2016 Pink Book Webinar Series

Measles, Mumps, and Rubella

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MMR– also known as…

Measles
(rubeola, red measles,
9 day measles)

Mumps
(epidemic
parotitis)

Rubella
(German measles
or 3 day measles)

Measles

- **Considered – the most contagious VPD**
  - Infectious agent-- a paramyxovirus
  - Nasopharynx is primary site of infection
- **Incubation period: 10-12 days**
- **Prodrome: 2-4 days**
  - 3 C's -- Cough, coryza, conjunctivitis
  - Koplik spots
  - Stepwise increase in fever up to 103°F-105°F
- **Rash**
  - 2-4 days after prodrome and 14 days after exposure
  - Begins on face and upper neck
    - Maculopapular rash becomes confluent
    - Fades in order of appearance
  - Persists 5-6 days


Koplik's spots

Measles Complications

Diarrhea	8%
Otitis media	7%
Pneumonia	6%
Encephalitis	0.1%
Seizures	0.6-0.7%
Death	0.2%

Based on 1985-1992 surveillance data

Mumps

- **Infectious agent: paramyxovirus**
  - Nasopharynx and regional lymph nodes are primary sites of infection; then can spread to meninges and glands (salivary, pancreas, testes, ovaries)
- **Incubation period: 12-25 days**
- **Prodrome– nonspecific: myalgia, anorexia, malaise, headache, and low-grade fever**
- **Parotitis in 9%-94%, typically occurs within 16-18 days**
- **Pre-vaccine era: 15%-27% of infections were asymptomatic**

Mumps

Mumps Complications

Orchitis	12%-66% in postpubertal males (prevaccine)
	3%-10% (postvaccine)
Pancreatitis	3.5% (prevaccine)
Unilateral deafness	1/20,000 (prevaccine)
Death	2/10,000 from 1966-1971
	No deaths in recent U.S. outbreaks

Rubella

- **Infectious agent: togavirus**
- **Incubation period: 14 days (range 12-23 days)**
- **Prodrome**
  - Rare in children
  - Low-grade fever in adults
- **Maculopapular rash 14-17 days after exposure**
- **Lymphadenopathy occurs before rash and lasts for several weeks**

Rubella Complications

Arthralgia or arthritis	Adult female – up to 70% Children—rare
Encephalitis	1/6,000 cases
Hemorrhagic manifestations (e.g. ,thrombocytopenic purpura)	1/3,000 cases
Orchitis, neuritis, progressive panencephalitis	Rare
	No deaths in recent U.S. outbreaks

