Preservatives may be added during the manufacturing process and helps in preventing the microbial growth but as the advancement in manufacturing processes occurred the need for adding preservatives during this step decreased significantly. Thimerosal is the widely used preservative in vaccines. It is a vaccine additive, added to some vaccines to prevent germs (like bacteria and fungi) from growing in them. It is a bacteriostatic and fungistatic organomercurial compound containing 50% mercury by weight and is used as a preservative since 1930. The antimicrobial properties of thimerosal ensures the safe use of vaccines in multi-dose vials, and the ability to package certain vaccines, such as influenza. Thimerosal is metabolized to thiosalicylate and ethylmercury. At concentrations found in vaccines, thimerosal meets the requirements for a preservative, that is, it kills the specified challenge organisms and is able to prevent the growth of the target fungi. Thimerosal in concentrations of 0.001% (1 part in 100,000) to 0.01% (1 part in 10,000) is found to be effective in killing and preventing growth of a broad spectrum of pathogens. A vaccine containing 0.01% thimerosal as an additive contains 50 micrograms of thimerosal for every 0.5 ml dose or roughly 25 micrograms of mercury for each 0.5 ml dose.

Most people don't have any side effects from thimerosal, but some people will have mild side effects like redness and swelling at the site where the shot was given, which will only last 1 to 2 days. It is very rare that one will have allergic reaction to thimerosal. Though a safe and effective concentration of thimerosal has been already determined for use in vaccines, increased exposure to thimerosal in first 3 years of immunization is linked to prevalence of autism in affected individuals. An increased risk of various neurodevelopmental disorders such as autism and ASD, was observed after ethylmercury exposure. However, various other studies by claiming an association between thimerosal and autism have been rejected on the basis of flawed study designs (The National Academies Press; 2004. 214 p).[4] Despite several years of reassuring studies, the thimerosal controversy continues.

The table given below provide some information about the amount of thimerosal that is approved by the FDA for addition in some influenza vaccines.

Vaccine	Tradename (Manufacturer)	Thimerosal Status Concentration**(Mercury)
Trivalent Influenza Vaccine	Afluria (multi-dose presentation) Seqirus Pty Ltd	0.01% (24.5 mcg/0.5 mL dose)
	Afluria (single-dose presentation) Seqirus Pty Ltd	None
	Fluad (single-dose presentation) Seqirus Vaccines Ltd	None
	Flublok (single dose presentation) Protein Sciences Corporation	None
	Fluvirin (multi-dose presentation) Seqirus Vaccines Ltd	0.01% (25 mcg/0.5 mL dose)
	Fluvirin (single-dose presentation) Seqirus Vaccines Ltd	Trace (<1 mcg/0.5mL dose) [1]
	Fluzone High Dose (single-dose presentation) Sanofi Pasteur Inc.	None
Quadrivalent Influenza Vaccine	Afluria Quadrivalent (multi-dose presentation) Seqirus Pty Ltd	0.01% (24.5 mcg/0.5 mL dose)
	Afluria Quadrivalent (single-dose presentation) Seqirus Pty Ltd	None
	Fluarix Quadrivalent (single-dose presentation) GlaxoSmithKline Biologicals	None
	Flublok Quadrivalent (single-dose presentation) Protein Sciences Corporation	None

Formaldehyde (methanal) and 2-phenoxyethanol are some other preservatives that have been found to be very successful in preserving vaccines. Formaldehyde preservation has been a concern due its safety issue. Higher concentrations of formaldehyde can lead to destruction in DNA base pairs and cause cancerous mutations in cells. Although formaldehyde is diluted during its manufacturing, residual quantities of formaldehyde can still be found in several current vaccines. Formaldehyde is one oof the major mutagens responsible for nasal cancer but the concentrations of formaldehyde found in vaccines is not sufficient enough to cause cancer (Mitkus et al., 2013)[5.] The average concentration of formaldehyde to which a newborn could be exposed to in the first two years of life may be as high as 0.7 – 0.8 mg but this concentration is still found to be safe as formaldehyde is essential in human metabolic activities and is essential for the synthesis of amino acids and DNA. Hence, human beings have traceable amounts of formaldehyde already present in them. The average amount of formaldehyde found in a healthy newborn is 1.1 mg which is 1500 times more than the concentration of formaldehyde that any child would be exposed to in a single vaccine. Formaldehyde is successfully used in preserving vaccines such as:

Hepatitis A (Havrix, Vaqta)

Quantity per dose:

