measles, mumps, and rubella virus vaccine live

Composition
(measles, mumps, and rubella virus vaccine live) is a live virus vaccine for immunization against measles (rubeola), mumps and rubella (German measles). M-M-R is a sterile lyophilized preparation of (1) ‘Attenuvax’ (measles virus vaccine live), a more attenuated line of measles virus, derived from Enders’ attenuated Edmonston strain and grown in cell cultures of chick embryo; (2) ‘Mumpsavax’ (mumps virus vaccine live), the Jeryl Lynn (B level) strain of mumps virus grown in cell cultures of chick embryo, and (3) ‘Meruvax’ II (rubella virus vaccine live), the Wistar RA 27/3 strain of live attenuated rubella virus grown in human diploid cell (WI-38) culture. The vaccine viruses are the same as those used in the manufacture of ‘Attenuvax’ (measles virus vaccine live), ‘Mumpsavax’ (mumps virus vaccine live) and ‘Meruvax’ II (rubella virus vaccine live). The three viruses are mixed before being lyophilized.

When reconstituted as directed, the dose for injection is 0.5 ml and contains not less than the equivalent of 1,000 TCID 50 (tissue culture infectious doses) of the U.S. reference measles virus; 20,000 TCID 50 of the U.S reference mumps virus; and 1,000 TCID 50 of the U.S. reference rubella virus.

Pharmaceutical form
Powder for injection fluid.

Pharmaceutical properties
Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that it is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95 percent, mumps neutralizing antibodies in 96 percent, and rubella HI antibodies in 99 percent of susceptible persons.

The RA 27/3 rubella strain in elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine and has been shown to induce a broader profile of circulating antibodies including antitheta and anti-iota precipitating antibodies. The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses. The virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus, and provide greater confidence for lasting immunity.

Vaccine induced antibody levels following administration of have been shown to persist for over 11 years.

Clinical particulars
Therapeutic indications
‘M-M-R II’ is indicated for simultaneous immunization against measles, mumps, and rubella in persons 15 months of age or older. A second dose of or monovalent measles vaccine is recommended (see: Revaccination).

Infants who are less than 15 months of age may fail to respond to the measles component of the vaccine due to presence in the circulation of residual measles antibody of maternal origin, the younger the infant, the lower the likelihood of seroconversion. In geographically isolated or other relatively inaccessible populations for whom immunization programs are logistically difficult, and in population groups in which natural measles infection may occur in a significant proportion of infants before 15 months of age, it may be desirable to give the vaccine to infants at an earlier age. Infants vaccinated under these conditions at less than 12 months of age should be revaccinated after reaching 15 months of age. Most infants 12-14 months of age respond readily, but a booster on school entry or later may be needed to avoid breakthrough cases in these infants. There is some evidence to suggest that infants immunized at less than one year of age
may not develop sustained antibody levels when later reimmunized. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization. Previously unimmunized children of susceptible pregnant women should receive live attenuated rubella vaccine, because an immunized child will be less likely to acquire natural rubella and introduce the virus into the household.

Non-pregnant adolescent and adult females
Immunization of susceptible non-pregnant adolescent and adult females of childbearing age with live attenuated rubella virus vaccine is indicated if certain precautions are observed (see below and Warnings and precautions). Vaccinating susceptible postpubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infection of the fetus and consequent congenital rubella injury.

Women of childbearing age should be advised not to become pregnant for three months after vaccination and should be informed of the reasons for this precaution.

It is recommended that rubella susceptibility be determined by serologic testing prior to immunization. If immune, as evidenced by a specific rubella antibody titer of 1:8 or greater (hemagglutination inhibition test), vaccination is unnecessary. Congenital malformations do occur in up to seven percent of all live births. Their chance appearance after vaccination could lead to misinterpretation of the cause, particularly if the prior rubella-immune status of vaccinees is unknown.

Postpubertal females should be informed of the frequent occurrence of self-limited arthralgia arthritis beginning 2 to 4 weeks after vaccination (see Side-effects).

Postpartum women
It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period (see Use in pregnancy and during lactation).

Revaccination
Children vaccinated when younger than 12 months of age should be revaccinated at 15 months of age. For children first vaccinated at age 15 months or older a second dose of ‘M-M-R II’ is recommended at approximately age 9.

Posology and method of administration
For subcutaneous administration do not inject intravenously
The dosage of vaccine is the same for all persons. Inject the total volume of the single dose vial (about 0.5 ml) or 0.5 ml of the 10 dose vial of reconstituted vaccine subcutaneously, preferably into the outer aspect of upper arm.

To reconstitute, only use the diluent supplied in the syringe, since it is free of preservatives or other antiviral substances which might inactivate the vaccine. Inject all the diluent in the syringe into the vial of lyophilized vaccine, and agitate to mix thoroughly.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

Contraindications
Do not give ‘MMR II’ to pregnant females: the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be avoided for three months following vaccination. (See: pregnancy and lactation).

Anaphylactic or anaphylactoid reaction to neomycin.
History of anaphylactic or anaphylactoid reaction to eggs (see: hypersensitivity to eggs).

Any febrile respiratory illness or other active febrile infection.
Active untreated tuberculosis.
infected with human immunodeficiency viruses but without overt clinical manifestations of immunosuppression may be vaccinated; however, the vaccinees should be monitored closely for exposure to vaccine-preventable diseases because immunization may be less effective than for uninfected persons. In selected cases confirmation of circulating antibody levels may be indicated to help guide appropriate protective measures, including immunoprophylaxis if immunity has waned to non-protective levels.

