CDC Home | Search | Health Topics A-Z

MMWR

Recommendations and Reports

November 23, 1990 / 39(RR15);1-18

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail.

Rubella Prevention -- Recommendations of the Immunization Practices Advisory Committee (ACIP)

These revised Immunization Practices Advisory Committee (ACIP) recommendations for the prevention of rubella update the previous recommendations (MMWR 1984;33:301-10,315-8) to include implementation of a new two-dose schedule for measles-mumps-rubella (MMR) vaccine. Current information about vaccine effectiveness, duration of immunity, vaccination in pregnancy, and progress in controlling congenital rubella syndrome (CRS) is also included. INTRODUCTION

Before licensure of rubella vaccine, rubella was a common childhood rash disease. Currently, it can be often overlooked or misdiagnosed because its signs and symptoms vary. The most common manifestations--postauricular and suboccipital lymphadenopathy, arthralgia, transient erythematous and sometimes pruritic rash, and low fever--may not be recognized as rubella. Similar exanthematous illnesses are caused by adenoviruses, enteroviruses, and other common respiratory viruses. Moreover, up to 30% of infections are subclinical and many are unrecognized. Transient polyarthralgia and polyarthritis sometimes accompany or follow rubella. Among infected adults (particularly among women), joint manifestations occur frequently (up to 70% of cases) and can be considered an expected manifestation of adult infection. Central nervous system complications and thrombocytopenia have been reported at rates of 1 per 6,000 cases and 1 per 3,000 cases, respectively. The former is more likely to occur among adults; the latter, among children.

By far the most important consequences of rubella are the miscarriages, stillbirths, fetal anomalies, and therapeutic abortions that result from rubella infection in early pregnancy, especially in the first trimester. Preventing fetal infection and consequent congenital rubella syndrome (CRS) is the objective of rubella immunization programs.

The most commonly described anomalies associated with CRS are auditory (sensorineural deafness), ophthalmic (cataracts, microphthalmia, glaucoma, chorioretinitis), cardiac (patent ductus arteriosus, pulmonary artery stenosis, atrial or ventricular septal defects), and neurologic (microcephaly, meningoencephalitis, mental retardation). In addition, infants with CRS frequently are retarded in growth and have radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, and purpuric skin lesions (blueberry-muffin appearance). Moderate and severe cases of CRS are readily recognizable at birth; mild cases (e.g., those with only slight cardiac involvement or deafness) may not be detected for months or years after birth or not at all. Although CRS has been estimated to occur among 20%-25% or more of infants born to women who acquire rubella during the first trimester, the actual risk of infection and subsequent defects may be considerably higher. If infants infected in the first trimester are followed for at least 2 years, up to 85% (1) will be found to be affected. The risk of any defect declines approximately 10%-24% for infections that occur between the 13th and 16th weeks of gestation, with

defects rarely occurring after infection beyond the 20th week. However, fetal infection without clinical stigmata of CRS can occur at any stage of pregnancy. Inapparent maternal rubella infection can also result in congenital malformations.

In 1983, the average lifetime expenditure associated with an infant with CRS was estimated to be more than $200,000 (2), which included costs associated with institutionalization of the retarded, blind, and/or deaf and the education of hearing- and sight-impaired teenagers and adolescents.

Postinfection immunity appears to be long-lasting. However, as with other viral diseases, reexposure to natural rubella occasionally leads to reinfection without clinical illness or detectable viremia. Because many rash illnesses may mimic rubella infection and many rubella infections are unrecognized, the only reliable evidence of immunity to rubella is the presence of specific antibody. Laboratories that regularly perform antibody testing are generally the most reliable because their reagents and procedures are strictly standardized (see Laboratory Diagnosis section).

Before rubella vaccines became available in 1969, most rubella cases occurred among school-age children. Because control of rubella in the United States was originally based on interrupting transmission, the primary target group for vaccination was children of both sexes. Secondary emphasis was placed on vaccinating susceptible adolescents and young adults, especially females. By 1977, vaccination of children greater than or equal to 12 months of age had resulted in a marked decline in the reported rubella incidence among children and had interrupted the characteristic 6- to 9-year rubella epidemic cycle. However, this vaccination strategy had less effect on reported rubella incidence among persons greater than or equal to 15 years of age (i.e., the childbearing ages for women). This age group subsequently accounted for greater than 70% of reported rubella patients with known ages. Approximately 10%-20% of this latter population continued to be susceptible. This proportion was similar to that of prevaccine years, and reported CRS continued at a low but relatively constant endemic level (an annual average of 32 reported confirmed and compatible* cases between 1971 and 1977).

- A confirmed case has at least one defect in categories A or B and laboratory confirmation of rubella infection. A compatible case has any two complications listed in A or one from A and one from B without laboratory confirmation.

    A. Cataracts/congenital glaucoma (either or both count as one),

    congenital heart disease, loss of hearing, pigmentary retinopathy.

B. Purpura, splenomegaly, jaundice, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease.

Beginning in the late 1970s, increased efforts were made to vaccinate junior and senior high school students effectively and to enforce rubella immunization requirements for school entry (3). Efforts were made to vaccinate all susceptible military recruits. Published accounts of rubella outbreaks in hospitals caused concern about the need to screen and/or vaccinate susceptible personnel. Many states stressed the need for ensuring proof of rubella immunity (i.e., documentation of vaccination or seropositivity) for college entrance. These efforts, combined with the 1977 Childhood Immunization Initiative and the 1978 Measles Elimination effort (which encouraged use of combined vaccines containing measles and rubella antigens), have led to decreases in reported rubella in all age groups (4,5). The value of this strategy is exemplified by the experience with vaccinating all military recruits, which has virtually eliminated rubella from military bases (6). Similar results could be achieved by ensuring proof of immunity of all employees, all college students and staff, all prison personnel, and all hospital personnel, including physicians, nurses, health-profession students, technicians, and dietary workers.

The number of rubella vaccine doses administered annually in the public sector to persons greater than or equal to 15 years of age increased more than tenfold from 28,000 doses in 1977 to greater than 300,000 doses per year from 1980 through 1988. It is likely that use of rubella vaccine for postpubertal adults was even higher in the private sector. By 1980, reported incidence rates among adolescents and young adults were lower than those among young children. Children less than 5 years of age have accounted for approximately one-fourth to one-

third of cases throughout the 1980s.

