Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

Varicella (Chickenpox) and Varicella Vaccines

September 2018

Varicella Zoster Virus

- Herpes virus (DNA)
- Primary infection results in varicella (chickenpox)
- Recurrent infection results in herpes zoster (shingles)
- Short survival in environment

MMWR 2007;56(RR-04)

Varicella Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Primary viremia 4 to 6 days after infection
- Multiple tissues, including sensory ganglia, infected during viremia

MMWR 2007;56(RR-04)

Varicella (Chickenpox) Clinical Features

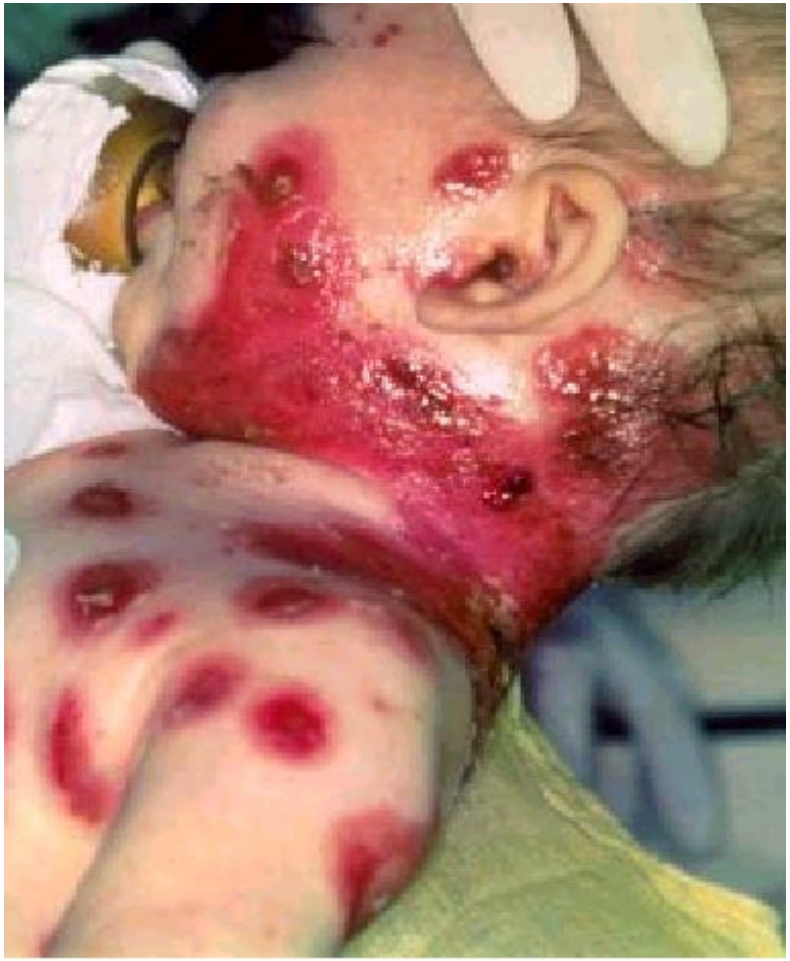
- Incubation period 14 to 16 days
- Mild prodrome for 1 to 2 days (adults)
- Rash generally appears first on the head; most concentrated on the trunk
- Successive crops over several days with lesions present in several stages of development

MMWR 2007;56(RR-04)

Varicella Complications

- **Bacterial infection of lesions**
- **Hemorrhagic varicella**
- **CNS manifestations**
- **Pneumonia (primary viral or secondary bacterial)**
- **Congenital varicella**
- **Perinatal varicella**
- **Prevaccine era:**
  - Hospitalization ~3 per 1,000 cases or 1,000/year
  - Death ~ 1 per 60,000 cases or 100/year

MMWR 2007;56(RR-04)



Varicella with a secondary bacterial infection

Increased Risk of Complications of Varicella

- Persons older than 15 years
- Infants younger than 1 year
- Immunocompromised persons
- Newborns of women with rash onset within 5 days before to 48 hours after delivery

MMWR 2007;56(RR-04)

Varicella Epidemiology

Reservoir	Human
Transmission	Person to person – respiratory tract secretions Direct contact with lesions
Temporal Pattern	Peak in late winter and spring (U.S.)
Communicability	1 to 2 days before until lesions have formed crusts May be longer in immunocompromised

MMWR 2007;56(RR-04)

Vaccines for the Prevention of Varicella (Chickenpox)

Product	ACIP Recommended Age Indications	ACIP Abbreviation
Varivax	12 months and older	VAR
ProQuad	12 months through 12 years	MMRV

Varicella Vaccine
Immunogenicity and Efficacy

- **In a pre-licensure clinical trial, 2 doses of vaccine were:**
  - 98% effective at preventing any form of varicella
  - 100% effective against severe varicella

- **In post-licensure studies, 2 doses of vaccine were:**
  - 88% to 98% effective at preventing all varicella

CDC Chickenpox About the Vaccine for Health Care Professionals www.cdc.gov/vaccines/vpd/varicella/hcp/about-vaccine.html, accessed 8/13/2018