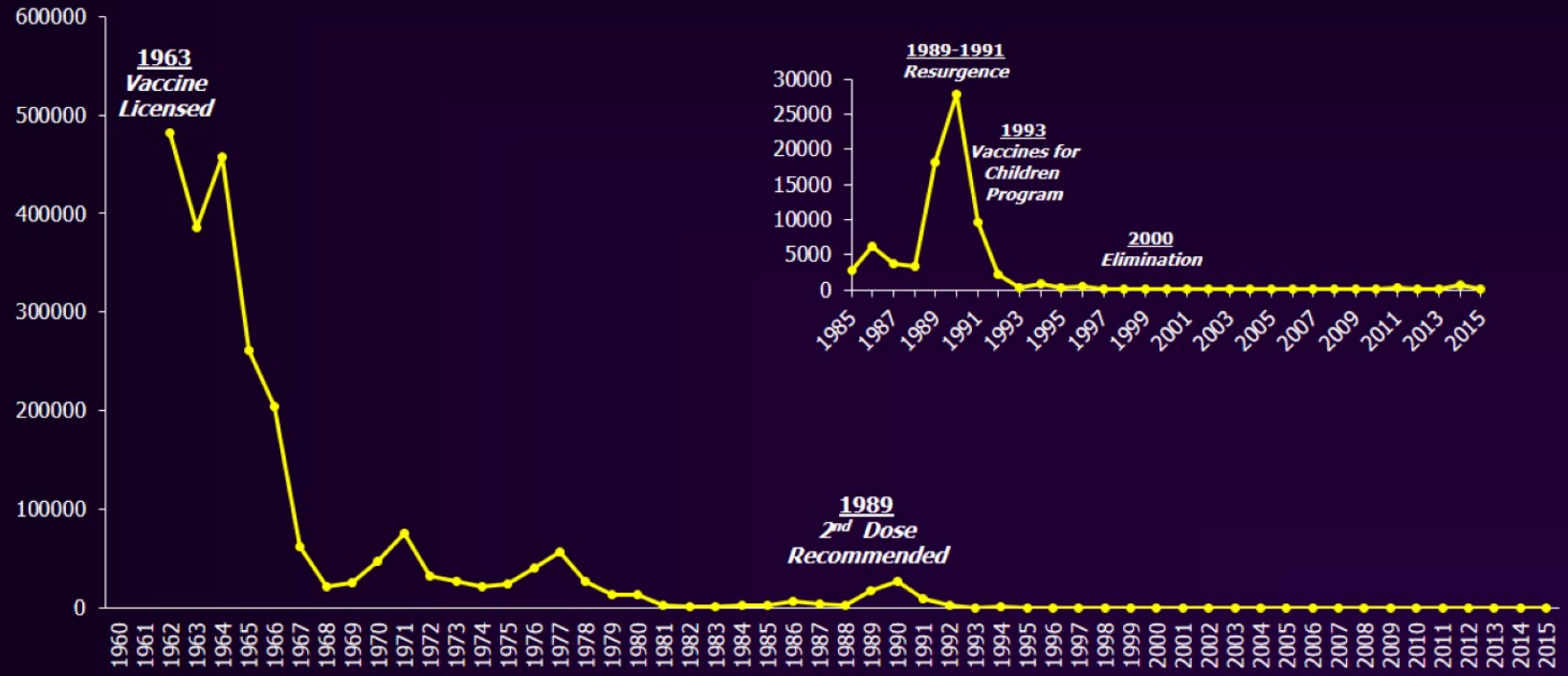
Congenital Rubella Syndrome

- **Infection may affect all organs**
  - Deafness
  - Eye defects
  - Cardiac defects
  - Microcephaly
  - Mental retardation
  - Bone alterations
  - Liver and spleen damage
- **May lead to fetal death or preterm delivery**
- **Severity of damage to fetus depends on gestational age**
- **Up to 85% of infants affected if infected during first trimester**

Epidemiology

	Measles	Mumps	Rubella
Reservoir	Human	Human	Human
Transmission	Respiratory Airborne	Airborne Direct contact with droplet or saliva	Respiratory
Temporal Pattern	Peaks in late winter/spring	Peaks in late winter/spring	Peaks in late winter/spring
Communicability	4 days before to 4 days after rash onset	Several days before and after onset of parotitis	7 days before to 5 to 7 days after rash onset

Reported Number of Measles Cases—United States, 1962-2015



CDC Immunization

Measles Cases by Year, 2010 - July 2016

Year	Cases
2010	63
2011	220
2012	55
2013	187
2014	667
2015*	189
2016**	48

- **2014**
  - 667 cases from 27 states
- **2015**
  - 189 people from 24 states and the District of Columbia
- 2016
  - 48 people from 13 states (Alabama, Arizona, California, Colorado, Florida, Georgia, Hawaii, Illinois, Massachusetts, Minnesota, Tennessee, Texas, and Utah)

Cases as of: *Jan 2, 2016, ** July 22, 2016

U.S. Economic Burden of Measles*

Year	Location	Number of cases (outbreaks)	Estimated public health cost^
2011	US	107 (16)	$2.7-5.3 million
2011	Utah	13 (2)	>$330,000
2008	California	12 (1)	$125,000
2008	Arizona	14 (1)	$800,000 (limited to cost for 2 hospitals to respond to 7 cases in their facilities)
2005	Indiana	34 (1)	$168,000
2004	Iowa	1	$142,000

www.ncbi.nlm.nih.gov/pubmed/24135574 www.nejm.org/doi/full/10.1056/NEJMoa060775 http://pediatrics.aappublications.org/content/125/4/747
http://jid.oxfordjournals.org/content/early/2011/04/25/infdis.jir115.full http://pediatrics.aappublications.org/content/116/1/e1