In 1988, 225 cases of postnatal rubella were reported, the lowest annual total ever reported to CDC. Only 38% (48 of 127) of rubella cases for which age was known were reported among persons greater than or equal to 15 years of age. The estimated incidence rate for persons greater than or equal to 15 years of age was the lowest ever reported--0.04 per 100,000 persons. Provisional data showed that a modest resurgence in annual number of reported rubella cases occurred in 1989. However, the 373 cases reported represented only a small fraction of the 60,000 cases reported in 1969 when vaccine became available.

With the decrease in incidence of rubella in postpubertal age groups, the reported number of infants born with CRS declined from 20-70 annual cases in the 1970s to only two cases in 1985, and CRS is on the verge of elimination (7). Nevertheless, the provisional data indicate that infants with CRS continue to be born (the number of reported births of children with indigenous CRS has ranged from 13 for 1986 to one for 1989). From 6% to 11% of postpubertal females may remain seronegative, according to data from premarital screening programs in selected states (8), and higher rates of seronegativity have been reported (9). Prevention of CRS and rubella in postpubertal populations continues to deserve attention (10). LIVE RUBELLA VIRUS VACCINE

The live rubella virus vaccine* currently distributed in the United States is prepared in human diploid cell culture. In January 1979, this vaccine (RA 27/3) replaced the HPV-77:DE-5 vaccine grown in duck embryo cell culture because it induced higher seroresponse, greater resistance to reinfection, and lower reaction rate. Although both subcutaneous and intranasal administration of the vaccine have been studied, the vaccine is licensed only for subcutaneous administration. The vaccine is produced in monovalent form (rubella only) and in combinations: measles-rubella (MR), rubella-mumps, and measles-mumps-rubella (MMR) vaccines.

*Official name: rubella virus vaccine, live.

In clinical trials, greater than or equal to 95% of susceptible persons who received a single dose of rubella vaccine when they were greater than or equal to 12 months of age developed antibody (11-13). Clinical efficacy and challenge studies have shown that greater than 90% of vaccinees have protection against both clinical rubella and viremia for at least 15 years (14-17). Available follow-up studies indicate that vaccine-induced protection is long-term, probably lifelong; therefore, a history of vaccination can be considered presumptive evidence of immunity.

Although vaccine-induced titers are generally lower than those stimulated by rubella infection (18,19), vaccine-induced immunity usually protects against both clinical illness and viremia after natural exposure. In studies that have attempted to reinfect persons artificially who received RA 27/3 vaccine, vaccinees demonstrated a resistance to reinfection similar to the resistance that follows natural infection (20). A small number of reports have indicated that viremic reinfection following exposure may occur in vaccinated individuals with low levels of detectable antibody (15). The frequency and consequences of this phenomenon are currently unknown but believed to be rare. These reports are to be expected, because there are also rare reports of clinical reinfection and fetal infection following disease-induced immunity (21).

Some vaccinees intermittently shed small amounts of virus from the pharynx 7-28 days after vaccination. However, studies of greater than 1,200 susceptible household contacts and experience gained over 20 years of vaccine use failed to identify transmission of vaccine virus. These findings indicate that vaccinating susceptible children whose mothers or other household contacts are pregnant does not present a risk. Rather, vaccination of such children provides protection for these pregnant women. VACCINE USE Rubella Immunity

Persons can be considered immune to rubella only if they have documentation of a) laboratory evidence of rubella immunity or b) adequate immunization with at least one dose of rubella vaccine on or after the first birthday. Many persons will receive two doses of rubella vaccine as a result of the new two-dose schedule for MMR vaccination, which is recommended to improve control of measles (22). Clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status. General Recommendations

Persons greater than or equal to 12 months of age should be vaccinated, unless they are immune. All children,

adolescents, and adults--particularly females--are considered susceptible and should be vaccinated if there are no contraindications (see section on PRECAUTIONS AND CONTRAINDICATIONS). Those who should be vaccinated include persons who may be immune to rubella but who lack adequate documentation of immunity. All vaccinations should be documented in the patient's permanent medical record (23).

Vaccinating susceptible individuals both protects them against rubella and prevents their spreading the virus. Vaccinating susceptible postpubertal females confers individual protection against rubella-induced fetal injury. Vaccinating adolescents or adults in high-risk population groups, such as those in colleges, places of employment, or military bases, protects them against rubella and reduces the chance of epidemics. Dosage

The dose of 0.5 ml of reconstituted vaccine (whether as a monovalent product or, preferably, in combination with measles and mumps antigens) should be administered subcutaneously. Age at Vaccination

Live rubella virus vaccine is recommended for all children greater than or equal to 12 months of age. It should not usually be given to younger infants, because persisting maternal antibodies may interfere with seroconversion. When the rubella vaccine is part of a combination that includes the measles antigen, the combination vaccine should generally be given to children at greater than or equal to 15 months of age to maximize measles seroconversion. A second dose of MMR is recommended at school entry, although in some localities the decision may be made to administer the second dose at older ages (e.g., entry to middle or junior high school) (21,24). Initial vaccination with MMR may be given at 12 months of age to children living in areas at high risk for measles transmission among preschool-age children (i.e., a county with greater than 5 cases among preschool-age children during each of the last 5 years, a county with a recent outbreak among unvaccinated preschool-age children, or a county with a large inner-city, urban population). These recommendations may be implemented for an entire county or in smaller, defined, high-risk areas (21). MMR may be administered to children before their first birthday if monovalent measles vaccine is not readily available. Infants vaccinated with MMR before the first birthday should be considered unvaccinated for purposes of determining the need for further vaccination. They should be revaccinated with rubella, measles, and mumps vaccines, preferably by starting the two-dose schedule of MMR with a first dose given generally at 15 months of age.