- Vaqta: 0.0004 mg (pediatric), 0.0008 mg (adult)

Hepatitis A - Hepatitis B (Twinrix)

Quantity per dose: ≤ 0.1 mg

Polio (IPOL®)

Quantity per dose: ≤ 0.02%

Japanese encephalitis vaccine (IXIARO)

Quantity per dose: < 200 ppm

2-Phenoxyethanol (2-PE) is a chemical substance widely used as a preservative in several vaccines. 2- Phenoxyethanol is a phenol containing compound, which has the ability to inhibit phagocytosis, which means it is toxic to all cells. Phenol present in 2- Phenoxyethanol is the major constituent which can disable body's immune response. 2-PE is a stable compound but is incompatible with acid chlorides and is a combustible

substance. It can cause systemic poisoning, kidney damage, convulsions, headache, shock, weakness, cardiac failure, kidney failure, or death.2-Pheoxyethelyneis effective against a broad spectrum of microorganisms, particularly *Pseudomonas aeuginosa*[6]. Ethylene oxide is also a constituent of 2-Phenoxyethanol which is an irritant to human skin and can lead to burns, blisters and dermatitis. 2-PE is also used in perfumes as a fixative, a topical antiseptic a bactericide and as insect repellent,

Quality Control of Vaccines

Quality control methods are significantly very important in producing a safe and effective vaccine. The first quality control test dates back to the 19th century which was the multi dilution test design assay with the use of reference preparation which depended upon ED_{50} was introduced between 1930 to 1950s. The following decades saw more and more quality control tests coming into existence for several vaccines. Potency assay is the most common and widely used quality control method which depends on one or several factors that are either directly or indirectly linked to the efficacy of the vaccine.

The common types of potency tests adopted by manufacturers involves enzyme linked immunosorbent assays (ELISAs), in-vitro titration of live organisms and in-vivo methods including immunization of small laboratory animals (for e.g.- rats and mice) which is then followed by challenge with a toxin/bacteria/virus or titration of immune sera to measure the antibody response. In-vitro potency assay is commonly used in live attenuated vaccines however, it is rarely used in inactivated vaccines. As the vaccines are produced in large batches, strict monitoring should be adopted by manufacturers to prevent any variations in different batches. The use of alternative methods as quality control methods has increased over several years. They are based on the 3R's - Replacement, Reduction, and Refinement of animal testing. Consequently, the manufacturers now encourage on following the 3R's. The potency test is fundamentally utilized for quality control assessment of vaccines dependent on an immunization challenge strategy in research-oriented animals. Several methods have been made to alter these animal models to improvise on its statistical significance. The quality control assessments of vaccines require high recurrence of tests with huge number of research-oriented animals. These potency tests are multi dose models that incorporate a test method with virulent microbes. Subsequently, animals suffer significant agony and pain during the testing time.[7]

Usually, using lab animals can be scientifically supported if the benefits for public or veterinary wellbeing are more in comparison to trouble to lab animals. Disregarding that, there is an overwhelming feeling in people that how the research-oriented lab animals can be replaced, decreased or refined of their utilization in biomedical examination and testing.

Government of their respective countries have set up several bodies that are responsible for reviewing of licensing applications, monitoring the performance of product and lot release. Accordingly, details of processes by which the vaccine is delivered and tested incorporating the in-process and eventual outcome testing are the essential objective of the producer[8]. However, achieving this objective relies generally upon the quality control tests led at different critical steps during the production process and utilization of Good Manufacturing Practices[9]

Traditional and conventional approaches and steps of quality control were based on the uniqueness of each individual batch of vaccine. Consistency in the of vaccine production implies to that each batch of the vaccine is of a similar quality and is within similar determinations of the batch which has been demonstrated to be safe and effective in human trials or in animal trials. However, a change in concentration away from dependence on eventual outcome testing will require the improvement of a control scheme for every item. Therefore, the development of alternative methods depending upon the principles based on 3Rs for potency testing of vaccines to establish consistency in different batches is crucial and of prime importance before the product moves to markets.

3R's in vaccine quality control

The principle of 3R's was first described by William Russel and Rex Burch in 1959[10]. The principle of 3R's describes:

- **Replacement –** It means implementing methods which can replace or avoid the use of animals.
- **Reduction –** It means adopting an alternative test design in order to minimize the number of animals per experiment.
- **Refinement –** It means moving to alternative methods that reduces suffering and improves animal welfare.

