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A Review Article on Vaccine Delivery System

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ABSTRACT :
Immunization is a cornerstone of public health policy and is demonstrably highly cost-effective when used to protect child health.Until the 20th century, infectious diseases were the leading cause of death and disability worldwide, and this is still the case in much of the developing world. Immunization has played a central role in radically reducing the incidence of many dangerous diseases, and some diseases have been wiped out entirely (e.g. smallpox). This article presents the World Health Organization's (WHO) recommendations on the use of various vaccines. Vaccines prevent an estimated two-three million deaths worldwide every year. But, a further 2 million lives could be saved annually with better global vaccine coverage. Vaccines prevent an estimated two – three million deaths worldwide every year. But, a further 2 million lives could be saved annually with better global vaccine coverage. The purpose of vaccination is to produce immunity. Vaccines contain the same germs that cause disease. (For example, measles vaccine contains measles virus.) But they have been either killed or weakened. A vaccine provides a conducted exposure to a pathogen, training and encourage the immune system so it can fight that disease quickly and effectively in future. The national Vaccine Injury Compensation Program covers routine vaccines for children (against a total of 16 diseases). Vaccines are safe and effective. Because vaccines are given to millions of wholesome people. Vaccines have one of the greatest impacts on public good health. The prevention of disease has had an enormous impact on commercial development by limiting the costs of curative care and saving billions of dollars in countries where diseases have been well controlled or eliminated.

KEYWORDS : Vaccine Delivery System, Nanotechnology, Severe acute respiratory syndrome coronavirus-2, Viral infectious diseases, Vaccine, Needle-free delivery, immunization, pathogen, vaccine injury compensation program.

I. INTRODUCTION :

Vaccines are the biological preparation that improves immunity to a particular disease. Vaccines are used to stimulate the body's immune response against diseases.Vaccines train your immune system to create antibodies. It is made from weakned or killed forms of the causative microbes or its toxin or one of its surface proteins.The recent outbreaks of various infectious diseases have emphasized the social need for the rapid development of vaccines. The continuous outbreaks of viruses such as severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), Ebola, and Zika have put the world in peril against infectious disease. In 2020, the unprecedently severe pandemic of coronavirus disease 2019 (COVID-19) greatly impacted social activities and the global economy.

- WHAT ARE VACCINES ???
  - A vaccine is a biological preparation that improves immunity to a particular disease.
  - A vaccine typically contains an agent that resembles a disease-causing microorganism and is often madefrom weakened or killed

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forms of the microbe, its toxins or one of its surface proteins.

- A vaccine contain agent that resemble a disease.
- The agent stimulate the body's immune system to recognize foreign agent, destroy it, and keep a record of it, so that the immune system can more easily recognize and destroy any ofthese microorganisms that it later encounters.
- Vaccines can be prophylactic (to prevent or ameliorate the effects of a future infection by any natural or wild pathogen), or therapeutic (vaccines against cancer).

➢ HISTORY OF VACCINES :

- The term VACCINE and VACCINATION are derived from aLatin word VARIOLAE VACCINAE.
- "The diary workers would never have the often fatal diseasesmallpox because they already have the cowpox.
- First vaccine was developed in 1878 for small pox by Edward Jenner. His innovations begun with successful use of cowpox material tocreate immunity against smallpox.
- The second generation of vaccines was introduced in 1 880s by Louis Pasteur who developed vaccines for chicken cholera and anthrax.
- Jenner took the pus from the hand of a milkmaid with cowpox, scratched it into the arm of an 8 year old boy and six weekslater inoculated (variolated) the boy with small pox, heobserved that boy did not catch smallpox.

➢ HOW VACCINES WORK ???

- Vaccines contain a component or weakened form of a bacteria or virus. The component or weakened form of bacteria or virus in the vaccine does not cause disease.
- Vaccines teach your body's defence (immune) system how to protect you against a specific type of bacteria or virus.
- Different vaccines protect against different types of bacteria or viruses.
- To ensure you have full and lasting protection, you may need to get more than one dose of some vaccines.

➢ COMPOSITION OF VACCINE :

Ingredients provide immunity,

l. Antigen :

Very small amount of weak or dead gems that can cause diseases. They help our immune system and learn how to fight against infections faster and more effectively.

Example: flu virus

2. Adjuvants :

Helps our immune system to respond strongly to vaccine. This increases immunity against the disease.

Example: Aluminum, paraffin oil, squalene, calcium phosphate hydroxide, IL-1, IL-2, IL-12.

Ingredients keep vaccines safe and long lasting

a) Preservatives: Protect the vaccine from outside bacterial or fungus.

Example

a) Phenol - Typhoid, Pneumococcal.
b) BenzthoniumCI-Anthrax
c) 2-phenoxy ethanol - Inactive Polio
d) Thimerosal - Influenza
e) Monosodium glutamate - acts as preservative and stabilizer

3. Stabilizers :

Stabilizer helps the active ingredients in vaccines to continue their work while vaccine is made, stored and moved. They keep the active ingredients from changing.