Older children who have not received rubella vaccine should be vaccinated promptly. Because a history of rubella illness is not a reliable indicator of immunity, all children should be vaccinated unless there are contraindications (see section on PRECAUTIONS AND CONTRAINDICATIONS). Vaccination of Women of Childbearing Age

The Immunization Practices Advisory Committee (ACIP) has weighed several factors in developing recommendations for vaccinating women of childbearing age against rubella. Although there may be concern about giving rubella vaccine during pregnancy, available data on previously and currently available rubella vaccines indicate that the risk of teratogenicity from live rubella vaccines is small. From January 1971 to April 1989, CDC followed to term 321 known rubella-susceptible pregnant women who had been vaccinated with live rubella vaccine within 3 months before or 3 months after conception. Ninety-four women received HPV-77 or Cendehill vaccines, one received vaccine of unknown strain, and 226 received RA 27/3 vaccine. None of the 324 infants (three of the mothers receiving RA 27/3 vaccine delivered twins) had malformations compatible with congenital rubella infection. This total included the five infants who were born to these susceptible women and who had serologic evidence of subclinical infection. (Three of the infants were exposed to HPV-77 or Cendehill vaccine; two were exposed to RA 27/3 vaccine.)

On the basis of the experience to date, the estimated risk of serious malformations attributable to RA 27/3 rubella vaccine, derived from the binomial distribution with 95% confidence limits, is from 0% to 1.6%. (If the susceptible infants exposed to other rubella vaccines are included, the risk is from 0% to 1.2%.) This risk is substantially less than the greater than or equal to 20% risk of CRS associated with maternal infection during the first trimester of pregnancy (25). Moreover, the observed risk with both the HPV-77 or Cendehill and RA 27/3 strains of vaccine is zero.

Rubella vaccine virus has been isolated from aborted tissue from one (3%) of 35 susceptible women who had been given RA 27/3 vaccine while pregnant, whereas virus was isolated from aborted tissue from 17 (20%) of 85 susceptible women who had been given HPV-77 or Cendehill vaccines while pregnant. This finding provides additional evidence that the RA 27/3 vaccine poses no greater risk of teratogenicity than did the HPV-77 or Cendehill vaccines.

The risk of vaccine-associated defects is negligible and should not ordinarily be a reason to consider interruption of pregnancy. Because birth defects, one-third of which are serious, are noted in 3% of all births, confusion about the etiology of birth defects may result if vaccine is administered during pregnancy.

As of April 30, 1989, CDC discontinued accepting new enrollees into its registry of women vaccinated with rubella vaccine during pregnancy. However, all suspected cases of CRS, whether presumed to be due to wild-virus or vaccine-virus infection, should continue to be reported through state and local health departments.

The continuing occurrence of rubella among women of childbearing age (9) and the lack of evidence for teratogenicity from the vaccine strongly indicate the need to continue vaccination of susceptible adolescent and adult females of childbearing age. However, because of concern about risk for the fetus, women of childbearing age should receive vaccine only if they state that they are not pregnant and are counseled not to become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against rubella, reasonable practices in a rubella immunization program include a) asking women if they are pregnant, b) excluding those who state that they are, c) explaining the concern about risk for the fetus to the others, and d) explaining the importance of not becoming pregnant during the 3 months following vaccination. Use of Vaccine Following Exposure to Rubella

There is no conclusive evidence that giving live rubella virus vaccine following exposure will prevent illness. However, a single exposure may not cause infection. Because postexposure vaccination will protect an individual exposed in the future, and because there is no evidence that vaccinating an individual who is incubating rubella is harmful, vaccination is still recommended, unless otherwise contraindicated. Use of Human Immune Globulin Following Exposure to Rubella

Immune globulin (IG) given after exposure to rubella will not prevent infection or viremia, but it may modify or suppress symptoms and create an unwarranted sense of security. The routine use of IG for postexposure prophylaxis of rubella in early pregnancy is not recommended. Infants with congenital rubella have been born to women who were given IG shortly after exposure. The only instance in which IG might be useful would be when a pregnant woman who has been exposed to rubella would not consider termination of pregnancy under any circumstances. Recent Administration of IG

Vaccine should be administered approximately 2 weeks before or deferred for approximately 3 months after receipt of IG, because passively acquired antibodies might interfere with the response to the vaccine. However, previous administration of anti-Rho (D) IG (human) or blood products does not generally interfere with an immune response and is not a contraindication to postpartum vaccination. In this situation, persons who have received the globulin or blood products should be serologically tested 6-8 weeks after vaccination to assure that seroconversion has occurred. Obtaining laboratory evidence of seroconversion in other vaccinees is not necessary. Vaccine Shipment and Storage

During storage, before reconstitution, rubella vaccine must be kept at a temperature of 2 C-8 C (35.6 F-46.4 F) or colder. It must also be protected from light, which may inactivate the virus. Reconstituted vaccine should be discarded if not used within 8 hours. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice. ADVERSE EVENTS

Vaccinees can develop low-grade fever, rash, and lymphadenopathy after vaccination. Arthralgia and transient arthritis occur more frequently in susceptible adults than in children, and more frequently in susceptible postpubertal females than in susceptible men. Arthralgia or arthritis are rare following vaccination of children with RA 27/3 vaccine (10). By contrast, approximately 25% of susceptible postpubertal females develop arthralgia following RA 27/3 vaccination, and approximately 10% have been reported to have arthritis-like signs

and symptoms (26-28). Rarely, transient peripheral neuritic complaints, such as paresthesias and pain in the arms and legs, have occurred (29).

When joint symptoms occur, or when pain and/or paresthesias not associated with joints occur, they generally begin 1-3 weeks after vaccination, persist for 1 day-3 weeks, and rarely recur. Adults with joint symptoms following rubella vaccination usually have not had to disrupt work activities. Infrequently, susceptible vaccinees, primarily adult females, reportedly have developed chronic or recurrent arthralgias, sometimes with arthritis or neurologic symptoms including paresthesias, carpal tunnel syndrome, and blurred vision. Onset of these symptoms occurred within 1 month of initial vaccination. One group of investigators has reported the frequency of chronic joint symptoms and signs in adult females to be as high as 5%-11% (30,31); however, other data from the United States and experience from other countries that use the RA 27/3 strain suggest that such occurrences are rare. In comparative studies, the frequency of chronic joint complaints is substantially higher following natural infection than following vaccination (31).