Measles Importation Infographic

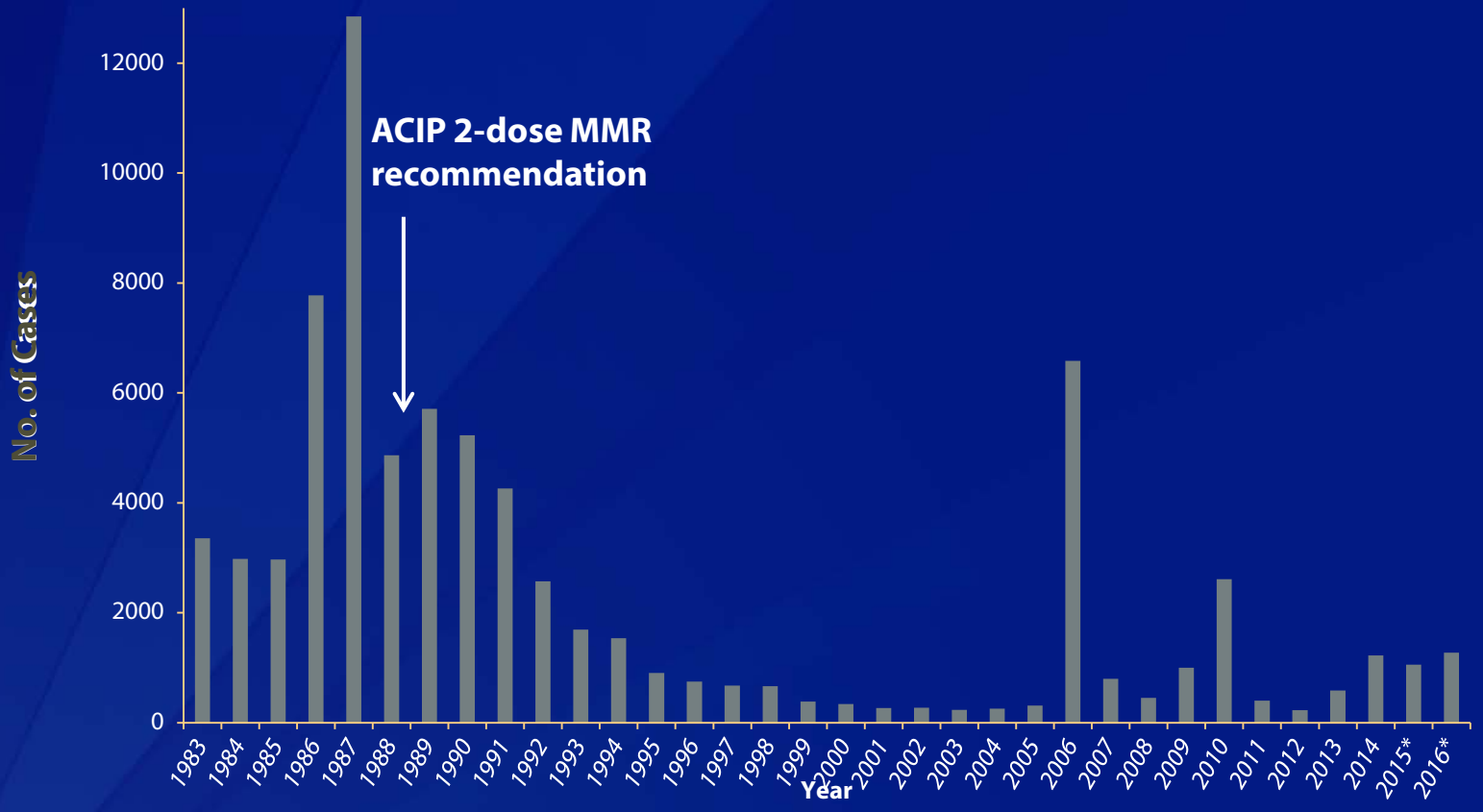
www.cdc.gov/measles/importation-infographic.html

Guidance for Healthcare Personnel

- **Be vigilant about measles**
- **Ensure all patients are up-to-date on measles-mumps-rubella vaccination**
- **Consider measles in patients with febrile rash illness and clinically compatible measles symptoms (cough, coryza, and conjunctivitis)**
- **Ask patients about:**
  - Recent travel internationally
  - Recent travel to domestic venues frequented by international travelers
  - Recent contact with international travelers
  - History of measles in the community
- **Promptly isolate patients with suspected measles**

www.cdc.gov/measles/hcp/index.html

Mumps Cases, United States, 1983-2016*



*2015 cases as of Jan 2, 2016. 2016 case count preliminary as of June 6, 2016 and subject to change.

