6 Cold Chain

Introduction

The system of transporting, storing and distributing vaccines in a potent state at the recommended temperature from the point of manufacture to the point of use is the cold chain. Vaccine potency once lost cannot be restored. The cold chain remains a highly vulnerable point for both National Immunization Programs and office practice in developing countries with tropical climates. Hence presently there is no substitute to rigorous maintenance of cold chain.

The essential components of a cold chain include

1. Personnel responsible for vaccine distribution.
2. Appropriate equipment to store and transport vaccines.
3. Appropriate transport facilities.
4. Maintenance of equipment.
5. Monitoring.

Temperature and Light Sensitivity of Vaccines

The correct temperature is the most important factor in maintaining the potency of vaccines. Unlike popular belief, vaccines are damaged by excessive cold in addition to heat.

Sensitivity of Vaccines to Heat

Each exposure to ambient temperature causes some degradation of the vaccine and subsequent exposures lead to cumulative impact. Vaccine potency cannot be restored after placing back at recommended temperatures. All vaccines are sensitive to heat but to different degrees. Live vaccines are

more susceptible and in decreasing order of sensitivity include two brands of varicella and MMRV (Varivax ™, ProQuad™, currently not available in India), Live Attenuated Influenza Vaccine, OPV, Measles, MMR, BCG, yellow fever, rotavirus and other brands of varicella/MMRV vaccines.

Sensitivity of Vaccines to Freezing

Cold injury is more common than assumed. Vaccines susceptible to damage by freezing include mainly all aluminum adjuvanted vaccines (DTwP, DTaP, TT, DT, Td, TT, Hepatitis B, combination vaccines, Hepatitis A, HPV, PCV 7) but also other vaccines including IPV, PPV 23, inactivated influenza vaccines, meningococcal vaccines, rotavirus vaccines, typhoid vaccines, Hib and brands of varicella vaccines except Varivax™. Vaccines that can be frozen without harm include OPV (vial must not be frozen and thawed repeatedly), and lyophilized measles, MMR, BCG vaccines, LAIV, certain brands of varicella and MMRV (Varivax ™, Proquad ™).

Sensitivity of Vaccines to Light

Lyophilized and reconstituted BCG, measles, MMR, varicella, rotavirus, human papilloma virus, most DTaP containing vaccines are particularly susceptible to light and need protection from strong light, sun light, ultraviolet and fluorescent neon lights.

Vaccine Vial Monitors

The Vaccine Vial Monitor (VVM) is a time and temperature sensitive colored label that provides an indication of the cumulative heat to which the vial has been exposed. VVMs were first introduced on OPV vials supplied to UNICEF and WHO in 1996. The VVM warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. It is used especially for temperature monitoring of OPV, which is the most thermo labile of all vaccines. The VVM is applied to the outside of a vaccine vial, and it applies only to that vial. It cannot be taken as a surrogate

marker for the potency of the vaccine in other vials of the same lot or in the same storage facility.

VVMs consist of a temperature sensitive material, which changes color gradually on being exposed to heat. This change of color is irreversible, and thus corresponds to the heat induced damage to the vaccine inside the vial. VVM's do not give any information on cold injury to vaccines. There are different types of VVMs available, to be used according to the heat stability characteristics of different vaccines.

Interpretation of the Color Change of VVM is as Follows

1. Inner square is white, or lighter than outer circle: If the expiry date has not passed, vaccine can be used.
2. Inner square matches color of outer circle or is darker than outer circle: vaccine should be discarded, regardless of the expiry date.

The vaccines can be used as long as the VVM has not changed color to the "discard" level. This is of tremendous help in outreach programs, where vaccine has to be carried to faraway places, or given door to door. Now VVMs are available for all vaccines and should be demanded from all manufacturers. VVMs are thus a low cost tool for assessing the adequacy and finding the weak links in the cold chain. They save children from receiving impotent, ineffective vaccines and avoid vaccine wastage.

Cold Chain Equipment

The cold chain involves two complementary aspects:

1. The set chain represented by the walk-in cold rooms, deep freezers and refrigerators and
2. The mobile chain represented by isothermic boxes and vaccine carriers.