The mechanism for joint abnormalities after vaccination is unclear. Joint destruction rarely has been reported (32). One group of investigators has reported that viral persistence in peripheral blood lymphocytes has occurred among a substantial number of these patients (33). This same group has postulated that defective immunity, in the form of partial antibody, detected by an enzyme immunoassay (EIA) kit but not by hemagglutination-inhibition (HI) assay, may facilitate viral persistence (30,34). No conclusive evidence has shown that immune complexes play a role in disease pathogenesis. Rubella virus has been isolated from both peripheral blood lymphocytes and synovial cells from children with chronic arthritis, primarily juvenile rheumatoid arthritis; however, a causal relationship has not been proven (35).

Available published data indicate that only susceptible vaccinees have side effects of vaccination (36). There is no conclusive evidence of an increased risk of these reactions for persons who are already immune when vaccinated. PRECAUTIONS AND CONTRAINDICATIONS Pregnancy

Pregnant women should not be vaccinated with rubella vaccine. If a pregnant woman is vaccinated or if she becomes pregnant within 3 months after vaccination, she should be counseled about the concern for the fetus, but rubella vaccination during pregnancy should not ordinarily be a reason to consider interruption of pregnancy. Febrile Illness

Vaccination of persons with severe febrile illness should be postponed until recovery. However, susceptible children with mild illnesses, such as upper respiratory infection, should be vaccinated. Considering the importance of protecting against rubella, medical personnel should use every opportunity to vaccinate susceptible individuals. Allergies

Hypersensitivity reactions rarely follow the administration of live rubella vaccine. Most of these reactions are considered minor and consist of wheal and flare or urticaria at the injection site.

Live rubella vaccine is produced in human diploid cell culture. Consequently, a history of anaphylactic reactions to egg ingestion needs to be taken into consideration only if measles or mumps antigens are to be included with rubella vaccine.

Since rubella vaccine contains trace amounts of neomycin (25 ug), persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive rubella vaccine. Most often, neomycin allergy is manifested as a contact dermatitis, which is a delayed-type (cell-mediated) immune response, rather than anaphylaxis. In such individuals, the adverse reaction, if any, to neomycin in the vaccine would be an erythematous, pruritic nodule or papule at 48-96 hours. A history of contact dermatitis to neomycin is not a contraindication to receiving rubella vaccine. No preparations of live rubella vaccine contain penicillin. Altered Immunocompetence

Replication of vaccine viruses can be enhanced in persons with immune deficiency diseases and in persons with immunosuppression, as occurs with leukemia, lymphoma, generalized malignancy, or resulting from therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids. Although there is no evidence that

wild rubella or rubella vaccine virus causes serious illness in immunocompromised persons, concern exists about the risk of any live virus vaccine, including rubella vaccine, for such persons. Therefore, such patients should not be given live rubella virus vaccine--except persons with symptomatic infection with human immunodeficiency virus (HIV), who can receive MMR (see below).

Patients with leukemia in remission who have not received chemotherapy for at least 3 months may be vaccinated with live virus vaccines. Short-term (less than 2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy (e.g., nasal, skin), long-term alternate-day treatment with low to moderate doses of short-acting systemic steroids, and intraarticular, bursal, or tendon injection of corticosteroids are not immunosuppressive in their usual doses and do not contraindicate rubella vaccine administration.

The growing number of infants and preschoolers with HIV infection has directed special attention to the appropriate immunization of such children. Asymptomatic children do not need to be evaluated and tested for HIV infection before decisions concerning vaccination are made. Asymptomatic HIV-infected persons in need of MMR should receive it. MMR should be considered for all symptomatic HIV-infected children, including children diagnosed as having acquired immunodeficiency syndrome (AIDS), because measles disease in these children can be severe. Limited data on MMR vaccination among asymptomatic and symptomatic HIV-infected children indicate that MMR has not been associated with serious or unusual adverse events, although antibody responses have been variable (37-39).

The administration of high-dose intravenous immune globulin (IGIV) to HIV-infected children at regular intervals is being studied to determine whether it will prevent a variety of infections. For those children who have received IGIV within the 3 months preceding vaccination, MMR vaccine may be ineffective. SIMULTANEOUS ADMINISTRATION OF CERTAIN LIVE VIRUS VACCINES

In general, the simultaneous administration of the most widely used live and inactivated vaccines does not impair antibody responses or increase rates of adverse reactions (40,41). The administration of MMR vaccine yields results similar to that of individual measles, mumps, and rubella vaccines at different sites or at different times.

Equivalent antibody responses and no clinically important increases in the frequency of adverse events occur when diphtheria-tetanus-pertussis vaccine (DTP), Haemophilus influenzae b conjugate vaccine (HbCV), oral polio vaccine (OPV), or inactivated polio vaccine (IPV) are administered with MMR either simultaneously at different sites or at separate times. Routine simultaneous administration of MMR, DTP, HbCV, and OPV (or IPV) to all children greater than or equal to 15 months who are eligible to receive these vaccines is recommended. Vaccination with MMR and HbCV at 15 months, followed by DTP and OPV (or IPV) at 18 months remains an acceptable alternative for children whose parents/caregivers are known generally to follow health-care recommendations. If the child might not be brought back for future immunizations, simultaneous administration of all vaccines (including DTP, OPV, MMR, and HbCV) appropriate to the age and previous vaccination status of the recipient is recommended. REPORTING OF ADVERSE EVENTS

The National Childhood Vaccine Injury Act of 1986 requires physicians and other health-care providers who administer vaccines to maintain permanent immunization records and to report occurrences of adverse events specified in the Act (22). These adverse events, as well as other adverse events that require medical attention, must be reported to the U.S. Department of Health and Human Services. Until November 1, 1990, separate systems for reporting adverse events existed for vaccines purchased with public funding and for vaccines purchased in the private sector. After November 1, 1990, all reportable events should be reported to the Vaccine Adverse Events Reporting System (VAERS). Adverse events other than those specified in the Act, especially events that are serious or unusual, should also be reported to VAERS. VAERS forms and instructions are available in the Food and Drug Administration's FDA Drug Bulletin and the Physicians' Desk Reference, or they may be obtained by calling VAERS at 1-800-822-7967. STRATEGIES FOR ELIMINATING CRS

The widespread vaccination of school-age children since 1969 has effectively prevented major epidemics of rubella and congenital rubella in the United States. With continued vaccination of children at levels approaching 100%, an immune birth cohort will eventually replace the 6%-25% of persons of childbearing age currently

susceptible to rubella, and rubella can be expected to disappear. Recent data suggest that the rates of rubella susceptibility among postpubertal females and in reported cases of rubella continue to decline (7,8). Because the process of replacing the adult cohort with immune persons will take years, cases of CRS can still be expected to occur (42-45).