Number of Mumps Cases by Year since 2010

Year	Cases
2010	2,612
2011	370
2012	229
2013	584
2014	1223
2015*	1057
2016**	1661

- **2009-2010 – 2 large outbreaks**
  - NYC– HS students in close-knit religious community; started with student returning from UK
  - Guam- mostly school-aged children
- **2011-2013 – several small outbreaks**
  - **college campuses**
  - California, Virginia, Maryland
- **2014 - several outbreaks**
  - National Hockey League
  - Ohio State University
  - Fordham University in NY
- 2015– 16 --several outbreaks
  - hundreds of university students
  - Iowa, Illinois

Cases as of: *Jan 2, 2016; ** July 22, 2016

Number of Rubella and Congenital Rubella Syndrome (CRS) Cases by Year since 2010

Year	Rubella	CRS
2010	5	0
2011	4	0
2012	9	3
2013	9	1
2014	8	0
2015*	2	1

*Cases as of August 28, 2015

- Median of 11 rubella cases annually 2005-2011
- 60% of rubella cases in U.S. in persons 20-49 years of age since 2004

Acceptable Presumptive Evidence of Immunity

Routine	Students (college/post-high school)	Healthcare personnel	International travelers
(1) Documented age-appropriate vaccination with live measles, mumps, rubella virus-containing vaccines, or (2) Laboratory evidence of immunity, or (3) Laboratory confirmation of disease, or (4) Born before 1957 (except rubella for women of childbearing age who could become pregnant)	(1) Documented 2 doses of live measles and mumps virus-containing vaccines; 1 dose rubella virus-containing vaccine, or (2) Laboratory evidence of immunity, or (3) Laboratory confirmation of disease, or (4) Born before 1957 (except rubella for women of childbearing age who could become pregnant)	(1) Documented 2 doses of live measles and mumps virus-containing vaccines; 1 dose rubella virus-containing vaccine, or (2) Laboratory evidence of immunity, or (3) Laboratory confirmation of disease, or (4) Born before 1957 (except rubella for women of childbearing age who could become pregnant)	(1) Documented age-appropriate vaccination with live measles, mumps, rubella virus-containing vaccines, or (2) Laboratory evidence of immunity, or (3) Laboratory confirmation of disease, or (4) Born before 1957 (except rubella for women of childbearing age who could become pregnant)

MMR Vaccine

Composition	Live attenuated viruses
Efficacy	Measles: 95% at 12 months 98% at 15 months Mumps: 88% (range 66%-95%) (2 doses) Rubella: 95% or more (1 dose)
Duration of immunity	Lifelong
Schedule	2 doses given SQ

MMRV (ProQuad) Vaccine

- Combined measles, mumps, rubella, and varicella vaccine
- 7 to 8 times as much varicella vaccine virus as monovalent varicella vaccine
- Approved only for children 12 months through 12 years of age

MMR Vaccine

- **First dose of MMR at 12-15 months**
- **12 months is the minimum age**
- **MMR given before 12 months should not be counted as a valid dose**
  - Infants as young as 6 months should receive MMR before international travel*
  - Revaccinate at 12 months of age or older

*ACIP off-label recommendation. *MMWR* 2013;62(RR-4)

MMR Vaccine (Second Dose)

- **Second dose of MMR at 4-6 years**
- **Second dose may be given at any time at least 4 weeks after the first dose**
  - Children older than 12 months of age can receive a second dose of MMR before international travel (minimum interval between doses is 4 weeks)
- **Intended to produce measles immunity in persons who failed to respond to the first dose (primary vaccine failure)**
- **May boost antibody titers in some persons**
- **People who received 2 doses of MMR vaccine as children according to the U.S. vaccination schedule are considered protected for life**

MMRV Recommendations

- **First dose at 12–47 months**
  - Either MMR and VAR or MMRV
  - Providers considering MMRV—discuss benefits/risks of both options with parents or caregivers
  - Unless parent or caregiver expresses preference for MMRV, CDC recommends MMR and varicella vaccines
- **Second dose at 15 months–12 years or first dose at 48 months and older**
  - MMRV generally preferred

Minimum Intervals

- MMR—2 doses of MMR can be separated by 4 weeks
- MMRV—2 doses of varicella vaccine must be separated by at least 3 months for children younger than 13 years of age