Example: sugar, gelatin

Ingredients used during production of vaccines.

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1. Cell culture material : To help the growth of vaccine antigen
Example: eggs
2. Inactivating ingredients (Germ killing) : To weaken or kill viruses, bacteria from growing in the vaccine.
Example:Formaldehyde
3. Antibiotics: It is used to help keep outside germs and bacteria from growing in the vaccine
Example: Neomycin

➢ TYPES OF VACCINES :

1. Whole organism vaccine :

Vaccine currently in use consists of inactivated (killed) or live but attenuated (avirulent) bacterial cells or viral particles.

A. Live attenuated vaccine :

They mimic an actual infection as the pathogen reproduces within host cell. The immunity is induced lifelong immunity is achieved without booster immunization. this long-term effectiveness occurs because attenuated viruses replicate in the body.
e.g. TB, BCG, yellow fever, rotavirus, measles

B. Iactivated killed vaccine :

Use microbes that have been killed by formalin or phenol. They are used against rabies, influenza, polio. They required booster dose.
E.g. whole-æell pertussis, inactivated poliovirus

2. Purified macromolecules as vaccine :

A. Toxoids :

It is defined as they modified toxins, detoxified by the use of moderate heat and chemical treatment so that their antigenic properties are retained. Toxoids are toxins whose toxicity has been removed.The toxin invades the bloodstream and is largely responsible for the symptoms of the disease. The toxin is used invaccine production and used as the antigen in the vaccine to elicit immunity. To increase the immune response, thetoxoid is absorbed to aluminumsalts, which serves as adjuvants.
e.g. tetanus toxoid, staphylococcus toxoid.

B.Conjugated vaccine :

They deal with the poor immune response of children to vaccines based on capsular polysaccharides.
e.g. Hemophilus influenza type B.

3. Multivalent subunit vaccine :

Microbes are producing desired antigenic action called as recombination vaccine.
e.g. hepatitis B, Hemophilus influenza type B, pneumonia

4. DNA vaccine :

Basics of DNA vaccine is first reported by Ulmer et al in 1993. The injection of DNA into animal does not generate an immune response but that DNA is expressed to yield a protein that can stimulate an immune response. They are composed of bacterial plasmid.
DNA is they introduced in to the tissue cells and that host responds to the antigenic materials the introduced DNA is lost from the recipient cells and antigen releases.
e.g. influenza and herpes, measles. HIV, Ebola etc.

5. Recombinant Vaccine :

The recombinant vaccine is developed through the DNA technology. These vaccines are produced by the insertion of genetic material which encoding the antigen that stimulates an immune response. Plasmid DNA is used as vaccine which is propagated in bacteria like E. coli and they get isolated and purified into the vaccine.
This method is used to prepare highly pure component vaccine (subunit vaccine). E.g. hepatitis B surface antigen from hepatitis B virus is isolated, sequenced, done by using yeast cell. First recombinant vaccine was developed in India by Shantha Biotechnic Pvt.Lld. Hyderabad in 1997. In recombinant vaccine genetic manipulation of the antigen itself is possible.
E.g. hepatitis

6. Miscellaneous vaccine :

A. Veterinary vaccine :

These are living or dead preparation of micro-organism used to stimulate active immunity in animals. Vaccine recommended on the basis of kind of exposure, diseases, stress, species and strain of animals. They are classified as killed, live and subunit vaccine.
e.g. anthrax vaccine, foot, Newcastle and mouth disease.

B. Peptide vaccine :

The first identification of peptide had vaccine potential was demonstrated in 1963 with a plant virus. Tobacco mosaic virus. (Ander 1963). In this study, a chemically isolated hexapeptide fragment from the virus coat proteins was coupled

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to bovine serum albumin and used to elicit rabbit antibodies which
neutralizes infection. This peptide vaccine is now widely used against rabies virus, polio virus, measle virus, influenza virus. Peptides are poor immunogens and this require carrier coupling to enhance immunogenicity. The free peptides are also effective when they are delivered in small, unilamellar liposomes. Peptide vaccines are based in vitro synthesized peptides of 20-30amino acids.

7. Viral vaccine :
Theseare suspension of viruses or preparation obtained from tissues or blood of animal or from cultures in fertile eggs, cells, tissue culture. They may be live, inactivated/ killed and may be freeze dried.

A) Poliomyelitis vaccine
B) Rabies vaccine
C) Small pox vaccine

➢ MECHANISM OF ACTION :

To initiate an adaptive immune response a number of signals are required by T Cells. Signals one is the vaccine derived, peptide antigen (Ag) bound to major histocompatibility class-Il (MHC) and class-L is displayed on surface of antigen presenting cells (APC's). signal two is also known as costimulation and together with signal one,induces immune response. Signal two involves cross linking of CD28 and other receptors on T cells by costimulatory molecules such as B7-1 (CD80), B7-2 (CD86) and other ligands are expressed by APC. signal 3 is provided by cytokines and is delivered from the APC to the T cell which determines differentiation into on effector cell. Both signal 2 and 3 are provided to T cell by activated cells (DC"s). Mature DC's are able to induce T cells clonal expansion and prime immune response.