Elimination of CRS can be hastened by expanding existing efforts to vaccinate susceptible adolescents and young adults, particularly females of childbearing age, along with continuing routine vaccination of children. In 1985-1988, 40%-60% of the rubella cases occurred in older, postadolescent populations, clearly indicating that rubella in postpubertal populations still occurs. Effective vaccination of all susceptible children in junior and senior high schools can be expected to contribute greatly to the elimination of CRS. Such efforts have resulted in decreases in the reported incidence of rubella in all persons and in the incidence of reported CRS.

The major components of a strategy to eliminate CRS are achieving and maintaining high immunization levels, accurate surveillance of rubella and CRS, and prompt outbreak-control measures. The following recommendations are presented to help preserve the level of rubella and CRS control already achieved and to bring about the further reduction in susceptibility that will be required to eliminate CRS. Ongoing Programs

The primary strategy for eliminating CRS in the United States is to interrupt rubella transmission by achieving and maintaining high immunization levels among all children. Official health agencies should take steps, including developing and enforcing immunization requirements, to ensure that all students in grades kindergarten through 12 are protected against rubella, unless vaccination is contraindicated. School-entry laws should be vigorously enforced. States that do not require proof of immunity of students at all grade levels should consider expanding existing laws or regulations to include the age groups not yet protected.

Recent age-specific data indicate that preschool-age children account for an important proportion of reported rubella cases. Proof of rubella immunity for attendance at day-care centers should be required and enforced. Licensure should depend on such requirements.

To hasten the elimination of CRS, continued effort should be directed toward vaccinating susceptible women of childbearing age. A multifaceted approach is necessary (46). General Principles --Voluntary vaccination programs have been less successful than mandatory programs. The military services require rubella immunity of recruits and have essentially eliminated rubella from military bases (6). In all settings where young adults congregate, men and women should be included in vaccination programs, because men may transmit disease to susceptible women. --If it is practical and if reliable laboratory services are available, women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility (so that vaccine is given only to proven susceptible women) can be effective but is expensive. Also, two visits to the health-care provider would be necessary--one for screening and one for vaccination. Accordingly, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing--and may be preferable, particularly when costs of serology are high and follow-up of identified susceptible women for vaccination is not assured. Vaccinated women should be counseled to avoid becoming pregnant for a 3-month period following vaccination. Routine serologic screening of men is not recommended. --Vaccine should be administered only if there is no contraindication to vaccination. --Health-care providers are encouraged to use MMR in routine childhood-vaccination programs and whenever rubella vaccine is to be given to persons also likely to be susceptible to measles and/or mumps. Premarital Screening and Vaccination

Routine premarital testing for rubella antibody identifies many susceptible women before pregnancy (47). Documented histories of rubella vaccination or serologic evidence of immunity should be considered acceptable proof of immunity. To ensure a significant reduction in susceptibility through premarital screening, more aggressive follow-up of women found to be susceptible is required. Postpartum Vaccination

Prenatal screening should be carried out on all pregnant women not known to be immune. Women who have just delivered babies should be vaccinated before discharge from the hospital, unless they are known to be immune

(48). Although such women are unlikely to become pregnant, counseling to avoid conception for 3 months following vaccination is still necessary. It is estimated that postpartum vaccination of all women not known to be immune could have prevented approximately 40% of recent CRS cases (4,6). Breast-feeding is not a contraindication to vaccination, even though virus may be excreted in breast milk, and infants may be infected (49-51). Women attending abortion clinics should be vaccinated after termination of pregnancy. Routine Vaccination in any Medical Setting

Vaccination of susceptible women of childbearing age should be part of routine general medical and gynecologic outpatient care, should take place in all family-planning settings, and should become routine before discharge from a hospital for any reason, if there are no contraindications (see section on PRECAUTIONS AND CONTRAINDICATIONS). Vaccination should be offered to adults, especially women of childbearing age, any time that contact is made with the health-care system, including when children are undergoing routine examinations or immunizations. Vaccination of Medical Personnel

Medical personnel, both male and female (e.g., volunteers, trainees, nurses, physicians), who might transmit rubella to pregnant patients or other personnel, should be immune to rubella. Consideration should be given to making rubella immunity a condition for employment (52-55). All medical personnel who have patient contact and who are beginning employment should have proof of rubella immunity or prior vaccination. Vaccination of Workers

Ascertainment of rubella-immune status and availability of rubella immunization should be components of the health-care program in places employing women of childbearing age (e.g., day-care centers, schools, colleges, prisons (56), companies (57), government offices, and industrial sites). Vaccination for College Entry

Colleges are high-risk areas for rubella transmission because of large concentrations of susceptible persons (58,59). Proof of rubella as well as measles immunity should be required for attendance for both male and female students. All students born in or after 1957 who enter institutions of post-high-school education should have documentation of receipt of two doses of measles vaccine (preferably given as MMR) and at least one dose of rubella vaccine or other evidence of measles and rubella immunity (21). Outbreak Control

Outbreak control will continue to play an important role in eliminating CRS. Aggressive responses to outbreaks may interrupt chains of transmission and will increase vaccination coverage among persons who might otherwise not be protected. Although methods for controlling rubella outbreaks are evolving, the main strategy should be to define target populations, ensure that susceptible persons are vaccinated rapidly (or excluded from exposure if a contraindication exists), and maintain active surveillance to permit modification of control measures if the situation changes.

Laboratory confirmation of rubella cases is important; however, control measures should be implemented before serologic confirmation. This approach is especially important in any outbreak setting involving pregnant women (e.g., obstetric-gynecologic and prenatal clinics). All persons at risk who cannot readily provide laboratory evidence of immunity or a documented history of vaccination on or after their first birthday should be considered susceptible and should be vaccinated if there are no contraindications.