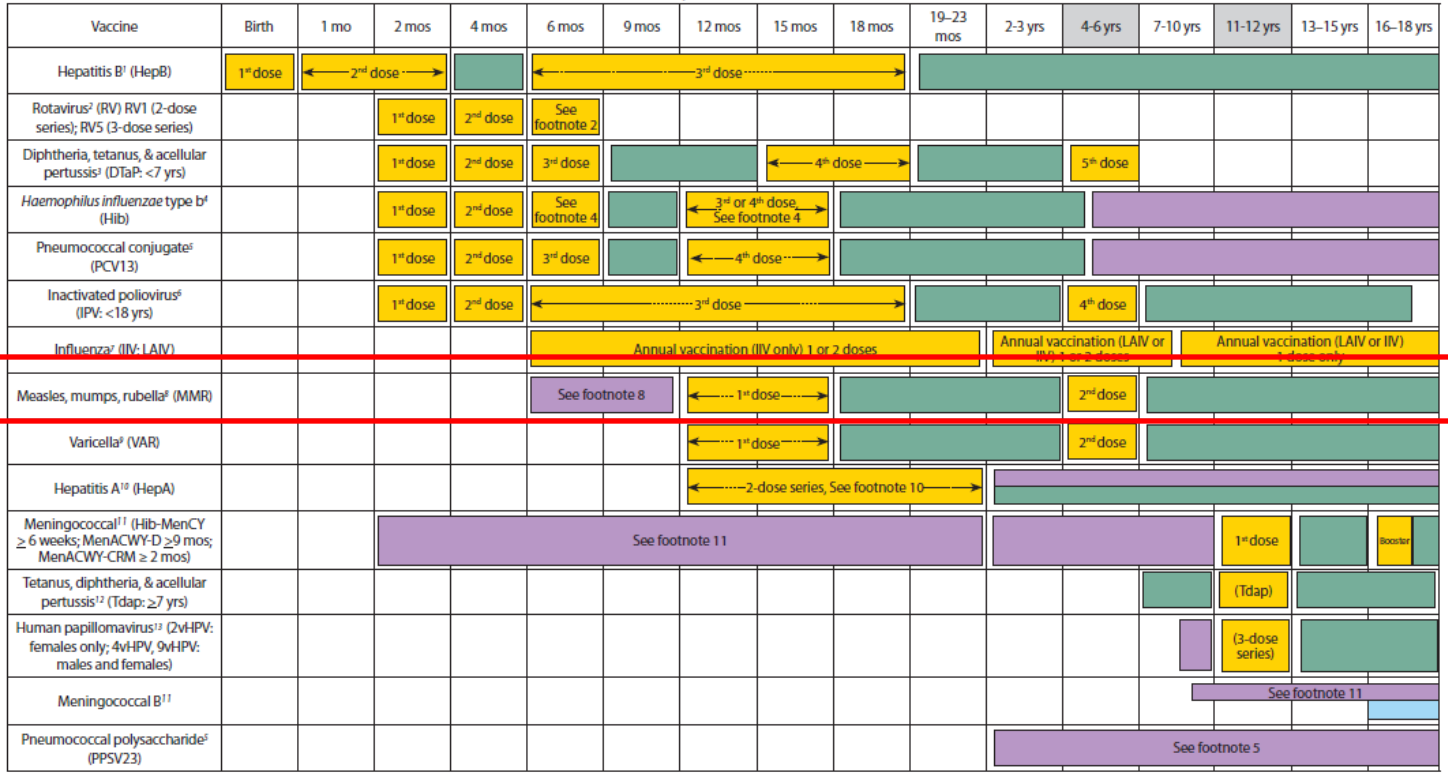
MMR Vaccine Failure

- Some recipients do not respond to the first dose
- Failure rate varies by component
- Caused by antibody, damaged vaccine, recording errors
- Most persons with vaccine failure will respond to second dose

Figure 1. Recommended immunization schedule for persons aged 0 through 18 years – United States, 2016.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded.



