IMMUNIZATION
OVERVIEWS

• Basic vaccine immunology
• Vaccination technique
• National immunization program (NIP),
• IAP Schedule
• Individual vaccines
ACTIVE IMMUNIZATION

Administration of all or part of microorganism or a modified product to stimulate immune response mimicking natural infection without risk to the recipient.
TYPES OF VACCINES

- Live attenuated: BCG, OPV, measles, varicella
- Killed / inactivated:
  - Whole cell: Hepatitis A, Rabies, whole cell pertussis (wP)
  - Subunit: Hepatitis B, acellular pertussis (aP)
  - Toxoid: Tetanus, diphtheria
  - Protein conjugated: Hib conjugate, pneumococcal conjugate
  - Polysaccharide: Typhoid (Vi), Pneumococcal polysaccharide
RESPONSE AFTER IMMUNIZATION

PROTEIN VS POLYSACCHARIDE VACCINES

• Protein antigens stimulate T cells in lymph nodes.
  – large quantity of high affinity antibodies are formed.
  – Memory cells are formed which produces a more rapid and higher antibody response on re-exposure.

• Polysaccharide antigens are T cell independent;
  – limited antibodies of lesser affinity are formed
  – No memory cells are produced so no booster effect on reexposure to same antigen.
RESPONSE TO VACCINES

- Live vaccines
  - Multifocal lymph node activation
  - Better immunogenicity
  - Less number of doses
  - May provide life long immunity after single dose itself

- Killed vaccines
  - Usually stimulate regional lymph nodes
  - Needs repeated doses to maintain optimum antibody level
  - Adjuvants may be added to increase immunogenicity
DETERMINANTS OF IMMUNE RESPONSE

• Type of vaccine: Live Vs inactivated
  Protein Vs polysaccharide

• Vaccine schedule: Adequate interval between priming doses; optimal interval between priming and boosting doses

• Age: Immunologic immaturity and interference by maternal antibody in early life.
TECHNIQUE OF VACCINE ADMINISTRATION

- Hands to be cleaned
- Separate needle and syringe for each injection
- Discard needle and syringe safely
- Avoid gluteal region for IM injection
- Gentle pressure at vaccination site for a few seconds after vaccination
- Wash hands
- Open plunger side
- Correct dose
- Correct site
- Safe disposal
# TECHNIQUE OF VACCINE ADMINISTRATION

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Needle size</th>
<th>Route</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles, MMR, Varicella</td>
<td>23-25 G, 5/8”</td>
<td>Subcutaneous</td>
<td>Outer triceps area (Posterior skin fold)</td>
</tr>
<tr>
<td>DPT, TT, Td, DTaP, Hep B, Hib, PCV, Hep A</td>
<td>22-25 G 1-2”</td>
<td>IM</td>
<td>Deltoid, vastus lateralis (anterolateral thigh)</td>
</tr>
</tbody>
</table>

BCG given intradermally over deltoid region
COLD CHAIN

• The cold chain is the system of storing and transporting vaccines at recommended temperatures from the point of manufacture to the point of use.
• Safe zone for short term storage: 2°C to 8°C
• Equipment for cold chain maintenance:
  - ILR/Refrigerator/Vaccine carrier
  - Temperature monitoring devices
DOMESTIC REFRIGERATOR AND VACCINE STORAGE

REFRIGERATOR SHOWING VACCINES STORED CORRECTLY IN CLINIC SETUP

FREEZING COMPARTMENTS
- ICE CUBES
- OPV VIALS

TOP
- BCG
- MEASLES

MIDDLE
- DPT / DT / TT
- TYPHOID
- HEPATITIS A
- HEPATITIS B
- VARICELLA

LOWER
- DILUENT

NOTHING IN DOOR

DIAL THERMOMETER (TOP SHELF)
VACCINE VIAL MONITOR (VVM)

• The combined effect of time and temperature cause the inner square of the VVM to darken gradually & irreversibly.

