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RUBELLA

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The name rubella is derived from Latin, meaning "little red." Rubella was initially considered to be a variant of measles or scarlet fever and was called "third disease." It was not until 1814 that it was first described as a separate disease in the German medical literature, hence the common name "German measles." Following a widespread epidemic of rubella infection in 1940, Norman Gregg, an Australian ophthalmologist, reported in 1941 the occurrence of congenital cataracts among 78 infants born following maternal rubella infection in early pregnancy. This was the first reported recognition of congenital rubella syndrome (CRS).

Rubella virus is classified as a togavirus, genus Rubivirus. It is most closely related to group A arboviruses, such as Eastern and Western Equine Encephalitis viruses. It is an enveloped RNA virus, with a single antigenic type that does not cross-react with other members of the togavirus group.

Rubella virus is relatively unstable and is inactivated by lipid solvents, trypsin, formalin, ultraviolet light, low pH, heat, and amantadine.

Epidemiology

Rubella is a human disease. There is no known animal reservoir. Although infants with CRS may shed rubella virus for an extended period, a true carrier state has not been described.

Transmission: Rubella is spread from person-to-person via airborne transmission or droplets shed from the respiratory secretions of infected persons. There is no evidence of insect transmission. Rubella may be transmitted by subclinical or asymptomatic cases (up to 50% of all rubella virus infections).

Temporal Pattern: In temperate areas, incidence is usually highest in late winter and early spring.

Communicability: Rubella is only moderately contagious. The disease is most contagious when the rash is erupting, but virus may be shed from seven days before to five to seven days or more after rash onset. Infants with CRS shed large quantities of virus from body secretions for up to one year and can therefore transmit rubella to persons caring for them who are susceptible to the disease.

Following vaccine licensure in 1969, rubella incidence fell rapidly. By 1983, fewer than 1,000 cases per year were reported in the USA.

The incubation period is 14 days with a range of 12 to 23 days.

Clinical Description

Symptoms are often mild, and up to 50% of infections may be subclinical or inapparent. In children, rash is usually the first manifestation and a prodrome is rare. In older children and adults, there is often a one to five day prodrome with low-grade fever, malaise, lymphadenopathy and upper respiratory symptoms preceding the rash. The rash of rubella usually occurs initially on the face and then progresses from head to foot. It lasts about three days and is occasionally pruritic. The rash is fainter than measles rash and does not coalesce. The rash is more prominent after a hot shower or bath. Lymphadenopathy may begin a week before the rash and lasts several weeks. Postauricular, posterior cervical and suboccipital nodes are commonly involved.

Arthralgia and arthritis occur so frequently in adults that they are considered by many to be an integral part of the illness rather than a complication. Other symptoms of rubella include conjunctivitis, testalgia, or orchitis. Forschheimer spots may be noted on the soft palate, but are not diagnostic for rubella.

Complications are not common, but tend to occur more often in adults than in children.

Arthralgia or arthritis may occur in up to 70% of adult women who contract rubella, but is rare in children and adult males. Fingers, wrists and knees are often affected. Joint symptoms tend to occur about the same time or shortly after appearance of the rash and may last for up to one month; chronic arthritis is rare.

Encephalitis occurs in one per 6,000 cases, more frequently in adults (especially in females) than in children. Mortality estimates vary from 0% to 50%.

Hemorrhagic manifestations occur in approximately one per 3,000 cases, occurring more often in children than in adults. These manifestations may be secondary to low platelets and vascular damage, with thrombocytopenic purpura being the most common manifestation. Gastrointestinal, cerebral or intrarenal hemorrhage may occur. Effects may last from days to months; most patients recover.

Additional complications include orchitis, neuritis and a rare late syndrome of progressive Panencephalitis.

Congenital Rubella Syndrome (CRS)

Following respiratory transmission of rubella virus, replication of the virus is thought to occur in the nasopharynx and regional lymph nodes. A viremia occurs five to seven days after exposure with spread of the virus throughout the body. Transplacental infection of the fetus occurs during viremia. Fetal damage occurs through destruction of cells as well as mitotic arrest.

