Congenital Rubella Syndrome
Last updated: September 5, 2018
Rubella is an acute viral disease often affecting susceptible children and young adults worldwide. Although it causes only a mild clinical illness in these groups, its public health importance is due to the teratogenic potential of the virus resulting in congenital rubella syndrome (CRS). From just before conception through the first 8–10 weeks of gestation, rubella infection of the pregnant woman can result in multiple fetal abnormalities in up to 90% of cases, and may result in miscarriage or stillbirth. CRS defects can affect any organ system, including ophthalmic, auditory, cardiac, neurologic, hepatic and haemotologic. After 18 weeks of gestation, the risk of CRS is low. The most common defects of CRS are hearing impairment and deafness, eye defects (cataracts, congenital glaucoma or pigmentary retinopathy) and cardiac defects. Infected infants can shed high amounts of rubella virus from body secretions for up to one year, thus potentially causing outbreaks. Infants that survive the neonatal period may face serious developmental disabilities (such as deafness) and have an increased risk for developmental delay (such as autism) and autoimmune diseases (diabetes type 1, thyroiditis).

In some cases of rubella infection during pregnancy, particularly after 20 weeks of gestation, the fetus can be infected but not develop the signs and symptoms of CRS. These infants are classified as congenital rubella infection (CRI), and also shed rubella virus.

Before introduction of rubella vaccination, epidemics of rubella have resulted in rates of CRS of 0.8–4.0 per 1,000 live births (1). Rubella vaccine has been highly effective at reducing the burden of CRS, and vaccination has led to elimination of rubella and CRS from several European and Western Pacific countries and the Pan American Health Organization Region. However, insufficient population vaccination coverage can result in a median age shift of rubella cases to young adults, which may result in more CRS cases.

### RATIONALE AND OBJECTIVES OF SURVEILLANCE

Surveillance for CRS complements rubella surveillance. Rubella surveillance cannot capture every case of rubella since it is frequently mild or asymptomatic. CRS is the most severe outcome of rubella, and the prevention of CRS is the primary reason for rubella vaccination. Thus, the goals for CRS surveillance are linked to national goals for rubella vaccination, including monitoring progress to achieve and maintain elimination. The objectives for CRS surveillance are to:

- document the burden of CRS prior to rubella vaccine introduction
- monitor the impact of rubella vaccine introduction in reducing the incidence of CRS
- detect and isolate affected infants rapidly
- mitigate the consequences of the disease for infants and their families through early provision of appropriate medical care
- demonstrate the elimination of CRS.

The key global objective of CRS surveillance is to provide data in support of rubella elimination in five of six WHO regions by 2020.
MINIMAL SURVEILLANCE
The minimal recommended standard is sentinel-site, case-based CRS surveillance with laboratory confirmation. The main target age group for CRS surveillance is infants < 12 months of age. All countries that have introduced rubella vaccine should have a CRS surveillance system that has the ability to capture the majority of infants with suspected CRS within the country. Because CRS is a constellation of congenital abnormalities that may have other causes, CRS surveillance requires a high level of specificity, and thus laboratory confirmation is critical (see Case definitions section). Surveillance systems based on aggregate reporting without laboratory confirmation are inadequate for CRS surveillance. Pregnancy registries can complement CRS surveillance systems, but are insufficient for identifying the majority of CRS cases, as rubella generally causes a mild or asymptomatic clinical illness.

ENHANCED SURVEILLANCE
The recommendation for enhanced surveillance is national case-based, surveillance system (passive, active or both) with laboratory confirmation.