Walk in cold rooms (WIC) and Walk—in freezers (WIF) are used for bulk storage of vaccines at the manufacturer site, or at major distribution points. They have two cooling units and standby generator sets, and are fitted with temperature recorders and alarm systems. Deep freezers are used for long

term storage of OPV/Measles/MMR vaccines. They are also used for making ice-packs for use in outreach programs. Ice lined refrigerators (ILR) are used where the power supply is intermittent. Most of the space is taken up by water which is frozen when electricity is available. Appropriate temperatures can be maintained for several hours.

Cold chain equipment commonly used in office practice including domestic refrigerators, cold boxes and vaccine carriers are discussed further in detail.

Domestic Refrigerator

The main compartment should have a temperature of 2 to 8° C, and the freezer compartment should maintain a temperature of –5 to –15° C. It should be large enough to store the largest inventory of a month and ideally CFC free. Ideally a double door refrigerator should be used. It is impossible to maintain optimum temperatures unless the refrigerator has two separate external doors for the two compartments. Without separate doors, either the freezer will be too warm, or the vaccines in the main compartment will suffer freezing damage. The doors should close snugly, be free of leakages of water and coolant, quiet and have features such as auto defrost and auto door closure. Bar and dormitory fridges should not be used. A voltage stabilizer is mandatory when voltage fluctuations are many and power cuts are frequent. A good well calibrated thermometer is a must; options include a stem thermometer, dial thermometer, digital thermometer, max/min thermometer or a data logger. The thermometer should be placed in both the freezer and the main compartment in the center and away from the walls, door, air vent or frozen packs and never in the door.

The vaccines can be placed as follows:

- Freezer compartment: BCG, OPV, Measles, and MMR.
- Top shelf: OPV, Measles and MMR.
- Middle shelf: DTwP, DTaP, DT, TT, Tdap, Combination vaccines, IPV, HPV, Typhoid, Hepatitis A, Hib, PCV7, influenza, rotavirus vaccines.

- Lower shelf: Hepatitis B and Varicella.
- Crispator: Diluents.
- Baffle tray: Should be kept empty. No vaccines should be stored in the door.

The following measures are recommended to maintain appropriate temperatures and ensure vaccine potency in domestic refrigerators.

- Temperatures should be recorded at least twice a day and a temperature log maintained regardless of temperature alarm, a chart recorder thermometer, or a digital data logger. Fast action should be taken in case of out of range temperatures. The log helps to identify recurring problems and loss of function in ageing units. Temperatures should be monitored twice a day for a week prior to using a new/repaired refrigerator for vaccine storage.
- The vaccine refrigerator should not be used for any other purpose including storage of food, beverages, pathology specimens and other medications. This will minimize the opening of the door. It is recognized that opening of the door can increase temperatures much as 2 to 5° C for as long as 2 to 8 minutes.
- The door should have a warning sticker in order to discourage unnecessary door opening.
- Access to the vaccine refrigerator should be restricted to anyone else than trained staff. A map of inside content of the refrigerator pasted on the outside of the door can minimize opened-door time while searching vaccine inside.
- Ice packs and jars/bottles of non-drinkable water should be kept in the freezer and the door of the main compartment and the lowest part (baffle tray) respectively. This increases the cool mass of the refrigerator and helps maintain temperature during power failures and cuts for at least 3 to 4 hours, and minimizes temperature fluctuations during door opening. The thermostat should be reset according to the ambient temperatures; e.g. to coolest during summers.
- The refrigerator should be kept at least 10 cm away from the floor and the walls so as to allow good air circulation.

- The vaccines should be kept in transparent labeled boxes that will help in minimizing time required for retrieving the vaccines. Each vaccine pack/vial must be labeled with the expiry date and the principle of FEFO (First expired first out) and FIFO (First in first out) followed.
- The refrigerator should not be overloaded and overstocked so as to allow good air circulation around the vaccines.
- The refrigerator should be checked regularly daily for door closure, monthly for coils, door seals, hinges and leveling and undergo maintenance on a periodic basis.
- In non frost free refrigerators regular cleaning and defrosting should be done weekly or whenever ice layer of more than 4 mm forms in the freezer. Thicker ice layer will hamper proper functioning of the unit. Vaccines should be transferred to a safe place during defrosting and cleaning.
- The power supply should be secured. The plug should have a sticker saying "Do Not Unplug." Staff must be trained never to turn off the refrigerator that holds vaccines.
- If power cuts are frequent, an alternative power source should be available capable for running for at least 72 hours.
- Rapid action should be taken in case of power failure or refrigerator malfunction. A plan must be in place for dealing with power failure. For short intervals, such as 2-3 hours, it is appropriate to just keep the refrigerator door closed, to maintain the temperature inside. For longer power cuts, it is necessary to move the vaccines, in a vaccine carrier, to a place where a working refrigerator is available. Refrigerator malfunctions need to be dealt with similarly. If the temperature inside is not within the acceptable range, the vaccines must be moved to another refrigerator, in a vaccine carrier. Regular training of staff and audit of practices should be done. Assign duties to specific trained staff to be hold responsible for the vaccine storage and identify back up staff. But all the staff should be versed with the plan to handle power failures and out of range temperatures.

