National Institute of Health
Islamabad, Pakistan

MEASLES VIRUS VACCINE, LIVE, ATTENUATED (DRIED)

Active Immunizing Agent For the Prevention of Measles (Rubeola)

Description

Measles Virus Vaccine, Live, Attenuated (Dried) is prepared in avian leucosis-free chick embryo fibroblast cultures from the Connaught strain, a strain of measles virus derived from the same original isolate as were other vaccine strains, such as Schwarz.[1,2] The Connaught strain was attenuated by sixty-nine passages in chick embryo fibroblast cultures.

The vaccine is freeze-dried in multiple-dose vials. Each dose contains not less than 1000 $TCID_{50}$[2] of measles virus and not more than 10 mcg streptomycin and not more than 0.5 mcg neomycin.

The vaccine fulfils the WHO Requirements for Measles Vaccine (Live).

Action

The clinical trial of Measles Virus Vaccine, Live, Attenuated (Dried) involved 5 lots of vaccine and was administered to 378 individuals between 11 and 17 months of age. Serologic response four weeks following vaccination equal to or greater than 1:8 by haemagglutination-inhibition test was demonstrated in 99% of the 374 vaccinees for whom serum samples were available.

Similar results were obtained in a previous clinical trial of 1142 vaccinees of whom 98% demonstrated post-vaccine serologic response equal to or greater than 1:8 by haemagglutination-inhibition test.

Indications

Measles Virus Vaccine, Live, Attenuated (Dried) is indicated for the active immunization of children against measles (rubeola).[3] It does not protect against German measles (rubella).

This vaccine is recommended routinely for all children at, or as soon as practicable after, their first birthday. Measles vaccine is also recommended for children and adolescents who have never had documented measles or received live attenuated vaccine after the age of 12 months, and for persons of any age known to be seronegative. Routine primary immunization of adults is not necessary because they are very likely to have acquired immunity by natural infection. However, vaccination may be advisable for high school and college persons in epidemic situations and for adults in isolated communities where measles is not endemic.

Children, who, in accordance with previous recommendations, received vaccine prior to 1 year of age, or who were given a dose of further attenuated vaccine accompanied by immune serum globulin, may not be fully protected. It is recommended that such children be re-vaccinated with live measles vaccine.

Despite the risk of reaction (see Adverse Reactions), children who have previously been given inactivated vaccine alone, or followed by live vaccine within 3 months, should be revaccinated with live vaccine to avoid the severe atypical form of natural measles that may occur.

> In countries where the incidence and mortality from measles is high in the first year of life, the recommended age for immunization against measles is as soon as possible after 9 months of age.

Contraindications

Measles Virus Vaccine, Live, Attenuated should NOT be administered to the following:

(a) individuals with acute febrile respiratory or other infections, or any acute illness,
(b) individuals with a history of sensitivity to streptomycin or neomycin,
(c) individuals with blood dyscrasias, lymphomas, or other generalized malignancies,
(d) individuals with untreated active tuberculosis,
(e) individuals undergoing treatment with immunosuppressive agents of any kind or with primary immunodeficiency, e.g. agammaglobulinaemia, dysgammaglobulinaemia, hypogammaglobulinaemia,
(f) pregnant women, since the possible effect of attenuated measles virus on the fetus is not known.

If a measles-susceptible woman is exposed to measles during pregnancy, one should consider the possibility of providing temporary passive immunity through the administration of immune serum globulin.

> The specific contraindications adopted by individual national health authorities should reflect a balance between the risk from the vaccine and the risk from the disease. Because the risk from the vaccine remains extremely low in comparison to the risk from the disease in many developing countries, authorities there may choose to offer immunization to children who are mildly to moderately ill or malnourished.

Precautions

Administer the vaccine **subcutaneously**, do NOT administer intravenously. Epinephrine Hydrochloride Solution (1:1000) should be available for immediate use in the event of an anaphylactoid reaction.

The vaccine should be given with caution to children with a history of febrile convulsions.

Live measles vaccine is grown in chick fibroblast cultures and not in eggs. Egg albumin and yolk components are absent from these cultures. Hypersensitivity reactions very rarely follow the administration of live measles vaccine. Most of these reactions are considered minor and consist of wheal and flare or urticaria at the injection site. With over 131 million doses of measles vaccine distributed in the U.S.A., there have been 3 reported cases of immediate allergic reactions which could potentially have been life threatening in children who had histories of anaphylactoid reactions to egg ingestion. Extreme caution should be exercised if the vaccine is administered to persons with a history of anaphylactoid reactions subsequent to egg ingestion. Egg allergies which are not anaphylactoid in nature and allergies to chicken and feathers do not appear to constitute an increased risk of reaction to the vaccine.[4] The attending physician must weigh the benefits of immunization against the potential risks of hypersensitivity reactions.

Administration of the vaccine should be deferred at least three months after administration of human immune globulin, plasma or whole blood. If repeated or large amounts of these substances have been given, a longer interval should be allowed.