Vaccine Vial Monitor

Stage 1 = good: Utilize
Stage 2 = good: Utilize
The central square is lighter than the surrounding circle

Stage 3 = bad: Don’t Utilize
Stage 4 = bad: Don’t Utilize
The central square is equal to, or darker than the surrounding circle
THERMOSENSITIVITY OF VACCINES

HEAT SENSITIVE

- BCG(recon.)
- OPV
- MEASLES
- BCG
- DPT
- DT, TT, HBV, JE

Most

Least
FREEZE SENSITIVE

- Aluminum adjuvanted vaccines should not be frozen. If frozen it desiccates, leads to decrease in potency and causes sterile abscess. eg. Hep B, Tseries vaccines, Hib.
- Hep B most freeze sensitive, freezes at – 0.5°C
- DPT, TT, DT freezes at -3°C.
- Do not keep these vaccines on ice pack.
- Ice pack temp. -20°C so condition it before using.
FREEZE DAMAGE

Never frozen | Frozen/thawed
Immediately after shaking

- Smooth and cloudy → Not smooth, granular particles

30 minutes after shaking

- Starting to clear → Almost clear
- No sediment → Thick sediment

Use vaccine | Do not use vaccine

Shake test | Conditioned ice pack
POLICY REGARDING MULTIDOSE AND REconstituted vaccines

- Opened reconstituted multi dose vials of measles and BCG vaccines must be discarded at the end of each immunization session or at the end of 4 hours whichever is earlier.

- Opened multi dose vials of DPT, TT, Hepatitis B and OPV vaccines may be used in subsequent immunization sessions up to a maximum of 1 month provided that the vaccines have been stored properly and the expiry date has not passed.
CONTRAINDICATIONS FOR VACCINATION

- Anaphylaxis following a previous dose or known allergic reaction to vaccine component
- Encephalopathy within 7 days of pertussis vaccine
- For some live vaccines – immuno-suppressed state
- Minor illnesses are not contraindications
ADVERSE EVENTS FOLLOWING IMMUNIZATIONS (AEFI)

• An untoward event following immunization that might or might not have been caused by immunization

• Types of adverse events:
  – Vaccine reaction
  – Immunization error
  – Anxiety reaction
  – Coincidental

• Serious AEFI: Death, disability, hospitalization
NATIONAL IMMUNIZATION SCHEDULE

• 1978: EPI (Expanded program of immunization) India introduced 6 vaccines-BCG, DPT, OPV, DT, TT,

• 1985: UIP (Universal immunization program) Targeted to immunize all infants with BCG, OPV, DPT and measles and TT for pregnant women

• Pulse polio program (National Immunization Day)

• Hepatitis B is given only in some states currently
# NATIONAL IMMUNIZATION SCHEDULE

<table>
<thead>
<tr>
<th>Age (Months)</th>
<th>Vaccines Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>BCG, OPV, Hep B1</td>
</tr>
<tr>
<td>6 weeks</td>
<td>DTwP1, OPV1, HepB2, Hib*</td>
</tr>
<tr>
<td>10 weeks</td>
<td>DTwP2, OPV2, HepB3, Hib*</td>
</tr>
<tr>
<td>14 weeks</td>
<td>DTwP3, OPV3, HepB4, Hib* +IPV</td>
</tr>
<tr>
<td>9-12 months</td>
<td>Measles / MR, JE1</td>
</tr>
<tr>
<td>16-24 months</td>
<td>DTwP B1, OPV4, Measles, JE2#</td>
</tr>
<tr>
<td>5-6 years</td>
<td>DTwP B2,</td>
</tr>
<tr>
<td>10 years</td>
<td>TT</td>
</tr>
<tr>
<td>16 years</td>
<td>TT</td>
</tr>
</tbody>
</table>

*JE vaccine given in select endemic districts

*Hib vaccine is given as pentavac in select states
PREGNANT WOMEN

• TT1 (early in pregnancy)
• TT2 (1 month later)
• TT booster (if vaccinated in past 3 years)

• Vitamin A
  9 months, 18 months then 6 monthly upto 5 yrs total
  9 doses
## IAP IMMUNIZATION SCHEDULE