➢ UPTAKE OF ANTIGENS :
Antigens generated by endogenous and exogenous antigenprocessing activate different effector functions.

- STAGES OF EXOGENOUS ANTIGEN UPTAKE :

UPTAKE
Access of native pathogens to intracellular pathways of degradation

DEGRADATION
Limited proteolysis of antigens to peptides

ANTIGEN-MHC COMPLEX FORMATION
Loading of peptides on MHC molecules

ANTIGEN PRESENTATION
Transport and expression of peptide-MHC complexes on the surfaces of cells for reorganization by T-Cells

- STAGES OF ENDOGENOUS ANTIGEN UPTAKE :

UPTAKE
Antigens/pathogens already present in the cells

DEGRADATION
Antigens synthesized in cytoplasm undergo limited proteolytic degradation in the cytoplasm

ANTIGEN-MHC COMPLEX FORMATION
Loading of peptide antigens onto MHC Class 1 Molecules is different to the loading on MHC Class-2 Molecules

PRESENTATION
Transport and expression of antigen-MHC Complex on the surface of cells for reorganization by T-cells

➢ EVALUATION TESTS FOR VACCINE :

1.Sterility Test :

Incubate the media for not less than 14 days at 30" to 37" in the test for detecting bacteria and at 20" to 25" in the test for detecting fungi. However, for live bacterial vaccines growth of the organism from which the vaccine was prepared is permitted.

2.Safety Test :

Inject at least 2 healthy, susceptible animals. The quantity to be injected in each animal is twice the appropriate vaccinating dose. Observe the animals for not less than 7 days. No animal exhibits an abnormal reaction.

3.Abnormal Toxicity :

Inject 0.5 ml subcutaneously into each of five mice and 2 mlintraperitoneally into each of two guinea pigs. If the vaccine being examined contains an adjuvant, inject 2 ml of the vaccine subcutaneously into each guinea pig. Observe the animals for 7 days. None of the animals shows significant local or systemic reaction. If one animal diesor shows signs of ill-health during the observation period repeat the test. None of the animals of the second groupdies or shows signs of

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ill health. This testmaybe omitted if a safety test is carried out on animals of the species forwhich the vaccine is intended.

4. Identification Test :

The identities of bacterial vaccines can be checked by precipitation and agglutination reactions. Inactivated viral vaccines are tested by observation of the specific antibody responses in vaccinated animals and live viral vaccinesby neutralization of their cytopathic effects by specific antisera.

5. Phenol Concentration :

Phenol is used as a preservative in different types of vaccines. Its concentration must not 0.5% w/v.

➢ UNIVERSAL IMMUNIZATION PROGRAMME (UIP) :

Experience with Smallpox Eradication Programme, it was experienced that immunization is the most powerful and cost-effective weapon for the prevention and control and even eradication of a disease. In 1974, WHO officially launched a global immunization programme, known_as Expanded Programme of Immunization (EPI) for the prevention and control of six killer diseases of children, namely; tuberculosis, diphtheria, pertussis, tetanus, poliomyelitis and meas|es,]all over the world. Expanded meant adding more disease controling antigens of vaccination schedules, extending coverage to all corners of a country and spreading services to reach the less privileged sectors of the society.The primary_healthcare concept as expressed in the|1978, AIma-Ata Declaration included immunization as one of the strategies for reaching the goal of "Health For All" by the year 2000. (The Government of India launched EPI in1978, with objective of reducing mortality and morbidity resulting from vaccine-preventable diseases of childhood and to achieve self-sufficiency in the production of vaccines.

- Significant Achievements have been made in India :

At the beginning of the programme, vaccine coverage ranged between 29 per cent for BCG and 41 per cent for DPT in 1985-1986. By the end of 2014, coverage levels had gone up significantly to about:

- 87 per cent for tetanus toxoid for pregnant women.
- About 91 per cent for BCG. tor neo nart
- 83 per cent for DPT three doses. ter chidren
- 83 per cent for measles.por pids
- 82 per cent for OPV three doses.or childrer
- 70 per cent for HepB3.
- 20 percent for Hib3.

Government of India has planned the State Programme Implementation Plan (PIP)part C to strengthen routine immunization,

It consists of:

- Support for alternate, vaccine delivery from PHC to sub-centre and outreach sessions.
- Arranging retired manpower to carry out immunization activities in urban slums and underserved areas, where services are deficient.
- Mobility support for district immunization officer as per state plan for monitoring and supportive supervision.
- Every six month, a review meeting at the state level with the districts.
- Training of ANM, cold chain handlers, mid-level managers, refrigerator mechanics etc.
- Support with ASHA, women self-help groups etc. for the mobilization of children to immunization session sites.
- Printing of immunization cards, monitoring sheet, cold chain cart, vaccine inventory charts, etc.