Acceptable Evidence of Varicella Immunity

- Written documentation of age-appropriate vaccination
- Laboratory evidence of immunity or laboratory confirmation of varicella disease
- U.S.-born before 1980*
- Health care provider diagnosis or verification of varicella disease
- History of herpes zoster based on health care provider diagnosis

*Birth year immunity criterion does not apply to health care personnel or pregnant women

MMWR 2007;56(RR-4):16-17

Varicella Vaccination and Children

- **Routine recommendations:**
  - Dose 1 at 12–15 months of age
  - Dose 2 at 4–6 years of age
- **Minimum interval between doses is 3 months for children younger than 13 years of age**

Varicella Vaccination and Adolescents

- **All persons 13 years of age and older without evidence of varicella immunity**
  - 2 doses separated by at least 4 weeks
- **Do not repeat first dose because of extended interval between doses**
- **Second dose recommended for persons of any age who have only received 1 dose**

Varicella Vaccine and Immunocompromised Persons

- **Single-antigen varicella vaccine may be administered to persons with isolated humoral immunodeficiency**
- **Consider varicella vaccination for:**
  - HIV-infected children with CD4 count of 15% or higher
  - HIV-infected older children with CD4 count of 200 or higher

Varicella Adverse Reactions

- **Local reactions (pain, erythema)**
  - Varicella:
    - 19% (children)
    - 24% (adolescents and adults)
  - Rash: 3%–4%
  - May be maculopapular rather than vesicular
  - Average 5 lesions
- **Systemic reactions not common**

MMWR 2007;56(RR-04)

Adverse Reactions

MMRV and MMR + VAR

- Fever is more common in the 5–12 days after vaccination with MMRV (22%) than with MMR + VAR (15%)
- Data from CDC Vaccine Safety Datalink sites indicate the rate of febrile seizures following MMRV (9 per 10,000 vaccinated) was approximately 2 times higher than among those receiving MMR + VAR at the same visit (4 per 10,000 vaccinated)
- Merck postlicensure surveillance has identified a similar trend

MMWR 2007;56(RR-04)

MMRV Vaccine

- For the first dose of measles, mumps, rubella, and varicella vaccines at age 12–47 months, either MMR vaccine and varicella vaccine or MMRV vaccine may be used

- Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers

MMWR 2010;59(RR-3)

MMRV Vaccine

- **Administer MMRV:**
  - For the second dose of measles, mumps, rubella, and varicella vaccines at age 15 months through 12 years
  - For the first dose at age 48 months or older

MMWR 2010;59(RR-3)

MMRV Vaccine

- **Unless the parent or caregiver expresses a preference for MMRV vaccine, CDC recommends that separate MMR vaccine and varicella vaccine should be administered for the first dose for children 12–47 months of age**

MMWR 2010;59(RR-3)

Varicella and MMRV Vaccine Contraindications

- Severe allergic reaction to a vaccine component or following a prior dose
- Pregnancy or planned pregnancy within 4 weeks*
- Immunosuppression
- Family history of altered immunocompetence

*ACIP off-label recommendation

MMWR 2007;56(RR-04)

General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP) Contraindications and Precautions section www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html, accessed 08/12/2018

Varicella and MMRV Vaccine Precautions

- **Moderate or severe acute illness with or without fever**
- **Recent blood product**
  - Varicella or MMRV vaccines should not be administered for 3–11 months after receipt of antibody-containing blood products
- **Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination**
  - Avoid use of these antiviral drugs for 14 days after vaccination)
- **Use of aspirin or aspirin-containing products**

MMWR 2007;56(RR-04)\
General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP) Contraindications and Precautions section www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html, accessed 08/12/2018

Varicella-Containing Vaccines Precautions

- MMRV only: personal or family (i.e., sibling or parent) history of seizures of any etiology

- These children generally should be vaccinated with separate MMR and varicella vaccines

MMWR 2007;56(RR-04)

Varicella-Containing Vaccines: Varivax (Var) and ProQuad (MMRV)

- **Storage:**
  - Lyophilized vaccine: In the freezer between -50°C and -15°C (-58°F and +5°F)
  - Diluent: At room temperature (68°F to 77°F, 20°C to 25°C) or in the refrigerator (36°F to 46°F, 2°C to 8°C)
- **Preparation: Reconstitute the vaccine with the diluent supplied by the manufacturer just before administering**

ProQuad package insert www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm123793.pdf, accessed 8/12/2018
Varivax package insert www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142812.pdf, accessed 8/12/2018

Varicella-Containing Vaccines: Varivax (Var) and ProQuad (MMRV)

- **Administration: Subcut injection**
  - Site: Fatty tissue of the anterolateral thigh or upper outer triceps of the arm
  - Needle length and gauge: 5/8-inch, 23- to 25-gauge needle

What Do You Think?