An effective means of terminating outbreaks and increasing rates of immunization quickly is to exclude from possible contact individuals who cannot provide valid evidence of immunity. Experience with measles-outbreak control indicates that almost all students who are excluded from school because they lack evidence of measles immunity quickly comply with requirements and are promptly readmitted to school. All persons who have been exempted from rubella vaccination because of medical, religious, or other reasons should also be excluded from attendance. Exclusion should continue until 3 weeks after the onset of rash of the last reported case in the outbreak setting. Less rigorous approaches, such as voluntary appeals for vaccination, have not been effective in terminating outbreaks.

Mandatory exclusion and vaccination of adults should be practiced in rubella outbreaks in medical settings because pregnant women may be exposed. This approach may be successful in terminating, or at least limiting, outbreaks. Vaccination during an outbreak has not been associated with substantial personnel absenteeism.

Vaccination of susceptible persons before an outbreak occurs is preferable, because vaccination causes far less absenteeism and disruption of routine work activities than does rubella infection. SURVEILLANCE

Surveillance of rubella and CRS has three purposes: a) to provide important data on program progress and long-term trends, b) to help define groups in greatest need of vaccination and in turn provide information for formulation of new strategies, and c) to evaluate vaccine efficacy, duration of vaccine-induced immunity, and other issues related to vaccine safety and efficacy.

As the rates of rubella and CRS decline in the United States, effective surveillance becomes increasingly important. Known or suspected rubella cases should be reported immediately to local health departments. Because an accurate assessment of CRS elimination can be made only through aggressive case finding, surveillance of CRS will have to be intensified.

Surveillance of rubella is complicated by the fact that the symptoms of the clinical disease are not distinctive and can be confused with a number of other illnesses. Thus, cases should be laboratory confirmed, particularly outside of the outbreak setting. Similarly, laboratory confirmation of suspected cases of CRS is also necessary, because the constellation of findings of CRS may not be specific. Laboratory Diagnosis Rubella Serologic Testing for Evidence of Immunity

Until recently, HI antibody testing was the most frequently used method of screening for the presence of rubella antibodies. However, the HI test has been supplanted in many settings by a number of equally or more sensitive commercial assays to determine rubella immunity. EIAs are the most commonly used of these newer commercial assays, but latex agglutination, immunofluorescence assay (IFA), passive hemagglutination, hemolysis-in-gel, and virus neutralization tests are also available.

When adults who have not produced detectable HI antibodies following vaccination have been examined more closely, almost all have had detectable antibody by a specific but more sensitive test (60,61). Similarly, a small number of children who initially seroconverted have subsequently lost detectable HI antibody during up to 16 years of follow-up (62-64). However, almost all had detectable antibody by more sensitive tests. Immunity in a number of these children was confirmed by documenting a booster response (i.e., absence of immunoglobulin M (IgM) antibody and a rapid rise in immunoglobulin G (IgG) antibody) following revaccination (13,65).

Although some individuals have antibody levels following previous vaccination or infection that are below levels detectable by HI antibody testing, the clinical significance of such low-level antibody has not been as well documented as that of higher levels of antibody. Limited data suggest that, on rare occasions, infection with viremia can occur in persons with low antibody levels. CRS following reinfection has been documented, although such instances have been rare (20). Further study is warranted to assess the appropriate interpretation of antibodies detectable only by these more sensitive tests (14,17). Nevertheless, available data continue to support the presumption that any antibody level that is measured by a licensed assay and is above the standard positive cutoff value for that assay can be considered evidence of immunity. Rubella

The diagnosis of acute rubella should be confirmed serologically. The presence of IgM antibody or a significant rise in IgG or total antibody levels is evidence of acute rubella infection (66). For HI assays, a fourfold rise in the titer of antibody indicates recent infection; for other types of assays, the criteria for a significant rise in antibody level vary by type of assay and by laboratory. The acute-phase serum specimen should be drawn as soon after rash onset as possible, preferably within the first 7 days. The convalescent-phase serum specimen should be drawn 10 or more days after the acute-phase serum specimen. If the acute-phase serum specimen is drawn more than 7 days after rash onset, a significant rise in antibody titer may not be detected by most commonly used tests. In this case, complement fixation (CF) testing may be especially useful, because CF antibodies appear in serum later than HI, EIA, or IFA antibodies. The acute- and convalescent-phase serum specimens should be tested simultaneously in the same laboratory.

Occasionally, significant rises may not be detected, even if the first specimen is drawn within the first 7 days after rash onset. Rubella infection may also be serologically confirmed by demonstrating rubella-specific IgM

antibody. If IgM is to be determined, one serum specimen should be drawn between 1 week and 2 weeks after rash onset. Although rubella-specific IgM antibody may be detected shortly after rash onset, IgM antibody is less likely to be detected if the specimen is drawn earlier than 1 week or later than 4-5 weeks following rash onset. False-negative IgM antibody test results may sometimes occur even when the specimen is appropriately drawn. False-positive IgM test results may also occur.

In the absence of rash illness, the diagnosis of subclinical cases of rubella can be facilitated by obtaining the acute-phase serum specimen as soon as possible after exposure. The convalescent-phase specimen should then be drawn 28 or more days after exposure. If acute- and convalescent-phase paired sera provide inconclusive results, rubella-specific IgM antibody testing can be performed, but results should be interpreted cautiously. Expert consultation may be necessary to interpret the data.

Confirmation of rubella infection in pregnant women of unknown immune status following rash illness or exposure may be difficult. A serum specimen should be obtained as soon as possible. Unfortunately, serologic results are often nonconfirmatory. Such situations can be minimized by performing prenatal serologies routinely. In addition, health providers should request that laboratories performing prenatal screening retain such specimens until delivery so that retesting, if necessary, can be done. Congenital Rubella

Suspected cases of CRS should be managed with contact isolation (see CDC "Guidelines for Isolation Precautions in Hospitals"). While diagnostic confirmation is pending, children with suspected CRS should be cared for only by personnel known to be immune. Confirmation by attempting virus isolation can be done by using nasopharyngeal and urine specimens. Serologic confirmation can be obtained by testing cord blood for the presence of rubella-specific IgM antibodies. An alternative but less rapid serologic method is to document persistence of rubella-specific antibody in an infant with suspected CRS, age 3 months or older, at a level beyond that expected from passive transfer of maternal antibody, i.e., a rubella antibody level in the infant that does not decline at the expected rate (the equivalent of one twofold dilution in HI titer per month). However, some infected infants may lose antibody because of agammaglobulinemia or dysgammaglobulinemia.