<table>
<thead>
<tr>
<th>Age (completed weeks/months/years)</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>BCG, OPV 0, HepB 1</td>
</tr>
<tr>
<td>6 weeks</td>
<td>DTwP1, IPV1, Hib1, HepB2, Rotavirus1, PCV 1</td>
</tr>
<tr>
<td>10 weeks</td>
<td>DTwP2, IPV2, Hib2, Rotavirus2, PCV 2</td>
</tr>
<tr>
<td>14 weeks</td>
<td>DTwP3, IPV3, Hib3, (Rotavirus 3), HepB3, PCV 3</td>
</tr>
<tr>
<td>9 months</td>
<td>OPV2, MMR1</td>
</tr>
<tr>
<td>9-12 months</td>
<td>Typhoid conjugate vaccine</td>
</tr>
<tr>
<td>Age</td>
<td>Vaccines</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>12 months</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>15 months</td>
<td>MMR2, Varicella, PCV Booster</td>
</tr>
<tr>
<td>16 to 18 months</td>
<td>DTwP B1/DTap B1, IPV B1, Hib B1</td>
</tr>
<tr>
<td>18 months</td>
<td>Hepatitis A 2</td>
</tr>
<tr>
<td>2 years</td>
<td>Typhoid 1</td>
</tr>
<tr>
<td>5 Years</td>
<td>DTwP B2/DTaP B2, OPV3, Typhoid B, Varicella 2</td>
</tr>
<tr>
<td>10 to 12 years</td>
<td>Tdap/Td HPV</td>
</tr>
</tbody>
</table>
INDIVIDUAL VACCINES

Vaccines under national immunization program
BCG VACCINE

- BCG is a live attenuated vaccine containing bovine tuberculosis bacilli
- Administered in the newborn period
- Protective against severe forms of childhood TB (Miliary and meningeal TB)
- 50-80% efficacy
- Can even be given to babies of HIV positive mothers in newborn period
BCG VACCINE ADMINISTRATION

- BCG is supplied as lyophilized powder in dark coloured multidose ampoules or vials (to be protected from light) with diluent
- Reconstituted vaccine dose is 0.1ml: intradermal route over left deltoid region using tuberculin syringe and 26G/27G needle
- Following local reaction, scar formation occurs in 6-12 weeks
ORAL POLIO VACCINE (OPV)

- 2 types of polio vaccines were developed in 1950’s: OPV by Albert Sabin and IPV (Inactivated polio vaccine-Injectable) by Jonas Salk
- OPV is used in NIP and also on NIDs
- Contains attenuated polio virus types 1, 2 and 3
- Highly heat sensitive
- Immunogenicity less in developing countries; multiple doses required
- Monovalent OPV – P1 or P3 (MOPV) and bivalent OPV (BOPV) – P1 + P3 in some areas they are more immunogenic than trivalent OPV
ORAL POLIO VACCINE

- OPV given at birth, 6, 10, 14, weeks, 16 - 24 months under NIS
- Also in NIDs (Pulse polio) and SNIDs to break circulation of wild polio virus
- Orally 2 drops
- Type I $10^6$ Type II $10^{5.5}$ and Type III $10^{5.5}$ doses
- Extremely rare, but serious adverse effects of OPV:
  - Vaccine associated paralytic polio (VAPP)
  - Vaccine Derived polio viruses (VDPVs)
DIPHTHERIA, TETANUS AND PERTUSSIS (WHOLE CELL) VACCINE – DTWP

• Contains diphtheria and tetanus toxoids and killed pertussis bacilli
• 3 primary doses at 6, 10 and 14 weeks and 2 boosters at 16-24 months and 5 years
• Effectiveness: Diphtheria and tetanus > 95%; pertussis 70-90%
• Tetanus boosters recommended at 10 and 16 years
ADVERSE EVENTS FOLLOWING DTWP

- Minor adverse events like pain, swelling, redness at injection site, fever and irritability in about 50% of vaccines
- More serious adverse events are rare
- Absolute contraindications:
  - Anaphylaxis to previous dose
  - Encephalopathy within 7 days of DTP
- Progressive neurological deficit – relative contraindication
MEASLES VACCINE