In addition, central government is supporting in supplies of auto- -disposable syringes, downsizing the BCG vial from 20 doses to 10 doses to ensure and that BCG is available in all immunization session sites, strengthening and maintenance of the cold chain system in the states and supply of vaccines and vaccine van.

- OBJECTIVES :
- To rapidly increase immunization coverage.
- To improve the quality of services.
- To establish reliable cold chain system to the health facility level.
- To introduce a district-wise system for monitoring of performance.
- To achieve self-sufficiencyin vaccine production.

UIP was given the status of a one of the five 'National. Technology Missions' In1986.Subsequently in 1992, UIP became a part of Child Survival and Safe Motherhood (CSSM) programme and then of Reproductive and Child Health (RCH) programme in 1997. A specific

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Immunization Strengthening Project (SP) was designed to run from 2000-2003, whichincluded three main components(polio eradication, strenthening routine immunization and stratergic framework for development).

- Guideline Principles of UIP :

The services provided through the UIP shall be guided by the following principles.

1. **Universal Immunization Coverage:** Sustaining demand and ensuring that all pregnant mothers, children and adolescents are immunized as per national schedule in line with the principles of universal health coverage.

2. Equitable Access: Ensuring that, the immunizations services reach outto the underserved, needy and most vulnerable populations while addressing regional inequalities across states.

3. High Quality Services and Innovation: Maintaining highest possible quality in vaccine procurement, storage, distribution and delivery services in an innovative and safe manner.

4. Sustainability and Partnerships: Committing resources financial, human and technical, that sustain immunization benefits to the people at all times and promoting partnerships across different sectors and organizations build synergies and expand the overall coverage of the programme.

5. Governance : Decentralized planning through a bottom uo approach to improve operational efficiency.

6. Management Excellence and Accountability : Implementation, oversight and accountability of interventions that optimize efficient use of resources.

- Key Roles of UIP :
  - Routine immunization
  - Campaigns (polio, measles and japanese encaphalitis)
  - Monitoring adverse events following immunization ADR
  - Vaccine and cold storage logistics.
  - Strategic communication
  - Immunization trainings

- Vaccines under UIP - Under UIP :

Following vaccines are provided:
1. BCG (Bacillus Calmette Guerin)
2. DPT (Diphtheria, Pertussis and Tetanus Toxoid)
3. OPV (Oral Polio Vaccine)
4. Measles
5. Hepatitis B
6. TT (Tetanus Toxoid)
7. JE vaccination (in selected high disease burden districts)
8. Hib containing Pentavalent vaccine (DPT + Hep B + Hib) (In selected States).

➢ PULSE POLIO IMMUNIZATION PROGRAMME :

Pulse Polio Immunization Programme was launched in the country in the year 1995.

- In this programme, children under five years of age are given additional oral polio drops in December and January every year on fixed days.
- From 1999-2000, house to house vaccination of missed children was also introduced.
- The NIDs rounds cover approximately 172 million children and SNIDs rounds cover that 40-80 million children. In addition, large scale multi-district mop-ups have been conducted.
- As result, only one case of polio was reported in. 2011 in the month of January conducted.
- As on 25th Feb 2012, India was removed from the list of polio endemic countries and on 27th March 2014, India was certified as polio-free country.

- Introduction to Vaccines :

1. Introduction of Hepatitis-B Vaccine:

- In 2010-2011, Government of India universalized hepatitis vaccination to all States/UTs in the country.
- Monovalent hepatitis B vaccine jS given as intramuscular injection to the infant at 6^{th}, 10^{th} and 14^{th} week along with primary series of DPT and Polio vaccines.
- In addition, one dose of hepatitis B is given at birth for institutional deliveries within 24 hours of birth.

2. Introduction of Japanese Encephalitis (JE) Vaccine:

- The programme was introduced in 2006 to cover 104 endemic districts in phased manner, using SA 14-14-2 vaccine, imported from China.
- Single dose of JE vaccine was given to all children between 1 to 15 years of age through campaigns.
- The JE vaccine is being integrated into routine immunization in the districts where campaign had already been conducted to immunize the

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new cohort of children byvaccinating with two doses at 9-12 months and 16-24 months.

3. Introduction of Measles Vaccine Second Opportunity:

- In order to accelerate the reduction of measles related morbidity and mortality,second opportunity for measles vaccination is being implemented.
- The National Technical Advisory Group on immunization recommended introduction of 2nd dose of measles vaccine to children between months and 10 years of agethrough supplementary immunization activity (SIA) for states where evaluatedcoverage of first dose of measles vaccination is less than 80 per cent.
- In states, with coverage of measles vaccination more than 80 per cent, the second dose of vaccine was given through routine immunization at 16-24 months.