Administration of attenuated live-virus measles vaccine may temporarily depress tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be scheduled before administering measles vaccine, or on the day of vaccination with reading 48 to 72 hours later. This avoids the possibility of a false-negative response. Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine. No studies have been reported to date on the effect of measles virus vaccines on untreated tuberculous children.[4]

To avoid any additional effect of possible adverse reactions, it is advisable that Measles Virus Vaccine, Live, Attenuated (Dried) be administered separately from other antigens. However, when circumstances such as foreign travel or limited access to patients call for

the administration of more than one vaccine, the following guidelines may be applied. Simultaneous administration of Measles Virus Vaccine, Live, Attenuated (Dried) and an inactivated vaccine or a live attenuated vaccine such as rubella, mumps or oral polio vaccine may be performed, provided the vaccines are administered by separate syringes and at different sites with observance of the precautions that apply to the individual vaccines.[3,4]

Adverse Reactions

Local erythema and/or swelling around the site of injection are not uncommon and regional lymphadenopathy may occur rarely.

Fever or mild rash, or both, may occur 5 to 12 days after administration of Measles Virus Vaccine, Live, Attenuated (Dried). Based on clinical trials the febrile response would be expected to be mild, ≤37.7°C (≤99.9°F) in 48–57%; moderate, 37.8–39.4°C (100°–102.9°F) in 39–47%; and high, >39.4°C (>102.9°F) in 4–5% of recipients. With high temperatures the possibility of development of convulsions is present.

Rash may occur in 12–16% of vaccinees and is usually minimal.

Reactions which may be temporally associated with administration of measles vaccine such as encephalitis and encephalopathy have been reported to occur approximately once per million doses. Following natural measles infections, the incidence of such neurological disorders is approximately one per thousand reported cases.[5]

There have been reports of subacute sclerosing panencephalitis (SSPE) in individuals who have no history of measles but who have received measles vaccine. However, studies have shown that the incidence of SSPE in measles vaccine recipients (about one case per million doses of vaccine distributed) is significantly less than the 5 to 10 SSPE cases per million cases of natural measles.[6,7] It would appear that measles vaccine significantly reduces the chance of developing SSPE by protecting against measles.

Local reactions characterized by marked swelling, redness and vesiculation at the injection site of attenuated live virus measles vaccines have occurred in children who have previously received killed measles vaccine. On rare occasions, more severe reactions have been reported. These included prolonged high fevers and extensive local reactions which required hospitalization.[4]

Dosage

One dose of 0.5 ml of Measles Virus Vaccine, Live, Attenuated (Dried) subcutaneously. The age at which the vaccine is administered should be in accordance with that specified by the country's health authority.

Administration

The vaccine should be administered by **subcutaneous** injection which may conveniently be made near the insertion of the deltoid muscle. The vaccine MUST NOT be injected intravenously. The site of the injection should be prepared with a suitable antiseptic.

CAUTION: A new sterile disposable syringe should be used for each injection of the vaccine because certain preservatives, antiseptics and detergents will inactivate the live measles virus in the vaccine.

If a new sterile disposable syringe is not available, a reusable syringe and needle which have been sterilized by one of the following methods may be used.

The syringe and needle must be thoroughly cleaned and rinsed with water before sterilizing in an autoclave at 121°C for 30 minutes or by boiling in water for at least 20 minutes. After being allowed to air cool, the syringe should be assembled with care avoiding contamination. Any water remaining in the syringe should be expelled.

Reconstitution of Freeze-Dried Vaccine and Withdrawal from Rubber-Stoppered Vial

DO NOT REMOVE THE RUBBER STOPPER FROM THE VIAL.

Apply a **sterile** piece of cotton moistened with a suitable antiseptic to the surface of the rubber stoppers of the vials of sterile diluent and vaccine and allow to dry. Draw into a **sterile** disposable syringe a volume of air equal to the volume of the sterile diluent in the vial. Pierce the centre of the rubber stopper in the vial of sterile diluent with the **sterile** needle of the syringe, invert the vial, slowly inject into it the air contained in the syringe, and, keeping the point of the needle immersed, withdraw into the syringe the contents of the sterile diluent vial. Then holding the syringe-plunger steady, withdraw the needle from the vial. Inject this volume of sterile diluent into the vial of freeze-dried vaccine. Shake gently to thoroughly mix the reconstituted vaccine. **Avoid foaming** since this will prevent the withdrawal of the proper dose. Withdraw the required dose (0.5 ml) of the reconstituted vaccine into the syringe.

Carefully insert the needle into the subcutaneous tissue. **In order to avoid intravenous injection**, pull back on the plunger of the syringe to make certain that no blood is withdrawn before injecting the vaccine.

Storage

The freeze dried vaccine should be stored and transported between 2° and 8°C (35° and 46°F).

The diluent should be kept cool during transport and storage. It should be cooled to 2° to 8°C before use.

The vaccine may be stored at −20°C if desired, but stability data indicate that potency is maintained when the vaccine is held at 2° to 8°C through to expiry date.

The vaccine should be used immediately after reconstitution and any reconstituted vaccine not used within eight hours MUST be discarded. Reconstituted vaccine must be protected from light and maintained at 2° to 8°C (35° to 46°F).

How Supplied

Measles Virus Vaccine, Live, Attenuated (Dried) is supplied in multiple-dose vials.

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