- **In the medication room, you notice a coworker using a stock vial of sterile water to reconstitute varicella and MMR vaccines. Is this an acceptable practice?**

  - Yes
  - No

Vaccines and Diluents

- **Diluent supplied by the manufacturer is specific to the corresponding vaccine in volume, sterility, pH, and chemical balance**
- **Only use the diluent supplied with the vaccine to reconstitute it**
  - Even if the diluent is composed of sterile water or saline
- **Never use a stock vial of sterile water or normal saline to reconstitute vaccines**

Vaccine Administration Error: Wrong Diluent

- **If a lyophilized vaccine is reconstituted with the wrong diluent, the dose is invalid and should always be repeated**
  - Inactivated vaccine: Repeat the dose as soon as possible
  - Live, attenuated vaccine: If the dose can't be repeated on the same clinic day, it should be repeated no earlier than 4 weeks after the invalid dose

Vaccine with Diluents Job Aid

Vaccines with Diluents: How to Use Them

Be sure to reconstitute the following vaccines correctly before administering them! Reconstitution means that the lyophilized (freeze-dried) vaccine powder or wafer in one vial must be reconstituted (mixed) with the diluent (liquid) in another.

- Only use the diluent provided by the manufacturer for that vaccine as indicated on the chart.
- ALWAYS check the expiration date on the diluent and vaccine. NEVER use expired diluent or vaccine.

Vaccine product name	Manufacturer	Lyophilized vaccine (powder)	Liquid diluent (may contain vaccine)	Time allowed between reconstitution and use, as stated in package insert*	Diluent storage environment
ActHIB (Hib)	Sanofi Pasteur	Hib	0.4% sodium chloride	24 hrs	Refrigerator
Hiberix (Hib)	GlaxoSmithKline	Hib	0.9% sodium chloride	24 hrs	Refrigerator or room temp
Imovax (RAB_{HDCV})	Sanofi Pasteur	Rabies virus	Sterile water	Immediately†	Refrigerator
M-M-R II (MMR)	Merck	MMR	Sterile water	8 hrs	Refrigerator or room temp
MenHibrix (Hib-MenCY)	GlaxoSmithKline	Hib-MenCY	0.9% sodium chloride	Immediately†	Refrigerator or room temp
Menomune (MPSV4)	Sanofi Pasteur	MPSV4	Distilled water	Single-dose vial: Immediately† Multidose vial: 35 days	Refrigerator
Menveo (MenACWY)	GlaxoSmithKline	MenA	MenCWY	8 hrs	Refrigerator
Pentacel (DTaP-IPV/Hib)	Sanofi Pasteur	Hib	DTaP-IPV	Immediately†	Refrigerator
ProQuad (MMRV)	Merck	MMRV	Sterile water	30 min	Refrigerator or room temp
RabAvert (RAB_{PCECV})	GlaxoSmithKline	Rabies virus	Sterile water	Immediately†	Refrigerator
Rotarix (RV1)‡	GlaxoSmithKline	RV1	Sterile water, calcium carbonate, and xanthan	24 hrs	Refrigerator or room temp
Varivax (VAR)	Merck	VAR	Sterile water	30 min	Refrigerator or room temp
YF-VAX (YF)	Sanofi Pasteur	YF	0.9% sodium chloride	60 min	Refrigerator
Zostavax (HZV)	Merck	HZV	Sterile water	30 min	Refrigerator or room temp

Always refer to package inserts for detailed instructions on reconstituting specific vaccines. In general, follow the steps below.

1 For single-dose vaccine products (exception is Rotarix‡), select a syringe and needle of proper length to be used for both reconstitution and administration of the vaccine. Following reconstitution, Menomune in a multidose vial will require a new needle and syringe for each dose of vaccine to be administered. For Rotarix, see the package insert.‡

2 Before reconstituting, check labels on both the lyophilized vaccine vial and the diluent to verify that
- they are the correct two products to mix together,
- the diluent is the correct volume (especially for Menomune in the multidose vial), and
- neither the vaccine nor the diluent has expired.

3 Reconstitute (i.e., mix) vaccine *just prior to use* by
- removing the protective caps and wiping each stopper with an alcohol swab,
- inserting needle of syringe into diluent vial and withdrawing entire contents, and
- injecting diluent into lyophilized vaccine vial and rotating or agitating to thoroughly dissolve the lyophilized powder.

4 Check the appearance of the reconstituted vaccine.
- Reconstituted vaccine may be used if the color and appearance match the description on the package insert.
- If there is discoloration, extraneous particulate matter, obvious lack of resuspension, or the vaccine cannot be thoroughly mixed, mark the vial as "DO NOT USE," return it to proper storage conditions, and contact your state or local health department immunization program or the vaccine manufacturer.

5 If reconstituted vaccine is not used immediately or comes in a multidose vial (i.e., multi-dose Menomune), be sure to
- clearly mark the vial with the date and time the vaccine was reconstituted,
- maintain the product at 2°–8°C (36°–46°F); do not freeze, and
- use only within the time indicated on chart above.

* If the reconstituted vaccine is not used within this time period, it must be discarded.
† For purposes of this guidance, IAC defines "immediately" as within 30 minutes or less.
‡ Rotarix vaccine is administered by mouth using the applicator that contains the diluent. It is not administered as an injection.

IAC. Vaccines with Diluents: How to Use Them http://immunize.org/catg.d/p3040.pdf

Questions?