4. Introduction of Pentavalent Vaccine (DPT + Hep-B + Hib):

- India introduced pentavalent vaccine containing DPT, hepatitis B and Hib vaccines intwo states viz. Kerala and Tamil Nadu under routine immunization programme fromDecember 2011.
- DPT and hepatitis B vaccination require 6 injections to deliver primary doses.
- With the introduction of pentavalent vaccine, a new antigen, i.e., Hib has been added which protects against haemophilus influenzae type (associated with pneumoniaand meningitis) and the number of injections are reduced to 3.
- The vaccine has been expanded to 6 more states, i.e., Haryana, Jammu and Kashmir, Gujarat, Karnataka, Goa and Puducherry in 2012-2013. Now pentavalent vaccine is being given in all states.

- Mission Indradhanush:
- The Government of India launched Mission Indradhanush on 25th December 2014, to cover children who are either unvaccinated or partially vaccinated against sevenvaccine_preventable_diseases, ie, iphtheria, whooping cough, tetanus, polio, tuberculosis, measles, and hepatitis B.
- The goal is to vaccinate all under-fives by the year 2020.
- 201 high focus districts were covered in the first phase. Of these, 82 districts are fromNational Health ProgrammeUttar Pradesh, Bihar, Madhya Pradesh and Rajasthan. These 201 districts have nearly
- 50 per cent of all unvaccinated children of the country. The drive was through"Catch-up" campaign mode. The mission was technically supported by WHO UNICEF,Rotary International and other donor partners.
- Government of India introduced "Intensified Mission Indradhanush IMI" in selected districts and urban areas of the country to achieve the target of more than90% coverage.
- IMI focus on children up to 2 years of age and pregnant women who have missedout on routine immunization. However, vaccination on demand to children up to 5 years of age will be provided during IMI rounds.
- Intensified Mission Indradhanush Immunization drive will be spread over 7 workingdays starting from 7th of every month. These 7 days do not include; holidays, Sundaysand the routine immunization days planned in that week.

- New Vaccines:
- In April 2016, India introduced the use of fractional dose IPV (flPV) into the routineimmunization programme in eight states (Odisha andhra Pradesh, Telangana,Karnataka, Tamil Nadu, Puducherry and Maharashtra).
- Since March 2017 has been scaled up nationwide in all 36 states. Two fractionaldoses of IPV 0.1 ml, are being given intradermally at 6 and 14 weeks.
- On 5 February 2017, The Ministry of Health and Family Welfare launched MeaslesRubella (MR) vaccination campaign in the country, following the campaign, Measles-Rubella vaccine will be introduced in routine immunization, replacing the currently given two doses of measles vaccine, at 9-12 months and 16-24 months of age in five States/UTs (Karnataka, Tamil Nadu, Pondicherry, Goa and Lakshadweep).
- In March 2016, the Rotavirus vaccine was first introduced in four states namely;Haryana, Himachal Pradesh, Andhra Pradesh and Odisha. On 18 Feb 2017, Union Minister for Health and Family Welfare announced the expansion of the Rotavirus vaccine under its

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UIP in five additional states of Assam, Tripura, Madhya Pradesh, Rajasthan and Tamil Nadu.

On 13 May 2017, Union Minister for Health and Family Welfare, announced the introduction of Pneumococcal Conjugate Vaccine (PCV) in the UIP. Currently, the vaccine is being rolled out to approximately 21 lakhs children in Himachal Pradesh and parts of Biharand Uttar Pradesh in the first phase. This will be followed by introduction in Madhya Pradeshand Rajasthan next year and eventually be expanded to the country in phased manner.

- IMMUNIZATION CHART :
  - For Pregnant Women :

Vaccine	When to give	Dose	Route	Site
Td-1	Early pregnancy	0.5ml	Intramascular	Upper arm
Td-2	4weeks after 1st dose	0.5ml	Intramascular	Upper arm
Td Booster	If received 2 Td dosese in a pregnancy within the last 3 years.	0.5ml	Intramascular	Upper arm

  - For Infants :

Vaccine	When to give	Dose	Route	Site
BCG	At birth or as early as possible till 1 year of age	0.1ml	Intradermal	Left upper arm
Hepatitis B-Birth dose	At birth or as early as possible within 24 hours	0.5ml	Intramuscular	Antero-lateral side of midthigh
OPV-0	At birth or as early as possible within first 15 days	2drops	Oral	Oral
OPV-1,2,3	6weeks, 10 weeks & 14weeks	2drops	Oral	Oral
fIPV 1 & 2	6weeks & 14weeks	0.1ml	Intradermal	Upper arm
Pentavalent vaccine-1,2&3	6weeks, 10weeks & 14weeks	0.5ml	Intramuscular	Antero-lateral side of midthigh
RVV 1,2&3	At 6weeks, 10weeks & 14weeks	5drops	Oral	Oral
PCV 1,2&Booster	At 6weeks, 14weeks & 9months	0.5ml	Intramuscular	Antero-lateral side of midthigh