• Live attenuated viral vaccine
• Supplied as lyophilised powder in dark coloured vials with diluent
• Reconstituted vaccine should be discarded after 4 hours
• Dose 0.5 ml: subcutaneous route
• Administered at 9 months of age
HEPATITIS B VACCINE

• To prevent chronic HBs Ag carrier state which can lead to chronic liver problems and mortality in adults
• Available as recombinant HBs Ag (Hepatitis B surface antigen) vaccine
• Dose: 0.5ml IM in <18 years of age; 1ml in > 18 years
• Various schedules are effective (>95% seroprotection)
  - Birth, 1 mo and 6 mo (IAP)
  - Birth, 6 wks, 14 wks
  - Birth, 6 wks, 10 wks, 14 wks (NIS)
  - 6 wks, 10 wks, 14 wks
• Birth dose necessary to prevent vertical transmission
VACCINES NOT UNDER CURRENT NIP RECOMMENDED BY IAP
MMR VACCINE

• Supplied in lyophilised form with diluent
• Each reconstituted dose of 0.5 ml contains live attenuated measles, mumps and rubella viruses
• Route of administration similar to measles vaccine, subcutaneous route
• IAP recommends 2 doses:
  – 1st dose at 9 months of age
  – 2nd at 15 months of age
HEMOPHILUS INFLUENZAE TYPE B (HIB) VACCINE

- Hib important pathogen in invasive infections such as meningitis and pneumonia
- Hib vaccine is a conjugate vaccine; each 0.5ml contains capsular polysaccharide bound to a protein (tetanus toxoid or nontoxic mutagenic diphtheria toxoid)
- Dose 0.5ml IM
- Schedule recommended: 3 doses below 6 months of age starting at 6 weeks: minimum interval of 4 weeks between doses; booster at 15-18 month of age
- Efficacy 90-100%
INACTIVATED POLIO VACCINE (IPV)

- Killed vaccine containing all the 3 types of polio virus; given by IM injection
- Sero conversion rates are 90-100% when given at 6, 10 and 14 weeks; a booster dose recommended at 15-18 months of age
- IAP recommends combined sequential OPV, IPV schedule for best protection and also to reduce to risk of VAPP
- IPV is to be introduced as single dose at 14 weeks with OPV
ACELLULAR PERTUSSIS VACCINE (AP)

- Instead of whole pertussis bacilli, some components like pertussis toxin, filamentous hemagglutinin and pertactin are included in the acellular DTaP vaccine.
- Dose and age recommendations are similar to DTwP vaccine.
- Minor and major side effects seen with DTwP are decreased by nearly 2/3 with DTaP.
- Absolute contraindications are similar to DTwP.
- Cost is a major factor.
- DTwP is found to be more efficacious hence now DTwP recommended for primary vaccination series.
TYPHOID VACCINE

- Vi Polysaccharide vaccine and conjugate typhoid vaccines are available.
- Vi polysaccharide 1st dose given after 2 years of age; To be repeated every 3 years.
- Efficacy 65-75%.
- Typhoid conjugate vaccine may be given at 9 months of age.
VARICELLA VACCINE

- Chickenpox generally a benign disease in children
- ↑ complications in neonates, adolescents and adults, pregnant women and immuno-compromised
- Varicella vaccine; live attenuated virus; lyophilised powder; to be reconstituted with the diluent
- Dose: 0.5ml; subcutaneous
- Currently 2 doses are recommended by IAP:
  - 1st at 15 month of age
  - 2nd between 4 – 6 years of age
HEPATITIS A VACCINE

- Hepatitis infection is relatively benign in young children <5 years of age and may be asymptomatic in many
- Hepatitis A can be severe in adults and in those with underlying chronic liver disease
- Vaccine is formalin inactivated (killed); Dose 0.5ml IM
- Recently a live attenuated vaccine also available; 1ml per dose IM
- IAP recommends 2 doses at 6-12 months interval; starting at > 1 year of age
- Protective efficacy 90-100%
PNEUMOCOCCAL VACCINE