The principle of 3R's is driven by 4 main drivers which are:

- **1st driver, science:** The scientific knowledge as well as technologies have evolved over the past decades and the in vitro technologies are now highly advanced and relevant than animal in vivo assay to evaluate the consistency of a vaccine.
- **2nd driver, animal welfare:** Animals are also living beings, yet large number of animals is used for testing vaccines and a large proportion of those animals are exposed to pain and agony, and there is a growing concern regarding the use of animals for laboratory purposes.
- **3rd driver, regulatory context:** 3R's became legal requirement in Europe; it started with EMA guidance in 1997[11] which was followed by a first directive in 2001 for veterinary as well as medicinal products[12].
- **4th driver, economics:** *In vivo* tests are human resource demanding and time consuming, also, they are expensive due to the animals themselves, and have long cycle times ranging from several weeks to months.

In vitro techniques, currently, are progressively being utilized in vaccine R&D and preclinical testing. Subsequently, interaction of antigenic structures with immune system cells can now be analyzed in vitro using cultures of, for example- Lymphocytes. However, the immune reaction is a profoundly complex process, including different cell types, like T and B cells, antigen processing cells and accessory cells, that adjust and quantify the reaction by producing cytokines[13]. As of now, it has not had the option to mimic this exceptionally complex cycle within a test tube. In spite of the fact that components of the immune responses can be studied in vitro, the verification of the final result still requires the utilization of a lab animal.

In viral vaccine development, animals are totally replaced by virus proliferation in continuous cell lines. Not for moral reasons but rather primarily to work on the safety as well as efficacy of the vaccines. These days, there are a couple of viral vaccines that actually need the utilization of animals for its production. For example, the Japanese encephalitis vaccine which is propagated in primary hamster kidney cells. The below given table shows the past and current available technologies used to produce several viral vaccines.

Viral Vaccine	Past production technology	Current production technology
Poliomyelitis	Primary of subcultured monkey kidney cells	Continuous cell lines (e.g. VERO cells)
Rabies	Baby rabbits, mice	Continuous cell lines
Influenza	Embryonated chicken eggs	Continuous cell lines
Smallpox	Calf skin	Continuous cell lines

Barriers to 3Rs

There are 2 major barriers for the 3R's principle, scientific barriers and regulatory barriers. The scientific obstacles are:

- The fact that in vivo measures are not approved according to ICH requirements[14].
- The inherent variability of *in vivo* assays

The regulatory hurdles are:

- the lack of harmonization of regulatory requirements, worldwide
- the complexity of regulatory changes that discourage and slow development and implementation of alternatives to animal testing; this is one of the main reasons why industry has not been able to fully implement alternative tests

Vaccine development and its quality control

Vaccine development and testing follows a standard arrangement of steps. The principal stages are exploratory in nature. Regulation and oversight increase as the vaccine clears its path through the former steps.

Exploratory Stage:

This stage includes essential lab research and often lasts for 2-4 years. researchers distinguish synthetic or natural antigens that may help prevent or treat an infection. These antigens could include virus like particles, weakened bacterial toxins or weakened viruses or bacteria.

Pre-Clinical Stage:

This stage involves animal testing and use of tissue culture for assessing the immunogenicity and safety of the vaccine. The animal used may include mice or monkeys. This stage gives an idea to the researchers about the immune responses produced by the vaccine, that can occur similarly in humans. It may also suggest the safe dosage for humans. This stage also involves performing challenge tests in which the vaccinated animal is infected with the target pathogen.

Clinical Studies with Human Subjects:

1. **Phase 1 trials-** The first time a vaccine is clinically tested, it usually involves a small group of healthy individuals. But in clinical trials of medicines treating terminal illnesses like cancer, individuals may be selected who are suffering from such disease. The objective of phase 1 trials is to examine and evaluate the immune response provoked in the host and to test whether the prepared vaccine is efficient and safe or not. The researchers may also adopt challenge method in this phase. The volunteers in this phase are carefully monitored under controlled conditions.
2. **Phase 2 trials-** This phase involves a larger group of individuals involving volunteers from high-risk groups. The trial is randomized and also includes a placebo group. This phase can help to understand the dosage, immunogenicity, efficacy, safety and the mode of immunization in a better way.
3. **Phase 3 trials-** This phase involves lakhs of participants from different medical backgrounds, age, gender etc. These trials are random and double blind. As several side effects may not surface in small groups, they become prominent in this phase which is helpful to determine the safety of the vaccine candidate. This phase is also significant in determining the efficacy of the developed vaccine.