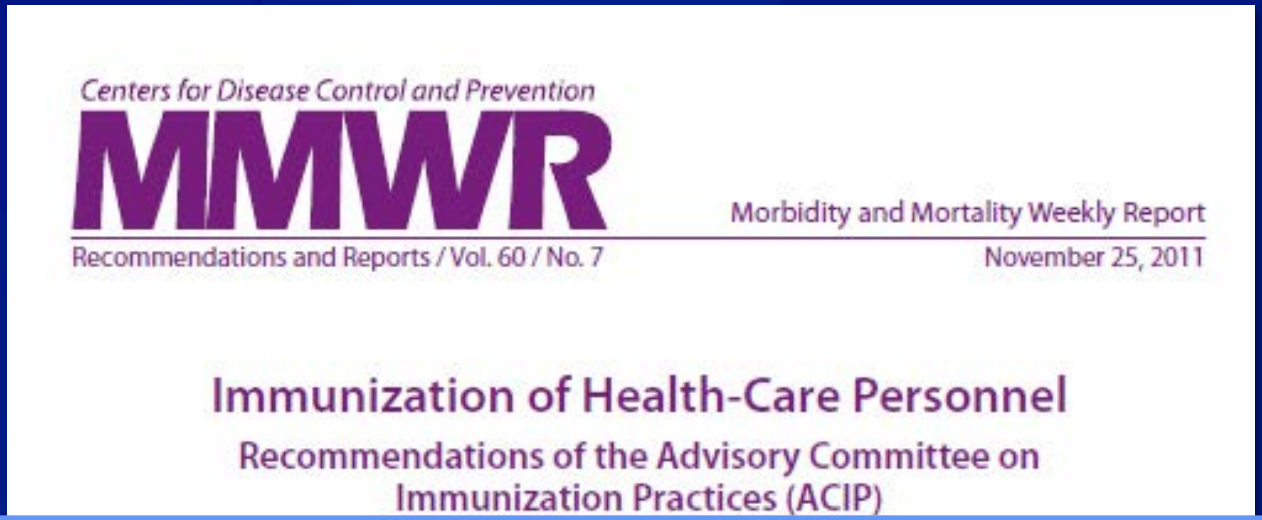
This schedule includes recommendations in effect as of January 1, 2016. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (http//www.cdc.gov/vaccines/acip), the American Academy of Pediatrics (http://www.aap.org), the American Academy of Family Physicians (http://www.aafp.org), and the American College of Obstetricians and Gynecologists (http://www.acog.org).

NOTE: The above recommendations must be read along with the footnotes of this schedule.

MMR Recommendations for Adults

- **Adults born in 1957 or later should receive 1 or more doses at least 28 days apart unless they have other evidence of immunity**
- **A routine second dose of MMR vaccine at least 28 days after the first dose is recommended for adults who are:**
  - College and post-high school students
  - Persons working in medical facilities
  - International travelers
- **Adults born before 1957 are generally presumed immune to measles, mumps, and rubella (except rubella for women of childbearing age who could become pregnant)**



All persons who work in medical facilities should be immune to measles, mumps, and rubella

www.cdc.gov/mmwr/pdf/rr/rr6007.pdf

Evidence of MMR Immunity for Healthcare Personnel Born in 1957 or After

- **Appropriate vaccination**
  - 2 doses of live measles- and mumps-containing vaccines (preferably MMR)
  - 1 dose of live rubella-containing vaccine (preferably MMR), or
- **Laboratory evidence of immunity, or**
- **Laboratory confirmation of disease**

www.cdc.gov/mmwr/pdf/rr/rr6204.pdf

Recommended Adult Immunization Schedule—United States - 2016

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended immunization schedule for adults aged 19 years or older, by vaccine and age group[1]

VACCINE ▼ / AGE GROUP ▶	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza[*,2]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap)[*,3]	Substitute Tdap for Td once, then Td booster every 10 yrs					
Varicella[*,4]	2 doses					
Human papillomavirus (HPV) Female[*,5]	3 doses					
Human papillomavirus (HPV) Male[*,5]	3 doses					
Zoster[6]					1 dose	
Measles, mumps, rubella (MMR)[*,7]	1 or 2 doses depending on indication					
Pneumococcal 13-valent conjugate (PCV13)[*,8]	1 dose					

VACCINE ▼ / AGE GROUP ▶	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years

Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications[1]

VACCINE ▼ / INDICATION ▶	Pregnancy	Immuno-compromising conditions (excluding HIV infection)[4,6,7,8,13]	HIV infection CD4+ count (cells/μL)[4,6,7,8,13]		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia and persistent complement component deficiencies[8,11,12]	Chronic liver disease	Diabetes	Healthcare personnel
			< 200	≥ 200							
Influenza*[,2]	1 dose annually										
Tetanus, diphtheria, pertussis (Td/Tdap)*[,3]	1 dose Tdap each pregnancy	Substitute Tdap for Td once, then Td booster every 10 yrs									
Varicella*[,4]	Contraindicated			2 doses							
Human papillomavirus (HPV) Female*[,5]		3 doses through age 26 yrs				3 doses through age 26 yrs					
Human papillomavirus (HPV) Male*[,5]		3 doses through age 26 yrs				3 doses through age 21 yrs					
Zoster[6]	Contraindicated			1 dose							
Measles, mumps, rubella (MMR)*[,7]	Contraindicated			1 or 2 doses depending on indication							
Pneumococcal 13-valent conjugate (PCV13)*[,8]		1 dose									