CASE DETECTION
- Facility-based surveillance is preferred because infants with the birth defects associated with CRS present to secondary, tertiary or specialty hospitals/sites, and the case definition requires clinical evaluation.
- If conducting sentinel-site CRS surveillance, establish a programme at selected sentinel hospitals and other sites that capture the majority of infants with suspected CRS. Tertiary care and specialty hospitals most likely to receive infants with cataracts, heart defects and hearing impairment should be prioritized as sentinel sites for establishing CRS surveillance. Later, surveillance can be expanded to include additional sites that have contact with more of the population.
- In most settings, a combination of passive and active approaches should be employed to increase the likelihood that all CRS cases will be captured by surveillance within the included health facilities. Specialists in ophthalmology, cardiology, ear/nose/throat and paediatrics should be sensitized on the process for reporting and investigating CRS cases.
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- During active surveillance visits to a site, conduct a review of medical records (including admission and discharge records) in units where infants who have manifestations consistent with CRS are likely to be seen (for example, neonatal ward, paediatric surgical ward, and eye, cardiac and ear clinics).
- As part of a comprehensive CRS surveillance system, test and follow up with pregnant women who were detected through fever-rash surveillance either as suspected measles-rubella cases or from exposure to confirmed rubella cases. Rubella in pregnancy registries can be used at the local level. These registries usually contain maternal demographic information, test results, contact information and pregnancy outcomes (delivery status of baby and birth defects). Infants identified as suspected or confirmed CRS should be included in the CRS surveillance system.
- Clinicians should notify public health of suspected CRS cases immediately.

**CASE DEFINITIONS AND FINAL CLASSIFICATION**

**SUSPECTED CASE DEFINITION FOR CASE FINDING**
- Any infant < 12 months of age that presents with any of the following:
  - congenital heart disease
  - suspicion of hearing impairment
  - one or more of the following eye signs: cataract (white pupil), congenital glaucoma (larger eyeball) or pigmentary retinopathy.
- Any infant < 12 months of age in whom a health worker suspects CRS, even without apparent signs of CRS, including maternal history of suspected or confirmed rubella during pregnancy.

**FINAL CLASSIFICATION**
Final classification of CRS cases depends, in part, on identifying Group A or Group B clinical signs of CRS.

**A.** Cataract(s), congenital glaucoma, pigmentary retinopathy, congenital heart disease (most commonly peripheral pulmonary artery stenosis, patent ductus arteriosus or ventricular septal defects), hearing impairment.

**B.** Purpura, splenomegaly, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease, jaundice that begins within the first 24 hours after birth.

Using these clinical signs, one of the final classifications listed below may be made.

**Laboratory-confirmed CRS:** A suspected CRS case with at least one sign from group A and meets the laboratory criteria for confirmation of CRS (see Laboratory section).

**Clinically compatible CRS:** A suspected CRS case without an adequate specimen in whom a qualified clinician detects at least two of the complications from group A OR one from group A and one from group B.

**Congenital rubella infection (CRI):** An infant who has none of the clinical signs of CRS from group A, but who meets the laboratory criteria for CRS.

**Discarded:** A suspected CRS case with an adequate specimen not meeting the laboratory-confirmed case definition, or a suspected case without an adequate laboratory specimen and not meeting the clinically compatible case definition.
OTHER DEFINITIONS FOR CRS CASES

- Source of infection
  - Endemic CRI/CRS: A confirmed case whose mother was exposed to endemic rubella transmission during gestation, as supported by epidemiological or genotyping evidence. A chain of rubella virus transmission that is continuous for ≥12 months within a country is defined as an endemic transmission.
  - Imported CRI/CRS: A confirmed case whose mother was exposed to rubella outside of the country during gestation, as supported by epidemiological or genotyping evidence.
  - Unknown source of CRI/CRS: A confirmed case not meeting the above endemic or imported CRI/CRS case definitions.

Figures 1a and 1b show how to classify suspected CRS cases by ELISA testing. Guidance for case confirmation by virus detection is in the Specimen collection section of this document.
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**SURVEILLANCE CLASSIFICATION OF SUSPECTED CRS CASE-PATIENTS ≥ 6 MONTHS TO < 12 MONTHS OF AGE**

**FIGURE 1b**

- **SUSPECTED CRS CASE**
  - < 6 MONTHS OF AGE
  - 6 TO < 12 MONTHS OF AGE

**BLOOD SAMPLE NOT OBTAINED**
- **SECOND BLOOD SAMPLE NOT OBTAINED**
  - DOES NOT MEET CLINICAL CRITERIA FOR CRS
    - DISCARDED
  - MEETS CLINICAL CRITERIA FOR CRS
    - CLINICALLY COMPATIBLE
    - DISCARDED

**BLOOD SAMPLE OBTAINED**
- **SECOND BLOOD SAMPLE OBTAINED**
  - IgG+ & IgM-
    - IgG-
      - DISCARDED
    - IgG+
      - CLINICALLY COMPATIBLE
  - IgG+ & IgM+
    - PRESENCE OF ≥ 1 DEFECT FROM GROUP A
      - INFECTION ONLY (CRI) CONFIRMED
    - NO DEFECTS FROM GROUP A
      - DISCARDED
  - IgG- & IgM- / IgM+
    - DISCARDED

*Every effort should be made to obtain a blood sample of adequate size (1ml) and that is kept cool during transport.