In some infants with CRS, virus can persist and be isolated for the first year of life. CRS precautions need to be exercised through the first year of life, unless nasopharyngeal and urine cultures are negative for rubella virus.
INTERNATIONAL TRAVEL

Persons without evidence of rubella immunity who travel abroad should be vaccinated against rubella because rubella is endemic and even epidemic in many countries throughout the world. No immunization or record of immunization is required for entry into the United States. However, international travelers should have immunity to rubella (i.e., laboratory evidence of rubella antibodies or verified rubella vaccination on or after the first birthday). Protection is especially important for susceptible women of childbearing age, particularly those planning to remain out of the country for a prolonged period.

References

1. Miller E, Cradock-Watson JE, Pollock TM. Consequences of

confirmed maternal rubella at successive stages of pregnancy. Lancet 1982;II:781-4.

2. White CC, Koplan JP, Orenstein WA. Benefits, risks and costs of immunization for measles, mumps and rubella. Am J Public Health 1985;75:739-44.

3. Nelson DB, Layde MM, Chatton TB. Rubella susceptibility in inner-city adolescents: the effect of a school immunization law. Am J Public Health 1982;72:710-3.

4. Orenstein WA, Bart KJ, Hinman AR, et al. The opportunity and obligation to eliminate rubella from the United States. JAMA 1984;251:1988-94.

5. Preblud SR, Serdula MK, Frank JA Jr, Brandling-Bennett AD, Hinman AR. Rubella vaccination in the United States: a ten-year review. Epidemiol Rev 1980;2:171-94.

6. Crawford GE, Gremillion DH. Epidemic measles and rubella in Air Force recruits: impact of immunization. J Infect Dis 1981;144:403-10.

7. Cochi SL, Edmonds LE, Dyer K, et al. Congenital rubella syndrome in the United States, 1970-1985. Am J Epidem 1989;129:349-61.

8. Stehr-Green PA, Cochi SL, Preblud SR, Orenstein WA. Evidence against increasing rubella seronegativity among adolescent girls. Am J Public Health 1990;80:88.

9. Schum TR, Nelson DB, Duma MA, Sedmak GV. Increasing rubella seronegativity despite a compulsory school law. Am J Public Health 1989;79:66-9. 10. Kaplan KM, Cochi SL, Edmonds LD, Zell ER, Preblud SR. A profile of mothers giving birth to infants with congenital rubella syndrome. Am J Dis Child 1990;144:118-23. 11. Balfour HH, Groth KE, Edelman CK. RA 27/3 rubella vaccine. Am J Dis Child 1980;134:350-3. 12. Grillner L, Hedstrom E-E, Bergstrom H, et al. Vaccination against rubella of newly delivered women. Scand J Infect Dis 1973;5:237-41. 13. Weibel RE, Villarejos VM, Klein EB, Buynak EB, McLean AA, Hilleman MR. Clinical and laboratory studies of live attenuated RA 27/3 and HPV 77-DE rubella virus vaccines (40931). Proc Soc Exp Biol Med 1980:165:44-9. 14. Balfour HH Jr, Groth KE, Edelman CK, Amren DP, Best JM, Banatvala JE. Rubella viraemia and antibody responses after rubella vaccination and reimmunization. Lancet 1981;I:1078-80. 15. O'Shea S, Best JM, Banatvala JE. Viremia, virus excretion, and antibody responses after challenge in volunteers with low levels of antibody to rubella virus. J Infect Dis 1983;148:639-47. 16. Greaves WL, Orenstein WA, Hinman AR, Nersesian WS. Clinical efficacy of rubella vaccine. Pediatr Infect Dis 1983;2:284-6. 17. Baba K, Yabuuchi H, Okuni H, et al. Rubella epidemic in an institution: protective value of live rubella vaccine and serological behavior of vaccinated, revaccinated, and naturally immune groups. Biken J 1978;21:25-31. 18. Orenstein WA, Herrman KL, Holmgreen P, et al. Prevalence of rubella antibodies in Massachusetts schoolchildren. Am J Epidemiol 1986;124:290-8. 19. Horstmann DM, Schluederberg A, Emmons JE, Evans BK, Randolph MF, Andiman WA. Persistence of vaccine-induced immune responses to rubella: comparison with natural infection. Rev Infect Dis 1985;7:580-5. 20. Plotkin SA, Farquhar JD, Ogra PL. Immunologic properties of RA 27/3 rubella virus vaccine. A comparison with strains presently licensed in the U.S. JAMA 1973;225:585-90. 21. Best JM, Banatvala JE, Morgan-Capner P, et al. Fetal infection after maternal reinfection with rubella: criteria for defining reinfection. Br Med J 1989;299:773-5. 22. CDC. Measles prevention. MMWR 1989;38(S9):1-18. 23. CDC. National Childhood Vaccine Injury Act: requirements for permanent vaccination records and for reporting of selected events after vaccination. MMWR 1988;37:197-200. 24. Committee on Infectious Diseases. American Academy of Pediatrics. Measles: reassessment of the current immunization policy. Pediatrics 1989;84:110-2. 25. Preblud SR. Some issues relating to rubella vaccine. JAMA 1985;254:253-6. 26. Polk BF, Modlin JF, White JA, DeGirolami PC. A controlled comparison of joint reactions among women receiving one of two rubella vaccines. Am J Epidemiol 1982;115:19-25. 27. Grillner L, Hedstrom E-E, Bergstrom H, et al. Vaccination against rubella of newly delivered women. Scand J Infect Dis 1973;5:237-41. 28. Best JM, Banatvala JE, Bowen JM. New Japanese rubella vaccine: comparative trials. Br Med J 1974;3:221-4. 29. Schaffner W, Fleet WF, Kilroy AW, et al. Polyneuropathy following rubella immunization: a follow-up and review of the problem. Am J Dis Child 1974;127:684-8. 30. Tingle AJ, Yang T, Allen M, Kettyls GD, Larke RPB, Schulzer M. Prospective immunological assessment of arthritis induced by rubella vaccine. Infect Immun 1983;40:22-8. 31. Tingle AJ, Allen M, Petty RE. Rubella-associated arthritis.