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MCV1/MR1	9completed months-to 12months.Give up to 5 years if not received at 9-12 months of age	0.5ml	Subcutaneous	Right upper arm
VitaminA	At 9completed months	1ml	Oral	Oral
Japanese Encephalitis	At 9completed months-12months	0.5ml	Subcutaneous	Left upper arm

- For Children and Adolescents :

Vaccine	When to give	Dose	Route	Site
DPT booster 1	16-24months	0.5ml	Intramuscular	Antero-lateral side of midthigh
MCV 2/MR 2	16-24months	0.5ml	Subcutaneuos	Right upper arm
OPV booster	16-24months	2drops	Oral	Oral
Japanese Encephalitis	16-24months	0.5ml	Subcutaneous	Left upper arm
Vitamin A	18months.Then, one dose every 6months up to age of 5years	2ml	Oral	Oral
DPT booster	5-6years	0.5ml	Intramuscular	Upper arm
Td	10 and 16 years	0.5ml	Intramuscular	Upper arm

➢ NATIONAL IMMUNIZATION SCHEDULE :

Year	Programme
1974	Expanded Programme of Immunization(EPI)
1985	Universal Immunization Programme(UIP)
1986	Technology Mission on Immunization
1992	Child Survival and Safe Motherhood(CSSM)
1997	Reproductive Child Health(RCH 1)
2005	National Rural Health Mission(NRHM)
2012	Year of Intensification of Routine Immunization
2013	Measles elimination and rubella/congenital rubella syndrome(CRS)control by 2020
2014	Polio Free Country

➢ SINGLE SHOT VACCINES :

- Single dose vaccine are given at a single contact point for preventing 4-6 diseases.
- To provide effective patient protection, many traditional vaccines requires multiple injections, which results in acostly and inconvenient regimen.
- These disadvantages have spurred the development ofsingle-shot vaccines that can provide protection againstinfection with only one injection.
- They will replace the need for a prime boost regimen, consequently eliminating the replaced visits to doctors.

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- The cost for single shot vaccines are higher as compared to normal vaccines.

Defination :

The single shot vaccine is a combination product of a Prime Component Antigen with an Microsphere Components andappropriate Adjuvants and an encapsulated antigen which will providethe booster immunizations by delayed release of the antigen.

- In order to increase the therapeutic activity of single shot vaccines vaccine adjuvant are used.
- Microsphere component that encapsulates antigen and provides the booster immunizations by delayed release of the antigen.
- The microsphere component uses OctoVAX microsphere technologv which is based on cross-linked modified dextran polymers.
- Dextrans are ideal polymers to form biocompatible hydrogels, Two major advantages of dextran microspheres as protein delivery systems, that the particles are prepared in the absence of organic solvents, and that degradation of the microspheres does not result ina pH drop.
- Several different dextrans have been developed for hydrogel formation. One of these dextran-based polymers is derivatized with hydroxy-ethyl methacrylate (Dex-HEMA).
- Which introduces hydrolytically sensitive carbonate ester groups that ensure biodegradation under physiological conditions.

➢ FORMULATION AND MANUFACTURING OF SINGLE SHOT VACCINE :-

VACCINE ADJUVANTS :-

Adjuvants are the substances added to vaccines to help them work better. Adding an adjuvant triggers the immune system to become more sensitive to the vaccine.

NEED FOR ADJUVANTS :-

- To increase the therapeutic efficiency.
- They form depot of antigen at the site of inoculation with slow release of antigens.
- It can improves the performance of vaccines by targeting the antigen to APC.

- Types of Adjuvants :-
- Geltypes :

eg. :-_aluminum hydroxide, calcium phosphate.

- Oil emulsion and emulsifier Particulate based type :

eg:- liposomes , biodegradable microspheres.

- Adverse effect of Single Shot Vaccine :
- Fever
- Pain around injection site
- Muscle aches

- Advantages of Single Shot Vaccine :
- Economic.
- With one Injection 4 to 6 Infections can be prevented.
- Patient compliance is Improved because, they would replace the need for a prime boost regimen, consequently eliminating the repeated visits to the doctor for mother and their children.
- Disadvantages of Single Shot Vaccine :
- The primary risk associated with vaccines, especially vaccines that utilize live organisms, so that the vaccine itself causes illness.
- The vaccine may behave as a super antigen and over stimulate the immune system.
- Some are not as effective as Multi-dose vaccines, because infection can occur due to micro organisms.