**Note:** For IgG+ sera, confirm that suspected case has a low likelihood of vaccination or of having postnatal rubella.

**WHO Vaccine-Preventable Diseases Surveillance Standards**
CASE INVESTIGATION

Suspected CRS cases should be investigated within 48 hours of detection. Use a standard case investigation form for investigation of all suspected cases and include clinical examination for CRS-related signs, especially those that benefit from early intervention. Specimens should be taken for laboratory confirmation of all suspected CRS cases.

Monitor the pregnancy outcomes for pregnant women with suspected or confirmed rubella. For those pregnancies that result in a live birth, ensure that the infant is followed up with appropriate clinical and laboratory evaluation, and placed under droplet and contact precautions to minimize potential spread.

After rubella elimination, a single case of domestically acquired CRS should lead to intensified rubella and CRS surveillance and an investigation to determine where the mother was exposed and the reason for insufficient immunity.

SPECIMEN COLLECTION

SERUM SPECIMENS

Serum specimens from infants for serological testing are the most common specimens used for CRS diagnosis. Collect specimens at first contact during the initial investigation; ideally, collect both a serum specimen for serologic testing alongside a sample for viral detection. As indicated below, additional samples may be needed in infants < 1 month of age or individuals > 6 months of age.

- If an infant is < 1 month of age with a high suspicion of CRS and a negative IgM serology, then a second specimen should be collected after one month to retest for IgM, as IgM seropositivity can be delayed until after the first month of life (false-negative for ages < 1 month).
- For infants ≥ 6 months of age but < 12 months with an initial positive rubella IgG serology, a second serum specimen for IgG should be collected after one month and tested in parallel with the initial serum specimen to assess if there is a sustained rubella IgG response.

If possible, 1 mL of blood in infants should be collected, although 0.5 mL can be acceptable in very small infants, or dried blood spots (≥ 3 fully filled circles).

SPECIMENS FOR VIRAL DETECTION

Specimens for viral detection are also acceptable for diagnosing CRS. The best results come from throat swabs, but nasal swabs, urine, serum or dried blood spots (in remote locations where serum transport is not possible) may also be used. Other specimens such as cerebrospinal fluid or cataracts are also possible sources of virus detection depending on the clinical picture, though performance characteristics of viral detection have not been established for these alternative specimen types and negatives do not necessarily rule out a case. Details on collection of these specimens can be found elsewhere (4).

STORAGE AND TRANSPORT

Whole blood/serum. Collection of whole blood is done by venipuncture using a sterile, plain collection tube or gel separator tube without additives. Whole blood can be stored at 4–8°C (never freeze whole blood) for up to 24 hours or for 6 hours at 20–25°C before the serum is separated from the clotted blood through centrifugation. After this time, whole blood must be transported to a facility equipped to separate the serum in order to avoid haemolysis.
Swabs should be collected using only synthetic fiber that have been used successfully to detect rubella virus. NP aspirates and nasal swabs are variations in virus isolation and detection but are more difficult to collect. NP swabs will serve as good samples for both viral detection and virus isolation for suspected oropharyngeal (throat swab) is the recommended sample for both viral detection and virus isolation. Nasopharyngeal (NP), nasal or throat swabs. Samples are kept at 4–8°C until the samples can be shipped to the laboratory within three days.

Oral fluid (OF). An adequate OF sample is one that is collected by gently rubbing along the base of the teeth and gums for at least one minute, which should allow the sponge to absorb about 0.5 mL of crevicular fluid. If the daily ambient temperature is below 22°C, OF samples should be collected within 24 hours. At higher temperatures, the OF samples should be kept at 4–8°C until the samples can be shipped to the laboratory. The OF samples are not considered a biohazard and can be shipped without special documentation from the site of collection to the laboratory.