Cold Box/Vaccine Carriers

These are used for transport of vaccines. They should have frozen ice packs lining the sides. To prevent cold injury conditioned icepacks should be used rather than frozen packs. The vaccine pack should not be placed in direct contact with the icepacks but should have an intervening layer of plastic/ bubble wrap/styroform peanuts. A thermometer should be placed in the cold box/vaccine carrier for recording temperatures. For keeping vaccines for longer durations the walls of the thermocol box should be 2 inches thick and have a snugly fitting lid.

Storage of Vaccines

Vaccines should be kept in original packaging till use to protect from light exposure. All vaccines currently available in India are safe at temperatures between 2 to 8° C. At a temperature of 2 to 8° C, most of these vaccines have a shelf life of 24 months. The manufacturer's instructions regarding shelf life of a given vaccine must be rigorously followed. BCG, OPV, Measles and MMR vaccines should be preferably kept frozen for long term storage (shelf life of 2 years). Even these vaccines, however, can be kept at 2 to 8° C for shorter periods, e.g. 6 to 12 months for OPV and 18 to 24 months for measles. Though vaccines may retain potency for variable amounts of time at ambient temperatures, there is no simple and cheap method that can be used in the field to assess whether a vaccine exposed to ambient temperature has retained at least the minimum required potency. Hence such vaccines are best discarded.

Aluminium adjuvanted vaccines (DTwP, DTaP, TT, DT, Td, TT, Hepatitis B, combination vaccines, Hepatitis A, HPV, PCV 7) and other vaccines including IPV, PPV 23, Hib, inactivated influenza vaccines, meningococcal vaccines, rotavirus vaccines, typhoid vaccines and other brands of varicella vaccines except Varivax ™ should be stored at 2 to 8°C, must never be frozen and if accidentally frozen should be discarded. The "Shake Test" can be used to determine if a

vaccine vial has been suspected to be frozen at any time. The vial should be shaken so that the sediments, if any, are completely mixed. A frozen control vial should be used to compare with the test vial. During the 15 minutes test time a non-viable test vial will show sediments settling as fast as the control frozen vial. Vaccine vial found in frozen state should be directly discarded and need not undergo shake test. Diluents should never be frozen. They can be stored at 2 to 25° C and can be kept in the door compartments.

Reconstituted lyophilized vaccines (BCG, Measles, MMR, Hib, rabies, rotavirus) whether single dose/multi dose must be stored at 2 to 8° C, protected from light and used within 4 to 6 hours. Multi dose vials of inactivated liquid vaccines once opened may be used till the expiry date on the container. OPV can be subjected to 10 cycles of freeze-thaw provided that the thawed material is kept refrigerated and the total cumulative duration of the thaw is not more than 24 hours. OPV would lose viability if kept at 22 to 25° C for more than a day. Opened vials of OPV, however, may be used in subsequent sessions at a given health facility if it has been preserved at 2 to 8° C. OPV vials used in the field setting or an outreach facility or during a pulse immunization session must be discarded at the end of the day. Vaccine vials should not be taken out to the field more than 3 times, after that these are best discarded irrespective of whether these have been opened or not.

Vaccines should be transported only in cold boxes or vaccine carriers—vacuum flasks should never be used for this purpose. During shipment and transportation, temperature and time sensitive monitor marks are used to check the cold chain. Transport is the most vulnerable time for the cold injury to vaccines.

Conclusion

The cold chain is the Achilles heel in immunization and should be given appropriate attention.