Prevention of CRS is the main objective of rubella vaccination programs in the United States. A rubella epidemic in the United States in 1964 to 1965 resulted in 12.5 million cases of rubella infection and about 20,000 newborns with CRS. The estimated cost of the epidemic was $840 million.

Infection with rubella virus can be disastrous in early gestation. The virus may affect all organs and cause a variety of congenital defects. Infection may lead to fetal death, spontaneous abortion, or premature delivery. The severity of the effects of rubella virus on the fetus depends largely on the time of gestation at which infection occurs. Up to 85% of infants infected in the first trimester of pregnancy will be found to be affected if followed after birth. While fetal infection may occur throughout pregnancy, defects are rare when infection occurs after the 20th week of gestation. The overall risk of defects during the third trimester is probably no greater than that associated with uncomplicated pregnancies.

Congenital infection with rubella virus can affect virtually all organ systems. Deafness is the most common and often the sole manifestation of congenital rubella infection, especially after the fourth month of gestation. Eye defects, including cataracts, glaucoma, retinopathy and microphthalmia may occur. Cardiac defects such as patent ductus arteriosus, ventricular septal defect, pulmonic stenosis and coarctation

of the aorta are possible. Neurologic abnormalities**,** including microcephaly and mental retardation and other abnormalities, including bone lesions, splenomegaly, hepatitis and thrombocytopenia with purpura may occur.

Manifestations of CRS may be delayed from two to four years. Diabetes mellitus appearing in later childhood occurs frequently in children with CRS. In addition, progressive encephalopathy resembling subacute sclerosing panencephalitis (SSPE) has been observed in some older children with CRS.

CRS infants may have low hemagglutination inhibition (HI) titers, but may have high titers of neutralizing antibody that may persist for years. Reinfection may occur. Impaired cell-mediated immunity has been demonstrated in some children with CRS.

Laboratory Tests

Many rash illnesses may mimic rubella infection and up to 50% of rubella infections may be subclinical. The only reliable evidence of acute rubella infection is the presence of rubella-specific IgM antibody, demonstration of a significant rise in IgG antibody from paired acute and convalescent sera, or a positive viral culture for rubella, or detection of rubella virus by RT-PCR.

Virus Detection & Isolation

Detection by RT-PCR has become the gold standard for laboratory confirmation, as it is highly sensitive and specific. Rubella virus can be isolated from nasal, blood, throat, urine and cerebrospinal fluid specimens from rubella and CRS cases. Virus may be isolated from the pharynx one week before and until two weeks after rash onset. However, maximum viral shedding occurs up to day four after rash onset. Ideally, samples should be obtained as soon as rubella is suspected. The best results are from throat swabs, but CSF may be used if rubella encephalitis is suspected.

Viral isolation is an extremely valuable epidemiologic tool and should be attempted for all suspected cases of rubella or CRS. It can give important information about the origin of the virus, which strains are circulating in the United States, and whether these strains are endemic. A state laboratory or CDC should be consulted for details of viral isolation.

Serology

Serologic tests are widely available as a method of confirming the diagnosis of rubella. However, the positive predictive value of these tests has greatly decreased as the incidence of rubella has decreased, so it is no longer the preferred method of confirmation. IgM tests may still be used as supportive evidence in addition to other methods of confirmation. IgG tests are less practical because of the two week delay between blood collection.

Acute rubella infection can be serologically confirmed by a significant rise in rubella antibody titer in acute and convalescent serum specimens or by the presence of serum rubella IgM. Sera should be collected as early as possible (within seven to ten days) after onset of illness and again 14 to 21 days (minimum of seven) days later. False-positive serum rubella IgM tests have occurred in persons with parvovirus infections, with a positive heterophile test for infectious mononucleosis, or with a positive rheumatoid factor. The serologic tests available for laboratory confirmation of rubella infections vary among laboratories. The state health department can provide guidance on available laboratory services and preferred tests.