Nasopharyngeal (NP), nasal or throat swabs. An oropharyngeal (throat swab) is the recommended sample for both viral detection and virus isolation for suspected cases. NP swabs will serve as good samples for both virus isolation and detection but are more difficult to collect. NP aspirates and nasal swabs are variations that have been used successfully to detect rubella virus. Swabs should be collected using only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts as they may contain substances that inactivate viruses and/or inhibit PCR testing.

The throat swab is collected by swabbing the posterior pharynx, avoiding the tongue. The NP swab has a flexible shaft. Tilt the patient’s head back and insert the swab into the nostril parallel to the palate. The swab should contact the mucosal surface. Place the sample in sterile tubes containing 2–3 mL of viral transport media (VTM) or phosphate-buffered saline (PBS). It is important to prevent the swabs from drying out. The throat and NP swabs may be refrigerated at 2–8°C for up to 48 hours and shipped on ice/frozen ice packs. If arrangements cannot be made for shipment within this timeframe, it is best to preserve the sample at -70°C. After freezing at -70°C, the samples are shipped on dry ice. Avoid freeze/thaw cycles. If storage at -70°C is not available, store samples at -20°C; viral viability will be lost, but the integrity of the viral RNA may be maintained and detected by RT-PCR.

Urine. Urine is collected in a suitable sterile, leak-proof container. The urine sample should be stored at 4–8°C until the urine can be centrifuged. Do not freeze the original urine sample prior to centrifugation. Whole urine samples may be shipped in sealed containers at 4°C, but centrifugation within 24 hours of collection is recommended. The urine is centrifuged at 500 x g (approximately 1500 rpm) for 5–10 minutes, preferably at 4°C and with the supernatant removed. Add sterile VTM, tissue culture medium or phosphate-buffered saline to the sediment to bring the final volume to 2 mL. If a pellet is not visible, remove all but 1 mL at the bottom of the centrifuge tube and mix with equal volume of VTM. Store the processed urine sample at 4°C and ship within 48 hours. Alternatively, the urine sample may be frozen at -70°C in viral transport medium and shipped on dry ice. If storage at -70°C is not available, samples can be stored at -20°C; viral viability will be lost, but the integrity of the viral RNA may be maintained and detected by RT-PCR.

Regardless of specimen type collected, all specimens should arrive to the laboratory within five days of collection, except in the case of oral fluids as noted above.
Laboratory confirmation of congenital rubella infection or syndrome in an infant meets one of the following criteria:

- for infants < 6 months of age, rubella IgM antibody detected
- for infants ≥ 6 months but < 12 months of age, rubella IgM and IgG antibody detected, OR a sustained rubella IgG antibody level, as determined on at least two occasions at least one month apart in the absence of receipt of rubella vaccine or exposure to wild-type rubella
- for infants any age < 12 months, rubella virus detection by viral culture or PCR in an appropriate clinical sample (throat, NP, or nasal swabs, blood, urine or cerebrospinal fluid specimens).

Although IgM antibodies may persist for up to one year, about 50% of CRS cases are IgM negative at 6 months of age, depending on test sensitivity. Because IgM may not be detectable in some infants tested shortly after birth, IgM-negative infants with suspected CRS should be retested at 1 month of age or shortly thereafter. Laboratory confirmation of CRS in an infant older than 6 months of age should not rely on the IgM test alone if the IgM result is negative. In such cases, as mentioned, serial IgG testing should be done after at least one month to check for a sustained level of IgG antibody over several months.

Genotype testing plays a similar role in CRS as it does in rubella surveillance, providing information potentially on the source of the virus. In a post-elimination setting, genotype testing should be conducted on every CRS case < 12 months of age. In an endemic setting, genotype testing should be conducted at least once for every chain of rubella transmission.