VACCINE ▼ / INDICATION ▶	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,8,15]	HIV infection CD4+ T lymphocyte count[4,6,7,8,15]		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies)[8,14]	Chronic liver disease	Diabetes	Healthcare personnel
			< 200 cells/μL	≥ 200 cells/μL							
Measles, mumps, rubella (MMR)[7,*]	Contraindicated			1 or 2 doses							

MMR Serologic Testing

- Serologic screening for measles, mumps, or rubella immunity before vaccination is not necessary and not recommended if a person has other acceptable evidence of immunity to these diseases
- Postvaccination serologic testing to verify an immune response is not recommended
- Documented age-appropriate vaccination supersedes the results of subsequent serologic testing

MMR Serologic Testing (2)

- If a person with 2 documented doses of measles- or mumps-containing vaccines is tested and determined to have negative or equivocal measles or mumps titer results, additional MMR vaccination is not recommended

- Such persons should be considered to have presumptive evidence of immunity

MMR Serologic Testing (3)

- If a person with 1 dose of rubella-containing vaccine is tested and determined to have negative or equivocal rubella titer results, additional MMR vaccination is not recommended, except for women of childbearing age
- Women of childbearing age with1 or 2 documented doses of rubella-containing vaccine and rubella-specific IgG levels that are not clearly positive should receive 1 additional dose of MMR vaccine (maximum of 3 doses) and do not need retesting

Postexposure Prophylaxis with MMR Vaccine

- **If given within 72 hours of exposure, MMR vaccine might protect or modify clinical course of measles (preferable to IG for persons ≥12months if given within 72 hours of exposure)**

- **If administered within 6 days of exposure, IG can prevent or modify measles in persons who are nonimmune**
  - Not indicated for persons who have received 1 dose of measles-containing vaccine at age ≥12 months, unless they are severely immunocompromised

www.cdc.gov/mmwr/pdf/rr/rr6204.pdf

Postexposure Prophylaxis with MMR Vaccine (2cont.)

- Postexposure MMR vaccination or IG not shown to prevent or alter the clinical severity of rubella or mumps and is not recommended

www.cdc.gov/mmwr/pdf/rr/rr6204.pdf

MMR Vaccine Contraindications and Precautions

- History of anaphylactic reaction to neomycin
- History of severe allergic reaction to any component of the vaccine
- Pregnancy
- Immunosuppression
- Moderate or severe acute illness
- Recent blood product
- Personal or family (i.e., sibling or parent) history of seizures of any etiology (MMRV only)

Vaccination of Women of Childbearing Age

- **Ask if pregnant or likely to become so in next 4 weeks***
- **Exclude those who say "yes"**
- **For others**
  - Explain theoretical risks
  - Vaccinate

*ACIP off-label recommendation; Vaccine package insert states 3 months

MMR Vaccine and HIV Infection

- MMR recommended for persons who do not have evidence of current severe immunosuppression
- Revaccination recommended for persons with perinatal HIV infection who were vaccinated before establishment of effective antiretroviral therapy (ART) with 2 appropriately spaced doses of MMR vaccine once effective ART has been established
- Prevaccination HIV testing not recommended
- MMRV not for use in persons with HIV infection

MMR Vaccine and Immunosuppressive Therapy

- **Low-dose steroids**
  - Vaccinate anytime
- **Leukemia in remission without chemotherapy for 3 months**
  - Vaccinate
- **Hematopoietic cell transplant (HCT) recipient who is immunocompetent**
  - Vaccinate 24 months after transplant

Tuberculin Skin Testing (TST)* or Tuberculosis Interferon-gamma Release Assay (IGRAs) and MMR or MMRV Vaccines

- Apply TST or IGRA testing at same visit as MMR or MMRV
- Delay TST or IGRA at least 4 weeks if MMR or MMRV given first
- Apply TST first and administer MMR or MMRV when skin test read (least favored option because receipt of MMR or MMRV is delayed)

*Previously called PPD

MMR Adverse Reactions

Fever	5%-15% (Measles)
Rash, pruritis, purpura	5% (Measles)
Joint symptoms (susceptible women)	25% (Rubella)
Thrombocytopenia	1/30,000–40,000 doses (Measles)
Lymphadenopathy	Rare
Allergic reactions (rash, pruritis, purpura)	Rare
Parotitis	Rare (Mumps)
Deafness	Rare (Mumps)
Encephalopathy	<1/1,000,000 doses (Measles)