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7-28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk. However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see: Nursing mothers).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

Children under treatment of tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine; no studies have been reported to date of the effect to measles virus vaccines on untreated tuberculous children.

As for any vaccine, vaccination with may not result in seroconversion in 100% of susceptible persons given the vaccine.

Interaction with other medicaments and other forms of interaction
Use with other vaccines:
Routines administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral poliovirus vaccine) concomitantly with measles, mumps and rubella vaccines is not recommended because there are insufficient data relating to the simultaneous administration of these antigens. However, the American Academy of Pediatrics has noted that in some circumstances,
evidence that it causes congenital malformations in humans. Mumps vaccine virus also has been shown to infect the placenta, but the virus has not been isolated from the fetal tissues from susceptible women who were vaccinated and underwent elective abortions; and (3) Reports have indicated that contracting of natural measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects.

M-M-R II should not be given less than one month before or after administration of other virus vaccines. Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin. It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with M-M-R II.

Effects on ability to drive and to use machines
There are no specific data. Some of the undesirable effects such as headache, dizziness and optic disturbances may effect the ability to drive or operate machinery.

Pregnancy and lactation
Animal reproduction studies have not been conducted with. It is also not known whether can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; further more, pregnancy should be avoided for three months following vaccination (see: Contraindications). In counselling women who are inadvertently vaccinated when pregnant or who become pregnant within 3 months of vaccination, the physician should be aware of the following: (1) In a 10 year survey involving over 700 pregnant women who received rubella vaccine within 3 months before or after conception (of whom 189 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with congenital rubella syndrome; (2) Although mumps virus is capable of infecting the placenta and fetus, there is no good evidence that it causes congenital malformations in humans.

Undesirable effects
The adverse reactions associated with the use of ‘M-M-R II’ are those which have been reported following administration of the monovalent vaccines.

Common:
Burning and/or stinging of short duration at the injection site.

Occasional:
Body as a whole: fever (38.3°C or higher)
Skin: Rash usually minimal but may be generalized. Generally, fever, rash or both appear between the 5th and 12th day.
Rare: Body as a whole: mild local reactions such as erythema, induration and tenderness; sore throat, malaise.
Digestive: parotitis, nausea, vomiting diarrhea.
Hematologic/Lymphatic: regional lymphadenopathy, thrombocytopenia, purpura.
Hypersensitivity: allergic reactions such as wheal...
and flare at injection site, anaphylaxis and anaphylactoid reactions, urticaria.
Musculoskeletal: arthralgia and/or arthritis (usually transient and rarely chronic, see below), myalgia.

Nervous/Psychiatric:
Febrile convulsions in children, afebrile convulsions or seizures, headache, dizziness, paresthesia, polyneuritis, Guillain-Barre syndrome, ataxia. Encephalitis/encephalopathy have been reported approximately once for every 3 million doses. In no case it has been shown that reactions were actually caused by vaccine. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with natural measles (one per two thousand reported cases).

Skin: erythema multiforme.
Special senses: forms of optic neuritis, including retrobulbar neuritis, papillitis and retinitis; ocular palsy, optic media, nerve deafness, conjunctivitis.

Urogenital: orchitis.
There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of natural measles but did receive measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine doses distributed. This is far less than the association with natural measles, 6-22 cases of SSPE per million cases of measles. The results of a retrospective case-controlled study conducted by the Center for Disease Control suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE. Local reactions characterized by marked swelling, redness and vesiculation at the injection site of attenuated live measles virus vaccines, and systemic reactions including atypical measles, have occurred in persons who received killed measles vaccine previously. ‘M-M-R II’ was not given under this condition: in clinical trials. Rarely, more severe reactions that require hospitalization, including prolonged high fevers and extensive local reactions, have been reported. Panniculitis has been reported rarely following administration of measles vaccine. Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of natural rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children.

Chronic arthritis has been associated with natural rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%, women: 12-20%), and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children (children: 0-3%, women: 12-20%), and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35-45 years), these reactions are generally well tolerated and rarely interfere with normal activities. Such reactions occur much less frequently after revaccination than primary vaccination.

Overdose
There are no data with regard to overdose.

Pharmaceutical particulars
List of excipients
Neomycin, water for injections. The product contains no preservatives. Sorbitol and hydrolyzed gelatin are added as stabilizers.

Incompatibilities
A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine.
Do not give immune globulin (IG) concurrently with -M-R II.

**Shelf life**
The expiry date has been printed on the package. It is recommended that the vaccine be used as soon as possible after reconstitution. Protect vaccine from light at all times, since such exposure may inactivate the virus. Store reconstituted vaccine in the vaccine vial in a dark place at 2-8°C and discard if not used within 8 hours.

**Special precautions for storage**
Before reconstitution, store at 2-8°C. Protect from light.

‘M-M-R II’ retains at least 8 times the immunizing dose even after 6 weeks at 22°C or 1 week at 37°C. Storage at temperatures above 2 to 8°C cannot be recommended due to the difficulty in monitoring the exact temperature and monitoring repeated exposures to time out of refrigeration. During shipment, to ensure there is no loss of potency, the vaccine must be maintained at a temperature of 10°C or less.

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