• S.pneumoniae – important cause of death due to severe pneumonia and bacterial meningitis in children
• 2 Vaccines:
  13 valent PCV (Pneumococcal conjugate vaccine)
  23 Valen PSV (Pneumococcal polysaccharide vaccine)
• PCV is T cell dependant and immunogenic in children < 2 years
• PCV recommended by IAP for routine immunization- 6,10, 14 weeks and booster 15-18 months; 0.5ml IM
• PSV in special groups after 2 years of age (sickle cell disease, asplenia, nephortic syndrome)
ROTA VIRUS VACCINE

- ROTA virus major cause of severe diarrhea related mortality in developing countries

- 2 live attenuated oral vaccines available:
  - Human monovalent vaccine (2 doses; 1ml each)
  - Human bovine reassorted pentavalent vaccine (3 doses; 2ml each)

- Schedule: 1st dose 6-8 weeks (not later than 14 Wks)
  - Interval between doses 4-8 weeks
  - Complete last dose before 32 weeks
RABIES VACCINE

- Rabies vaccines currently used are the modern tissue culture vaccines: Purified chick embryo cell vaccine (PCEV), Purified vero cell vaccine (PVCV), Human diploid cell vaccine (HDCV)
- Equal efficacy
- Post exposure prophylaxis started as soon as possible
- Standard protocol (Essen): Days 0,3,7,14 and 30
- Dose: 1ml IM; anterolateral thigh or deltoid muscle
  - ID route
- Updated Thai red cross regime 2-2-2-0-2-0
JAPANESE ENCEPHALITIS (JE) VACCINE

- JE risk is highest in children aged 1 – 15 years and in rural areas
- Cell culture derived live SA-14-14-2 Chinese vaccine
- Dose 0.5ml subcutaneous, 2 dose 9 months and 18 months
- Given to children aged 1-15 years in selected districts of UP, Assam, West Bengal, Kerala and Karnataka
HUMAN PAPILLOMA VIRUS (HPV) VACCINE

- Vaccine for prevention of cervical cancer
- HPV types 16 and 18 are responsible for 70% of cervical cancer worldwide, including India
- 2 vaccines available in India – Quadrivalent (16,18,6,11) and Bivalent (16,18) vaccines
- Protective efficacy 93-99%
- IAP recommends routine HPV vaccination for girls at 10-12 years of age
- 3 doses: 0,2 and 6 months (Quadrivalent)
  0,1 and 6 months (Bivalent)
THE MYTHS AND FACTS ABOUT IMMUNIZATION

• The Myth
  • Too many vaccines might overload the immune system

• The Fact
  • The immune system can simultaneously respond to over 10 million antigens at any one time
  • Natural infections present more antigens
THE MYTHS AND FACTS

• The myth
• Combination vaccines may be less effective than vaccines administrated separately
• The fact
• The DTPw-HB-Hib combination formulations
• Excellent immunological response
POINTS TO REMEMBER - IMMUNIZATION

• Vaccines as per schedule as per chronological age in pre terms and low birth weight babies
• Need not restart even after lapse of usual interval
• Minor illnesses, malnutrition not contra indications
POINTS TO REMEMBER - IMMUNIZATION

• Minimum 4 weeks gap between 2 primary doses of the same vaccine.

• Minimum of 4 weeks gap between 2 live vaccines

• Killed vaccine can be given any time after or before any vaccine
POINTS TO REMEMBER - IMMUNIZATION

• Stick to proper guidelines – dose, route
• Maintain cold chain
• Inform parents about benefits and anticipated reactions
• Use reconstituted vaccines in 4 hrs
• Disposable – Auto disabled syringe
• Anterolateral thigh or deltoid
• Keep basic resuscitation ready drugs / equipments
SOURCE

• IAP recommendations 2014, IP
• IAP Guide Book on Immunization 2011 by
  IAP Committee on Immunization 2009 -2011

• IAP text book of Pediatrics 4th edition
• Editor Dr.A.Parthasarathy
THANK YOU