➢ MUCOSAL VACCINE DELIVERY SYSTEM :

- Mucosal surfaces ares is the major portal entry for many human pathogens.
- The adult human mucosa lines the surfaceS of the digestive,respiratory and genitourinary tracts,covering an immense surface area(m2) that is -200 times greater than that of the skin.
- It is estimated that 70% of infectious agents enter the host by mucosal routes
- The mucosal immune system consists of integrated network of tissues, lymphoid and nonlymphoid cells, and effector molecules such as antibodies, chemokines, cytokines.
- Mucosal surfaces are typically categorized as type I or type II mucosae.

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Type of Mucosae	Location
Type I	Lung and gut
Type II	Mouth, Esophagus and cornea
Both Type I and Type II	Female genital tract, type I (endocervix, uterus) and type II (vagina, ectocervix)

- It is well associated with lymphatic system hence it is known as mucosa associatedlymphatic tissue(MALT)
- Its a wider term and it consists of manysubdivisions namely gut associated lymphatictissue(GALT),bronchus associated lymphatictissue(BALT),nasal associated lymphatictissue(NALT).

- Mucosal Types :

1. Sublingal mucosa
2. Intranasal mucosa
3. Oral mucosa
4. Vaginal mucosa
5. Rectal mucosa
6. Ocular mucosa
7. Respiratory tract mucosa
8. Gastrointestinal mucosa

- Mucosal Delivery of vaccines :

- Most licensed vaccines are administered via parenteral route and are unable to elicit protectivemucosal immunity.
- Therefore mucosal immunization may be more favourable in providing protective immunityagainst mucosal pathogens.
- Among different approaches for effective mucosal vaccination,particulate delivery systems can beemployed.
- Particulate delivery systems protects the immunogenic material during the delivery.
- Facilitates specific target oriented delivery
- Allows incorporation of several adjuvant materials.
- Efficient delivery of vaccine antigens assists in uptake by APCs to generate protective mucosalimmunity.

➢ TRANSDERMAL VACCINE DELIVERY SYSTEM :

- The skin is the largest and most accessible organ of the body.
- Vaccine administration on the skin offers many advantages including ease of access, a potential for generation of both systemic and mucosal immune response.
- Formulations approaches such as liposomes, physical penetration enhancers such as electroporation, and technologies that create micron-sized pores in the skin, such as microneedles.
- The World Health Organization estimates that,

✓ 32% of Hepatitis B Virus infections
✓ 40% of Hepatitis C Virus infections
✓ 5% of Human Immunodeficiency Virus infections

in developing countries are attributable to unsafe injection practices

- The development of needle free immunization methods has thus become an

important goal in global health care.

- Dermal vaccination or transcutaneous immunization is a needle free method ofvaccine delivery which has the potential,

✓ To reduce the risk of needle-borne diseases
✓ To improve access to vaccination by simplifying procedures
✓ Trained personnel and use of sterile equipment not required
✓ To assist in the implementation of multiple boosting and regimens.

- SKIN AS A SITE OF VACCINE DELIVERY :

- The skin has multiple barrier properties to minimize water loss from the body and prevent the permeation of environmental contaminantsinto the body.
- These barriers can be considered as

-Physical barriers
-Enzymatic barriers.
-Immunological barriers.

- DESIGN AND STRATERGY FOR TRANSDERMALVACCINE DELIVERY :

I. Liquid jet injections
II. Energy based approaches
III. Epidermal power immunization
IV. Colloidal carriers

➢ IDEAL PROPERTIES OF VACCINE :

1. Vaccines gives life long immunity
2. Vaccine should be stable
3. It should effective in all subjects

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4. Rapid induce immunity
5. It should be cheap
6. It should be safe
7. Broadly protective agaist disease
8. It should be chemically inert

➢ PROS OF VACCINE :

1. Prevents an infected person from spreading disease.
2. Provide immunity to fight against harmful disease.
3. Protect drug against degradation.
4. Virosomes are biodegradable, bio compatible and non-toxic.
5. Enable drug delivery into cytoplasm of target cell.
6. Prevent epidemic and pandemics
7. Prevent the potential greater cost treating the infected patient.
8. Promote fusion activity in the endolysosomal pathway.
9. No auto immunogenic.
10. No disease transmission risk

➢ CONS OF VACCINE :

1. Shelf life is too short.
2. Vaccine can cause serious and sometime fetal side effect.
3. Booster injection can be inconvenient.
4. Can be unpleasant or painful.
5. Not guaranteed to work or provide 100% protection
6. Only humoral immunity can be induced.
7. Inactivation may after antigenicity.

➢ SIDE EFFECTS OF VACCINES:

1) Tiredness
2) Headache
3) Fever
4) Shivering
5) Swelling at injection site
6) Dizziness
7) Body rash
8) Chills
9) Pain
10) Irritability

II. CONCLUSION :

It is clear from this article that, from the past few years the whole field of vaccine research has been changed significantly. Immunochemist plays vital role to form more defined and efficacious products. Immunization policy needs to be national in scope. Implementation of Immunization policy must be flexible at the state and local levels. The importance of vaccination to young generation can have long lasting beneficial effects in the population. The childhood Immunization schedule may become more complex over time as scientific progress are made and new vaccines are developed. Because of the benefits and number of effects vaccination, the vaccines become more popular now a days. Vaccines proves that it is much comfortable for patients as we are taken it via different delivery routes such as needle free vaccine delivery system.