MMRV Adverse Reactions

- **Similar to MMR**
- **Higher risk for fever and febrile seizures 5-12 days after the first dose among children 12-23 months of age**
  - 1 additional febrile seizure occurred 5-12 days after vaccination per 2,300-2,600 children compared to children who received first dose as MMR and varicella vaccine separately
- **Fever of 102°F or higher**
  - 22% of MMRV recipients
  - 15% with separate injections
- **Increased risk of febrile seizures has not been observed following use of MMRV as the second dose in the MMR and varicella series**

MMRV Vaccine Precaution

- **Children who have a personal or family history of febrile seizures or family history of epilepsy are at increased risk for febrile seizures**
  - The risk for such seizures is approximately 1 case for every 3,000-4,000 doses of MMR vaccine administered
- **Children with a personal or family history of seizures generally should be vaccinated with separate MMR and varicella vaccines**

Rubella Vaccine Arthropathy

- Acute joint symptoms in about 25% of vaccinated, susceptible adult women
- Frank arthritis-like signs and symptoms occur in about 10% of recipients
- Rare reports of chronic or persistent symptoms
- Population-based studies have not confirmed association

MMR Vaccine and Autism

"The evidence favors a rejection of a causal relationship at the population level between MMR vaccine and autism spectrum disorders (ASD)."

- Institute of Medicine, April 2001

Vaccine Storage and Handling MMR Vaccine

- **Store 36°F-46°F (2°C-8°C) (may be stored in the freezer)**
- **Store diluent at room temperature or refrigerate**
- **Protect vaccine from light**
- **Discard if not used within 8 hours after reconstitution**
  - Do not fill syringe with reconstituted vaccine until ready to administer

Vaccine Storage and Handling MMRV Vaccine

- **Store frozen between -58°F and +5°F (-50°C and -15°C)**
  - Use of dry ice may subject MMRV to temps colder than recommended
- **Store diluent at room temperature or refrigerate**
- **Vaccine may be stored at refrigerator temperature (between 36°F and 46°F, 2°C and 8°C) for up to 72 continuous hours after removal from freezer**
- **Protect vaccine from light at all times**
- **If not used immediately, the reconstituted vaccine may be stored at room temperature, protected from light, for up to 30 minutes**
- **Discard reconstituted vaccine if it is not used within 30 minutes**
- **Do not freeze reconstituted vaccine**

(August 2016) Resources for Measles, Mumps, Rubella

- **ACIP Recommendations**

  www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mmr.html
  www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mmrv.html

- **CDC Pink Book (Epidemiology and Prevention of Vaccine-Preventable Diseases (13th edition)--**

  www.cdc.gov/vaccines/pubs/pinkbook/meas.html
  www.cdc.gov/vaccines/pubs/pinkbook/mumps.html
  www.cdc.gov/vaccines/pubs/pinkbook/rubella.html

- **FDA Vaccine Package Inserts**

  www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123789.pdf
  www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123793.pdf
  www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123796.pdf

- **MMR Infection/Disease**
  - **Manual for Surveillance of Vaccine-Preventable Diseases**
    www.cdc.gov/vaccines/pubs/surv-manual/index.html,
  - **www.cdc.gov/measles/index.html**
  - **www.cdc.gov/mumps/index.html**
  - **www.cdc.gov/vaccines/vpd-vac/rubella/default.htm#disease**

- **MMR Vaccination**
  - **www.cdc.gov/vaccines/vpd-vac/measles/default.htm**
  - **www.cdc.gov/vaccines/vpd-vac/mumps/default.htm**
  - **www.cdc.gov/vaccines/vpd-vac/rubella/default.htm**

Additional Resources:

- **Acceptable evidence of MMR immunity** (Table 3, page 19)
  www.cdc.gov/mmwr/pdf/rr/rr6204.pdf
- **MMR dosing intervals (CDC Pink Book):**
  Recommended intervals between administration of immune globulin preparations and measles-or varicella-containing vaccine

- **2013 Infectious Disease Society of America Guidelines:**

  http://cid.oxfordjournals.org/content/58/3/e44.full.pdf+html

- **Economic evaluation:** Zhou F et al. An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. J Infect Dis. 2004 May 1;189, Suppl 1:S131-45.

- **Immunization Action Coalition**

  www.immunize.org/measles/
  www.immunize.org/mumps/
  www.immunize.org/rubella/

- **Children's Hospital of Philadelphia Vaccine Education Center**

  www.chop.edu/service/vaccine-education-center/a-look-at-each-vaccine/mmr-measles-mumps-and-rubella-vaccine.html

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