I. Comparative study of joint manifestations associated with natural rubella infection and RA 27/3 rubella immunization. Ann Rheum Dis 1986;45:110-14. 32. Tingle AJ. Postpartum rubella immunization. Reply (Letter). J Infect Dis 1986;154:368-9. 33. Chantler JK, Ford DK, Tingle AJ: Persistent rubella infection and rubella-associated arthritis. Lancet 1982;1323-5. 34. Tingle AJ, Chantler JK, Kettyls GD, et al. Failed rubella immunization in adults: association with immunologic and virological abnormalities. J Infect Dis 1985;151:330-6. 35. Chantler JK, Tingle AJ, Petty RE. Persistent rubella infection with chronic arthritis in children. New Engl J Med 1985;313:1117-23. 36. Lerman SJ, Nankervis GA, Heggie AD, Gold E. Immunologic response, virus excretion, and joint reactions with rubella vaccine: a study of adolescent girls

and young women given live attenuated virus vaccine (HPV-77:DE-5). Ann Intern Med 1971;74:67-73. 37. Krasinski K, Borkowsky W. Measles and measles immunity in children infected with human immunodeficiency virus. JAMA 1989;261:2512-6. 38. McLaughlin P, Thomas PA, Onorato I, et al. Use of live virus vaccine in HIV-infected children; a retrospective survey. Pediatrics 1988;82:229-30. 39. ACIP. Immunization of children infected with human immunodeficiency virus--supplementary ACIP statement. MMWR 1988;37:181-3. 40. Deforest A, Long SS, Lischner HW, et al. Simultaneous administration of measles-mumps-rubella vaccine with booster does of diphtheria-tetanus-pertussis and poliovirus vaccines. Pediatrics 1988;81:237-46. 41. Eskola J, Peltola H, Takala AK, et al. Efficacy of Haemophilus influenzae type b polysaccharide-diphtheria toxoid conjugate vaccine in infancy. New Engl J Med 1987;317:717-22. 42. Dales LG, Chin J. Public health implications of rubella antibody levels in California. Am J Public Health 1982;72;l67-72. 43. Dales LG, Chin J. An outbreak of congenital rubella. West J Med 1981;135:266-70. 44. Lamprecht C, Schauf V, Warren D, Nelson K, Northrop R, Christiansen M. An outbreak of congenital rubella in Chicago. JAMA 1982;247:1129-33. 45. CDC. Rubella and congenital rubella--United States, 1985- 1988. MMWR 1989;38:173-8. 46. Robertson S, Cochi AL, Bunn GA, Morse DL, Preblud SR. Preventing rubella: assessing missed opportunities for immunization. Am J Public Health 1987;77:1347-9. 47. Lieberman E, Faich GA, Simon PR, Mullan RJ. Premarital rubella screening in Rhode Island. JAMA 1981;245:1333-5. 48. Preblud AR, Orenstein WA. Postpartum rubella immunization. J Infect Dis 1986;154:367-9. 49. Buimovici-Klein E, Hite RL, Bryne T, Cooper LZ. Isolation of rubella virus in milk after postpartum immunization. J Pediatr 1977;91:939-41. 50. Klein EB, Byrne T, Cooper LZ. Neonatal rubella in a breast-fed infant after postpartum maternal infection. J Pediatr 1980;97:774-5. 51. Landes RD, Bass JW, Millunchick EW, Oetgen WJ. Neonatal rubella following postpartum maternal immunization. J Pediatr 1980;97:465-7. 52. The Advisory Committee on Infections within Hospitals of the American Hospital Association. Recommendations for the control of rubella within hospitals. Infect Control 1981;2:410-1,424. 53. Polk BF, White JA, DeGirolami PC, Modlin JF. An outbreak of rubella among hospital personnel. N Engl J Med 1980;303:541-5. 54. McLaughlin MC, Gold LH. The New York rubella incident: a case for changing hospital policy regarding rubella testing and immunization. Am J Public Health 1979;69:287-9. 55. Greaves WL, Orenstein WA, Stetler WC, Preblud SR, Hinman AR, Bart KJ. Prevention of rubella transmission in medical facilities. JAMA 1982;248:861-4. 56. CDC. Rubella outbreaks in prisons--New York City, West Virginia, California. MMWR 1985;34:615-8. 57. CDC. Rubella in universities--Washington, California. MMWR 1982;32:394-5. 58. CDC. Rubella in colleges--United States, 1983-1984. MMWR 1985;34:228-31. 59. CDC. Rubella outbreak among office workers--New York City. MMWR 1983;32:349-52. 60. O'Shea S, Best JM, Banatvala JE, Marshall WC, Dudgeon JA. Rubella vaccination: persistence of antibodies for up to 16 years. Br Med J 1982;285:253-5. 61. Serdula MK, Halstead SB, Wiebenga NH, Herrmann KL. Serological response to rubella revaccination. JAMA 1984;251:1974-7. 62. Chu SY, Bernier RH, Stewart JA, et al. Rubella antibody persistence after immunization: sixteen-year follow-up in the Hawaiian Islands. JAMA 1988;259:3133-6. 63. Hillary IB, Griffith AH. Persistence of antibody 10 years after vaccination with Wistar RA 27/3 strain live attenuated rubella vaccine. Br Med J 1980;280:1580-1. 64. Weibel RE, Buynak EB, McLean AA, Roehm RR, Hillemann MR. Persistence of antibody in human subjects for 7 to 10 years following administration of combined live attenuated measles, mumps, and rubella virus vaccines. Proc Soc Exp Biol Med 1980;165:260-3. 65. Robinson RG, Dudenhoeffer FE, Holroyd HJ, Baker LR, Bernstein DI, Cherry JD. Rubella immunity in older children, teenagers, and young adults: a comparison of immunity in those previously immunized with those unimmunized. J Pediatr 1982;101:188-91. 66. Herrmann KL. Available rubella serologic tests. Rev Infect Dis 1985;7:S108-12.

SAFER·HEALTHIER·PEOPLE™
Morbidity and Mortality Weekly Report
Centers for Disease Control and Prevention
1600 Clifton Rd, MailStop E-90, Atlanta, GA 30333,
U.S.A

USA.gov Government Made Easy

Department of Health
and Human Services

This page last reviewed 5/2/01