REFERENCE :

[1]. Ryan F. Donnelly. Vaccine delivery systems. HUMAN VACCINES & IMMUNOTHERAPEUTICS 2017, VOL. 13, NO. 1, 17–18.
[2]. Angela S Clem. Fundamentals of Vaccine Immunology. Glob Infect Dis. 2011 Jan-Mar; 3(1): 73–78.
[3]. Ross S. Federman. Understanding Vaccines: A Public Imperative.Yale J Biol Med. 2014 Dec; 87(4): 417–422.
[4]. Lu Zhang, Wei Wang,and Wang. Effect of Vaccine Administration Modality on Immunogenicity and Efficacy. Expert Rev Vaccines. 2015; 14(11): 1509–1523.
[5]. Cortes-Perez NG1, Ah-Leung S, Bermúdez-Humarán LG, Corthier G, Langella P, Wal JM, Adel-Patient K. Allergy therapy by intranasal administration with recombinant Lactococcus lactis Producing bovine beta-lactoglobulin.nt Arch Allergy Immunol. 2009;150(1):25-31.
[6]. https://www.amarujala.com/lifestyle/fitness/16-march-2019-national-vaccination-day-know-important-vaccine-for-your-child
[7]. http://tut2learn.com/2017/03/national-vaccination-day/
[8]. Mark Doherty, Philippe Buchy, Baudouin Standaert, CarloGiaquinto, DavidPrado-Cohrs. Vaccine impact: Benefits for human health.elsevierVolume 34, Issue 52, 20 December 2016, Pages 6707-6714
[9]. D.K. Sanghi, Rakesh Tiwle. A DETAIL COMPREHENSIVE REVIEW ON VACCINES, International Journal of Research and Development in Pharmacy and Life Sciences, Vol. 3, No.2, pp 887-895.

[10]. GA Poland, IG Ovsyannikova, and RB Kennedy. Personalized Vaccinology: A Review. HHS Public Access, Vaccine. 2018 August 28; 36(36): 5350–5357.
[11]. Frank DeStefano, Heather Monk Bodenstab, Paul A Offit. Principal Controversies in Vaccine Safety in the United States.Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731.
[12]. Teena Mohan, Priyanka Verma & D. Nageswara Rao. Novel adjuvants & delivery vehicles for vaccines development: A road ahead. Indian J Med Res 138, November 2013, pp 779-795.
[13]. Daisy Arora, Sushmita Rana, GD. Gupta Amit Chaudhary, Bhupendra Singh. Oral Mucosal Immunization Recent Advancement and Exploit Dendritic Cell Targeting. Journal of Drug Delivery & Therapeutics. 2019; 9(3):704-711
[14]. Vaccines and vaccination.National Office of Animal Health Available at: https://www.noah.co.uk/briefingdocument /antibiotic- resistance-2/ (accessed 26 November 2018).
[15]. Grace DMF, Ochungo P, Kruska R et al. Mapping of poverty and likely zoonoses hotspots. Zoonoses Project 4. Nairobi, Kenya: International Livestock Research Institute (ILRI), 2012.
[16]. Ullas PT, Desai A, Madhusudana SN (2012) Rabies DNA Vaccines: Current Status and Future. World Journal of Vaccines 2(1): 36-45.
[17]. Elgert KD. Immunology: Understanding the immune system. 2nd ed.United states: Wiley-Blackwell; 2009 (629).
[18]. Carino GP. Vaccine delivery. In: Mathiowitz E, editor. Encyclopedia of Controlled Drug Delivery. Vol.2. United States:Wiley Interscience;1999 (996).
[19]. Leo De Leede, Rianne Roukema, Bas Kremer "Advances in Single-Shot Vaccine Development" Biopharm International Volume 2009.
[20]. Vivek Shrivatsava & U.K.Jain "Design of Single Dose Control Relese Device for Antigen Delivery based on Poly(Lactic-co-Glycolic acid)"
[21]. International journal of Pharmaceutical Sciences & Nanotechnology, volume 3, 2010.
[22]. Adam.A.Walters, Christos Krastew, Adrian V.S.Hill & Anita Milicic 'Next Generation Vaccines; Single Dose Encapsulated vaccines for Improved Global Immunization Coverage & Efficacy" Journey forPharmacy And Pharmacology Nov 9,2014.
[23]. Textbook of Social and Preventive Pharmacy
[24]. Textbook of Drug Delivery sytem
[25]. www.Google.com
[26]. Wikipedia
[27]. Yashodahospitals
[28]. medscape.com