Enzyme-linked immunosorbent assays (ELISA). ELISA is sensitive, widely available and relatively easy to perform. It can also be modified to measure IgM antibodies.

Hemagglutination inhibition (HI) test was once the "standard" and most commonly used technique. It is sensitive and simple to perform and allows for either screening or diagnosis (if paired acute and convales-

cent sera are tested). A four-fold rise or greater in HI antibody titer in paired sera is diagnostic of recent infection. The test may be modified to detect rubella-specific IgM antibody indicative of recent infection.

Immunofluorescent antibody assay (IFA) is a rapid and sensitive assay. Commercial assays for both IgG and IgM are available in the United States. Care must be taken with the IgM assay to avoid false-positive results due to complexes with rheumatoid antibody.

Surveillance

Rubella and CRS are conditions reportable within 24 hours of diagnosis.

Clinical case definition

An illness that has all the following characteristics:

- Acute onset of generalized maculopapular rash
- Temperature greater than 99.0ºF (greater than 37.2ºC), if measured
- Arthralgia/arthritis, lymphadenopathy, or conjunctivitis

Laboratory criteria for diagnosis

- Isolation of rubella virus from a clinical specimen, or
- Detection of rubella-virus-specific nucleic acid by polymerase chain reaction, or
- Significant rise in serum rubella immunoglobulin G antibody level between acute- and convalescent-phase specimens, by any standard serologic assay, or
- Positive serologic test for rubella immunoglobulin M antibody

Case classification

Suspected: any generalized rash illness of acute onset

Probable: a case that meets the clinical case definition, has no or noncontributory serologic or virologic testing, and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case

Epidemiologic Classification of Internationally-Imported and U.S.-Acquired

Internationally imported case: An internationally imported case is defined as a case in which rubella results from exposure to rubella virus outside the United States as evidenced by at least some of the exposure period (12 to 23 days before rash onset) occurring outside the United States and the onset of rash within 23 days of entering the United States and no known exposure to rubella in the U.S. during that time. All other cases are considered U.S.-acquired cases.

U.S.-acquired case: A U.S.-acquired case is defined as a case in which the patient had not been outside the United States during the 23 days before rash onset or was known to have been exposed to rubella within the United States.

U.S.-acquired cases are subclassified into four mutually exclusive groups:

Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.

Imported-virus case: a case for which an epidemiologic link to an internationally imported case was not identified but for which viral genetic evidence indicates an imported rubella genotype, i.e., a genotype that is not occurring within the United States in a pattern indicative of endemic transmission. An endemic genotype is the genotype of any rubella virus that occurs in an endemic chain of transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.

Endemic case: a case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of rubella virus transmission continuous for ≥12 months within the United States.

Unknown source case: a case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S.

Note: Internationally imported, import-linked and imported-virus cases are considered collectively to be import-associated cases.

States may also choose to classify cases as "out-of-state-imported" when imported from another state in the United States. For national reporting, however, cases will be classified as either internationally imported or U.S.-acquired.

Comments

Serum rubella IgM test results that are false positives have been reported in persons with other viral infections (e.g., acute infection with Epstein-Barr virus [infectious mononucleosis], recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor. Patients who have laboratory evidence of recent measles infection are excluded.

Investigation

The purpose of investigation is to identify rubella cases and suspected cases as soon as possible, to differentiate between other rash illnesses, and prevent transmission to the susceptible population (especially pregnant women).

- The case should be excluded from school or child care or work (for adults) for seven (7) days after onset of the rash.
- Identify childbearing-age female contacts, especially those who are or could be in the first trimesterof a pregnancy. Such contacts should be tested serologically for susceptibility or early infection (IgMantibody) and advised accordingly, if immune status is not already known. Refer these women to theirprivate physician for follow-up. If the pregnant female is a health unit client, the female should be informed of symptoms and instructed to notify the health unit if any symptoms occur.
- Live rubella virus vaccine given after exposure does not prevent illness. However, immunization ofnonpregnant individuals may be indicated because, if the current exposure fails to result in infection, the immunization will protect the individual in the future. Immunization of a person incubating natural rubella is not contraindicated.