Approval and Licensure:

After passing phase 3 trials successfully, the vaccine manufacturer then submits the application for approval of vaccine to the licensing authority – Drug controller general of India (DCGI). Then the DCGI inspects the factory where the vaccine will be manufactured and approve the labeling of the vaccine. After licensure and approval, the DCGI may conduct its own tests to ensure the safety of manufactured vaccine. After this, the production of vaccine is still under strict eye of the concerned designated authorities.

Cancer vaccines

Cancer vaccines exists for both, treating cancer as well as preventing it from coming back. Some cancers can be caused due to viruses such as HPV. Vaccines can help preventing infection of HPV in humans along with cancer caused by the virus. Most of the cervical, anal and penile cancer is occurred because of HPV thus, vaccinating children and adults against HPV can be found to be helpful in preventing these cancers. Also, people suffering from some chronic illnesses like hepatitis B virus are more susceptible of developing liver cancer. Getting vaccinated against HBV can be helpful in preventing liver cancer in such individuals.

Vaccines which treat existing cancers are known as therapeutic vaccines. These vaccines are used as a part of immunotherapy. These vaccines provoke the immune response of the body to fight against the cancer. These vaccines can:

- Destroy cancerous cells.
- Prevent any further differentiation of the tumor cells.
- Stop a tumor from spreading further in the body.

Working of cancer vaccines

Our immune system finds some antigens present on the cellular surface to be harmful for our body. The immune response tries to get rid of these harmful antigens which forms a memory in the body that helps to fight against the same disease in future. The therapeutic vaccines help our immune system to efficiently identify and the destroy antigens. Tumor cells have cancer specific antigens on their surface which, normal cells don't have. These vaccines have cancer specific antigen molecules in them which, when given to a person helps their immune system to identify, destroy and eliminate those cells having these antigens on their surface.

Some cancer vaccines are customized which means they are made for a specific cancer for a particular individual. These vaccines are produced on the basis of cancer found in that person and by taking sample of the tumor cells. Other disease vaccines are not customized and hence does not focus on certain malignancy antigens that are not specific to a particular individual. Radio-specialists give these vaccines to individuals whose tumors have those antigens on the surface of the tumor cells.

Almost every cancer vaccine is administered only after successful clinical trials. In 2010, the FDA approved sipuleucel –T (Provenge) for people suffering from with metastatic prostate cancer which is prostate cancer that has spread. Sipuleucel-T is administered to each individual through a set of steps:

- WBCs are removed from the person's blood plasma. They help our body to fight infection.
- These cells are manipulated in a laboratory so as to target specific malignant cells.
- These manipulated cells are then administered intravenously.

Another therapeutic vaccine Bacillus Calmette-Guérin (BCG) which consists weakened bacteria that activates immune system to treat early-stage bladder cancer.

T-VEC (Talimogenelaherparepvec) is a therapeutic vaccine approved to treat last stage melanoma cancer. It is produced from herpes virus that has been manipulated in lab to produce cytokines. The cytokines provoke the immune system and causes some flu-like symptoms for a very short period of time.

Cancer vaccines under clinical trials

- **Cancer VAX:** It is a polyvalent melanoma vaccine being used along with surgical treatments to treat stage 3 melanoma cancer. In order to enhance the immunogenicity, it is given in combination to BCG.
- **Onyvax:** It is a monoclonal antibody 105AD7 anti-idiotype therapeutic vaccine used for treating advanced colorectal adenocarcinoma. The vaccine is administered with BCG with alum adjuvant.

Cancer vaccines come with some potential side effects which include skin reaction at the injection site or moderate flu-like symptoms, nausea etc.[15]

Conclusion

Vaccines have been proven to save millions of lives since decades now. Safe administration of vaccines can help a person prevent terminal

illnesses such as cancers, polio etc. By advancement in technology, vaccine manufacturing has got more efficacious. Quality control checks are now done at a much faster than before. The use of preservatives such as thimerosal has also reduced because the production as well as the need of multi dose vials has been replaced by single shot vaccines. Authentic license and approval by respective authorities for the vaccines have helped several countries raise their economies such as India, which is one of the largest producers of vaccines including vaccines for COVID-19. Vaccines should only be approved when it has passed all the necessary tests and came out to be safe as well as effective against the disease. The major challenge in developing vaccines is the ever-changing genome of the virus due to mutations.

The immunization advancement for Cancer is an excellent methodology of analysts to battle the most fearful illness all throughout the planet. Future advancement and improvement in this space definitely give the humanity wonderful weapons to battle with a wide range of malignant growth.

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