

K. Rubella (see Chapter 11)

Diagnostic tests used to confirm acute or recent rubella infection or CRS include **serologic testing** and **virus isolation**.

Serologic testing

Sera should be collected as early as possible (within 7–10 days) after onset of illness, and again at least 7–14 days (preferably 2–3 weeks) later. IgM antibodies may not be detectable before day 5 after rash onset. In case of a negative rubella IgM and IgG in specimens taken before day 5, repeat serologic testing. Virus may be isolated from 1 week before to 2 weeks after rash onset. However, maximum viral shedding is up to day 4 after rash onset.

False-positive serum rubella **IgM tests** have occurred in persons with parvovirus infections or positive heterophile test (indicating infectious mononucleosis), or with a positive rheumatoid factor (indicating rheumatologic disease).^{28,29} When a false-positive rubella IgM is considered, a rheumatoid factor, parvovirus IgM, and heterophile test should be done to rule out a false-positive rubella IgM test result.

The serologic tests available for laboratory confirmation of rubella infections and immunity vary among laboratories. The following tests are widely available and may be used for screening for rubella immunity and/or laboratory confirmation of disease. The state health department can provide guidance on available laboratory services and preferred tests.

Enzyme immunoassay (EIA). Most of the diagnostic testing done for rubella antibodies use some variation of the EIA, which is sensitive, widely available, and relatively easy to perform. EIA is the preferred testing method for IgM, using the capture technique; indirect assays are also acceptable.

Hemagglutination inhibition (HI) test. This once was the gold standard and most commonly used technique and allows for either screening or diagnosis (if paired acute and convalescent 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 primary infection.

Latex agglutination (LA) test. The 15-minute LA test appears to be sensitive and specific for screening when performed by experienced laboratory personnel.

Immunofluorescent antibody (IFA) 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.

Virus isolation

Rubella virus can be isolated from nasal, blood, throat, urine, and cerebrospinal fluid specimens from rubella and CRS cases. The best results come from throat swabs. Efforts should be made to obtain clinical specimens for virus isolation from all cases (or from at least some cases in each outbreak) at the time of the

initial investigation. Virus may be isolated from 1 week before to 2 weeks after rash onset. However, maximum viral shedding is up to day 4 after rash onset.

Molecular typing

Rubella virus isolates are very important for surveillance. Molecular epidemiologic surveillance provides important information on:

- Origin of the virus
- Virus strains circulating in the U.S.
- Whether these strains have become endemic in the U.S.

In obtaining specimens for rubella molecular typing, collect throat swabs within 4 days of rash onset. Specimens for molecular typing from CRS cases should be collected as soon as possible after diagnosis. Appropriate specimens from CRS cases for molecular typing include throat swabs, cerebrospinal fluid, and cataracts from surgery. Strains for virus isolation should be sent to CDC for molecular typing as directed by the state health department.

Reverse transcription polymerase chain reaction (RT-PCR)

In the United Kingdom, there has been extensive evaluation of RT-PCR for detection of rubella virus in clinical specimens, documenting its usefulness.^{30,31} Clinical specimens obtained for virus isolation and sent to CDC are routinely screened by RT-PCR.

L. Congenital rubella syndrome (CRS) (see Chapter 12)

Diagnostic tests used to confirm CRS include serologic assays and isolation of the virus. Laboratory confirmation can be obtained by any of the following:

- Demonstration of rubella-specific IgM antibodies in the infant's cord blood or sera. In infants with CRS, IgM antibody persists for at least 6-12 months. In some instances, IgM may not be detected until at least 1 month of age (thus, infants with symptoms consistent with CRS who test negative shortly after birth should be retested at 1 month of age).³²
- Documentation of persistence of serum rubella IgG titer beyond the time expected from passive transfer of maternal IgG antibody.
- Isolation of rubella virus, which may be shed from the throat and urine for a year or longer.
- Detection of rubella virus by reverse-transcription polymerase chain reaction (RT-PCR).