- Persons who have had a documented case of rubella and who are in need of measles and/or mumps vaccine shall be given MMR.
- The use of Immune Globulin for postexposure prophylaxis of rubella is not recommended.
- If a pregnant female is not immune to rubella and does not develop rubella as a result of exposure, she should be instructed to receive the MMR vaccine after delivering the baby, preferably while still in the hospital. Be sure to flag her record accordingly.
- Special follow-up is needed for schools, hospitals, child care centers, colleges, etc.

Case associated with a school or child care center

- Contact the school or child care center
  -to determine if any additional cases are occurring
  -to evaluate or have the school nurse evaluate immunization records of those enrolled
  -to arrange with the school or child care center to notify parents of students whose records do not indicate immunization against rubella or other disease under containment procedures.
- Recommend that children with inadequate immunization or no records, be excluded until acceptable proof of immunization is provided or until the outbreak is contained.
- Follow-up on all suspected cases.

Immunization

Three rubella vaccines were licensed in the U.S. in 1969: HPV- 77:DE-5 (duck embryo), HPV-77:DK-12 (dog kidney), and Cendehill (rabbit kidney) strains. The HPV-77:DK-12 was later removed from the market because there was a higher rate of joint complaints following vaccination with this strain. In January 1979, the RA 27/3 (human diploid fibroblast) strain (Meruvax-II) was licensed and all other strains were discontinued.

Characteristics:
The RA 27/3 rubella vaccine is a live attenuated virus. It was first isolated in 1965 at the Wistar Institute from a rubella-infected aborted fetus. The virus was attenuated by 25 to30 passages in tissue culture, using human diploid fibroblasts. It does not contain duck, chicken or egg protein. Vaccine virus is not communicable, except in the setting of breastfeeding, even though virus may be cultured from the nasopharynx of vaccinees.

Rubella vaccine is available as a single antigen preparation, combined with mumps vaccine, or combined with measles and rubella vaccines. The Advisory Committee on Immunization Practices (ACIP) recommends that combined measles-mumps-rubella vaccine (MMR) be used when any of the individual components is indicated.

Vaccination Schedule And Use
At least one dose of rubella vaccine, as combination MMR vaccine, separated by at least four weeks, are routinely recommended for all children. All persons born in or after 1957 should have documentation of at least one dose of MMR. The first dose of MMR should be given on or after the first birthday. Any dose of rubella-containing vaccine given before 12 months of age should not be counted as part of the series. Children vaccinated with rubella-containing vaccine before 12 months of age should be revaccinated with two doses of MMR vaccine, the first of which should be administered when the child is at least 12 months of age.

A second dose of MMR is recommended to produce immunity to measles in those who failed to respond to the first dose. Data indicate that almost all of the persons who do not respond to the measles component of the first dose will respond to a second dose of MMR. Few data on the immune response to the rubella and mumps components of a second dose of MMR are available. However, most persons who do not respond to the rubella or mumps component of the first MMR dose would be expected to respond to the second dose of MMR. The second dose is not generally considered a booster dose because a primary immune response to the first dose provides long-term protection. Although a second dose of vaccine may

increase antibody titers in some persons who responded to the first dose, available data indicate that these increased antibody titers are not sustained. The combined MMR vaccine is recommended for both doses to assure immunity to all three viruses. The second dose of MMR vaccine should routinely be given at age four to six years, before a child enters kindergarten or first grade. The adolescent health visit at age 11 to 12 years can serve as a catch-up opportunity to verify vaccination status and administer MMR vaccine to those children who have not yet received two doses of MMR (with the first dose administered no earlier than the first birthday). The second dose of MMR may be administered as soon as one month (*i.e.,* minimum of 28 days) after the first dose. All older children not previously immunized should receive at least one dose of rubella vaccine as MMR.

Adults born in 1957 or later who do not have a medical contraindication should receive at least one dose of MMR vaccine unless they have documentation of vaccination with at least one dose of measles-, rubella-, and mumps-containing vaccine or other acceptable evidence of immunity to these three diseases. Some adults at high risk of measles exposure may require a second dose of measles vaccine. This second dose should be administered as combined MMR vaccine. Efforts should be made to identify and vaccinate susceptible adolescents and adults, particularly women of childbearing age who are not pregnant. Particular emphasis should be placed on vaccinating both males and females in colleges, places of employment, and healthcare settings.

Rubella Immunity

Persons generally can be considered immune to rubella if they have documentation of vaccination with at least one dose of MMR or other live rubella-containing vaccine administered on or after their first birthday, have serologic evidence of rubella immunity, or were born before 1957. Persons who have an "equivocal" serologic test result should be considered rubella-susceptible unless they have evidence of adequate vaccination or subsequent serologic testing indicates rubella immunity. Although only one dose of rubella-containing vaccine is required as acceptable evidence of immunity to rubella, children should receive two doses of MMR vaccine according to the routine childhood vaccination schedule. Birth before 1957 provides only presumptive evidence of rubella immunity; it does not guarantee that a person is immune to rubella. Only a positive serologic test for rubella antibody or documentation of appropriate vaccination should be accepted for women who may become pregnant.

Clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status**.** Because many rash illnesses may mimic rubella infection and many rubella infections are unrecognized, the only reliable evidence of previous rubella infection is the presence of serum rubella IgG. Laboratories that regularly perform antibody testing are generally the most reliable because their reagents and procedures are strictly standardized. Occasionally, an individual with a history of documented rubella vaccination is found to have a negative serum IgG by ELISA. Such persons may be given a dose of MMR vaccine and do not need to be retested for serologic evidence of rubella immunity. Although birth before 1957 is generally considered acceptable evidence of measles and rubella immunity, medical facilities should consider recommending a dose of MMR vaccine to unvaccinated workers born before 1957 who do not have laboratory evidence of rubella immunity. Rubella vaccination or laboratory evidence of rubella immunity is particularly important for healthcare workers who could become pregnant, including those born before 1957. This recommendation is based on serologic studies which indicate that among hospital workers born before 1957, 5% to 9% had no detectable measles antibody.

Serologic screening need not be done before vaccinating for measles and rubella unless the medical facility considers it cost effective. Serologic testing is appropriate only if tracking systems are used to ensure that tested persons who are identified as susceptible are subsequently vaccinated in a timely manner. If the return and timely vaccination of those screened cannot be assured, vaccination should be performed without prior testing. Serologic testing for immunity to measles and rubella is not necessary for persons documented to be appropriately vaccinated or who have other acceptable evidence of immunity. Neither rubella vaccine nor immune globulin is effective for postexposure prophylaxis of rubella. Vaccination after exposure is not harmful and may possibly avert later disease.

Adverse Reactions Following Vaccination

Rubella is a very safe vaccine. Most adverse reactions reported following MMR vaccination are attributable to the measles component (such as fever and rash). The most common complaints following rubella vaccination are fever, lymphadenopathy, and arthralgia. These adverse reactions only occur in susceptible persons and are more common in adults, especially in women.

Joint symptoms**,** such as arthralgia (joint pain) and arthritis (joint redness and/or swelling), are associated with the rubella component of MMR. Arthralgia and transient arthritis occur more frequently in susceptible adults than in children and more frequently in susceptible women than in men. Acute arthralgia or arthritis are rare following vaccination of children with RA 27/3 vaccine. By contrast, approximately 25% of susceptible postpubertal females develop acute arthralgia following RA 27/3 vaccination, and approximately 10% have been reported to have acute arthritis-like signs and symptoms. Rarely, transient peripheral neuritic complaints, such as paresthesias and pain in the arms and legs, have been reported.
When acute joint symptoms occur, or when pain and/or paresthesias not associated with joints occur, the symptoms generally begin one to three weeks after vaccination, persist for one day to three weeks, and rarely recur. Adults with acute joint symptoms following rubella vaccination rarely have had to disrupt work activities.

Data from studies in the United States and experience from other countries using the RA 27/3 strain rubella vaccine have not supported an association between the vaccine and chronic arthritis. One study among 958 seronegative immunized and 932 seronegative unimmunized women aged 15 to 39 years, found no association between rubella vaccination and development of recurrent joint symptoms, neuropathy, or collagen disease. The ACIP continues to recommend the vaccination of all adult women who do not have evidence of rubella immunity.

Contraindications And Precautions To Vaccination

Persons who have experienced a severe allergic reaction (*i.e.*, hives, swelling of the mouth or throat, difficulty breathing, hypotension, shock) following a prior dose of rubella vaccine or to a vaccine component (e.g., gelatin, neomycin), should generally not be vaccinated with MMR.

Women known to be pregnant or attempting to become pregnant should not receive rubella vaccine. Although there is no evidence that rubella vaccine virus causes fetal damage, pregnancy should be avoided for four (4) weeks after rubella or MMR vaccination.

Persons with immunodeficiency or immunosuppression, resulting from leukemia, lymphoma, generalized malignancy, immune deficiency disease, or immunosuppressive therapy should not be vaccinated. However, treatment with low dose (<2 mg/kg/day), alternate day, topical, or aerosolized steroid preparations is not a contraindication to rubella vaccination. Persons whose immunosuppressive therapy with steroids has been stopped for one month (three months for chemotherapy) may be vaccinated. Rubella vaccine should be considered for persons with asymptomatic or mildly symptomatic HIV infection.

Persons with moderate or severe acute illness should not be vaccinated until the illness has resolved. Minor illness (*e.g.*, otitis media, mild upper respiratory infections), concurrent antibiotic therapy and exposure or recovery from other illness are not contraindications to rubella vaccination.

Receipt of antibody-containing blood products (*e.g.,* immune globulin, whole blood or packed red blood cells, intravenous immune globulin) may interfere with seroconversion to rubella vaccine. Vaccine should be given two weeks before, or deferred for at least three months following administration of an antibody-containing blood product. If rubella vaccine is given as combined MMR, a longer delay may be necessary before vaccination.

Previous administration of human anti-Rho(D) immune globulin (RhoGam) does not generally interfere with an immune response to rubella vaccine and is not a contraindication to postpartum vaccination. However, women who have received anti-Rho immune globulin should be serologically tested six to eight

weeks after vaccination to assure that seroconversion has occurred. Although vaccine virus may be isolated from the pharynx, vaccinees do not transmit rubella to others, except occasionally in the case of the vaccinated breastfeeding woman. In this situation, the infant may be infected, presumably through breast milk, and may develop a mild rash illness, but serious effects have not been reported. Infants infected through breastfeeding have been shown to respond normally to rubella vaccination at 12 to 15 months of age. Breastfeeding is not a contraindication to rubella vaccination and does not alter rubella vaccination recommendations.

Rubella Vaccination Of Women Of Childbearing Age

Women who are pregnant or intend to become pregnant within four weeks should not receive rubella vaccine. The ACIP recommends that vaccine providers ask a woman if she is pregnant or likely to become pregnant in the next four weeks. Those who are pregnant or intend to become pregnant should not be vaccinated. All other women should be vaccinated after being advised of the theoretical risks of vaccination during pregnancy and the importance of not becoming pregnant during the four weeks following vaccination. ACIP does not recommend routine pregnancy screening of women before rubella vaccination.

If a pregnant woman is inadvertently vaccinated or if she becomes pregnant within four weeks after vaccination, she should be counseled about the concern for the fetus (see below), but MMR vaccination during pregnancy should not ordinarily be a reason to consider termination of the pregnancy.

Evaluation of the effectiveness of prevaccine pregnancy prevention counseling in women of childbearing age in Hawaii revealed that the pregnancy rate for all women 15 to 44 years old in Hawaii was 122.8 per1,000 per year and the pregnancy rate among vaccinees 15 to 44 years of age who were counseled was 14.0 per1,000 peryear. The efficacy of counseling is 88.6% ([122.8-14.0]/[122.8 x 100]). While pregnancy is a contraindication to rubella vaccination, some women have been inadvertently vaccinated while pregnant or soon before conception. When rubella vaccine was licensed, this situation was of concern because of the known teratogenicity of the wild virus strain. To define the risk, if any, the Centers for Disease Control and Prevention (CDC) maintained a registry from 1971 to 1989 of women vaccinated during pregnancy to determine whether CRS would occur in infants of such mothers.

Subclinical fetal infection has been detected serologically in approximately 1% to 2% of infants born to susceptible vaccinees, regardless of the vaccine strain. However, based on data collected by the CDC in the Vaccine in Pregnancy (VIP) Registry, no evidence of CRS occurred in offspring of the 321 susceptible women who received rubella vaccine and who continued pregnancy to term. The observed risk of vaccine-induced malformation was 0%, with a maximum theoretical risk of 1.6%, based on 95% confidence limits (1.2% for all types of rubella vaccine). Since the risk of the vaccine to the fetus appears to be extremely low, if it exists at all, routine termination of pregnancy is not recommended. Individual counseling for these women is recommended. As of April 30, 1989, the CDC discontinued the VIP registry. The ACIP continues to state that pregnant women should **not** be vaccinated, because of the small theoretical risk to the fetus of a vaccinated woman.

Vaccine Storage And Handling

Measles-mumps-rubella (MMR) vaccine must be shipped with refrigerant to maintain 10^{o}C (50^{o}F) or less at all times. Vaccine must be refrigerated immediately on arrival and protected from light at all times. The vaccine must be stored at refrigerator temperature (2 ^{o}C to 8^{o}C [35 ^{o}F to 46^{o}F]), but may be frozen. Diluent may be stored at refrigerator temperature or at room temperature. After reconstitution, MMR vaccines must be stored at refrigerator temperature and protected from light. Reconstituted vaccine should be used immediately. If reconstituted vaccine is not used within eight hours, it must be discarded.

Control

CRS elimination

Although the CRS case count is low, rubella transmission continues to occur, and increased in 1989 and 1990.

The elimination of CRS will require several interventions:
- –Achievement and maintenance of high immunization levels.
- –Intensive surveillance of rubella and CRS.
- –Prompt outbreak control when rubella occurs.

Vaccination Of Susceptible Postpubertal Females

Elimination of indigenous rubella and CRS can be achieved by expanding and intensifying efforts to vaccinate susceptible adolescents and young women of childbearing age, particularly those born outside the United States.

These efforts should include vaccinating in family planning clinics, sexually transmitted disease (STD) clinics, and as part of routine gynecologic care; maximizing use of premarital serology results; emphasizing immunization for college students; vaccinating women postpartum and post-abortion; immunizing prison staff, and when possible, prison inmates, especially women inmates; offering vaccination to at-risk women through the Special Supplemental Program for Women, Infants and Children (WIC); and vaccination programs in the workplace, particularly those employing persons born outside the United States.

Hospital Rubella Programs

Emphasis should be placed on vaccinating susceptible hospital personnel, both male and female (volunteers, trainees, nurses, physicians, etc.) . Ideally, all hospital employees should be immune. It is important to note that screening programs alone are not adequate. Vaccination of susceptible staff must follow.

Use Of Combination Vaccines

The use of combination vaccines such as MR and MMR vaccines and the two-dose schedule of MMR vaccine for measles control will increase the level of rubella seropositivity in children and adults. Persons already immune to rubella should not have adverse events attributable to rubella vaccine; those not already immune are in need of vaccination against rubella.

Hospital precaution and isolation: Standard precautions.