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Laboratory Networks

WHO coordinates the Global Measles and Rubella Laboratory Network (GMRLN). Regional and global reference laboratories can provide specialized testing such as viral isolation with molecular techniques to those countries that are unable to perform this in their own laboratories. Ensure that samples are tested in a WHO accredited or proficient laboratory, or in laboratories with quality assurance support from national labs in GMRLN. If this is not possible, then use a laboratory that has an established a recognized quality assurance programme such as ISO 15189 or ISO 17025 accreditation, or Clinical Laboratory Improvement Amendments (CLIA) certification.
DATA COLLECTION, REPORTING AND USE

RECOMMENDED DATA ELEMENTS

- **Demographic information**
  - **Child**
    - Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
    - Unique case identifier
    - Place of residence (city, district, and province)
    - Age/date of birth
    - Sex
    - Age when case detected
    - Race and/or ethnicity, if appropriate in country setting
    - Country of birth
  - **Mother**
    - Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
    - Age at birth of affected child
    - Country of birth (for help determining mother’s rubella vaccination status)

- **Reporting Information**
  - Place of reporting (e.g., name of health facility, county, district)
  - Date of notification
  - Date of case investigation

- **Clinical**
  - Health care worker suspects CRS?
  - **Signs and Symptoms**
    - Cataracts (unilateral, bilateral)
    - Hearing impairment
    - Developmental delay
    - Congenital heart defect (please specify)
    - Congenital glaucoma
    - Pigmentary retinopathy
    - Purpura
    - Radiolucent bone disease
    - Hepatosplenomegaly
    - Meningoencephalitis
    - Microcephaly
    - Jaundice < 24h from birth
    - Other
  - Outcome (patient survived, died, unknown)
  - Date of death

- **Laboratory methods and results (performed on infant)**
  - Types of specimen(s) collected
  - Date(s) of specimen(s) collection
  - Date(s) specimen(s) sent to laboratory
  - Date(s) specimen(s) received in laboratory
  - Serology and/or viral detection results for each specimen type
  - Genotype
    - Follow up specimen collection #1: type, date, result
    - Follow up specimen collection #2: type, date, result

- **Maternal history**
  - Gravida (number of pregnancies)
  - Para (number of pregnancies carried to viable gestational age)
  - History of rubella-like illness during pregnancy?
    - If yes, month (or weeks) of gestation
    - Was rubella diagnosed by a health care worker at the time of illness?
      - If yes, confirmed by laboratory?
    - Identified as part of pregnancy tracking register?
» Was the mother directly in contact with someone with confirmed rubella during pregnancy? If yes, what month of gestation?

» Vaccination history of mother
  • Number of doses of rubella containing vaccine given
  • Dates of vaccination

Location and exposure history
» If location of exposure unknown, did mother travel outside the country of residence during pregnancy? (If yes, list countries visited and month of gestation)

Classification
» Final case classification (laboratory-confirmed CRS, clinically compatible CRS, CRI, discarded)
» Source (imported, endemic, unknown)

REPORTING REQUIREMENTS AND RECOMMENDATIONS
CRS cases should be reported separately from clinical rubella cases. The clinician should transmit the case notification form or set of core information to the local epidemiologist or public health personnel. After case investigation is completed, case-based data should be transmitted from local levels to higher administrative levels of the surveillance system, including to the national level/MOH. CRS should be reported annually by every WHO Member State in the Joint Reporting Form (JRF). CRS is not currently reportable under International Health Regulations (IHR 2005).

RECOMMENDED DATA ANALYSES
» Final case counts by final case classification, month/year and geographic area (province, district, etc.); confirmed cases by source of infection (endemic, imported/import-related, unknown)
» CRS incidence (number of CRS cases per 1 000 live births) by year
» Clinical characteristics (types of birth defects) and outcome of CRS cases

» Maternal characteristics including age group, race/ethnicity, country of birth, location of exposure, vaccination status, gravida/para

» Number of CRS cases with maternal history of rubella-like illness in pregnancy (including month or week of gestation during illness, whether this was clinically compatible or laboratory-confirmed, and whether she was included in a pregnancy registry)

» Proportion of cases clustered or associated with a rubella outbreak

» Spot maps of confirmed CRS cases by year

» Age of CRS case at time of diagnosis (< 1 month, 1–5 months, 6–11 months)

» Number of infants with follow-up samples to confirm clearance of virus

CRS surveillance data should be triangulated with rubella surveillance data. For instance, after a rubella outbreak in women of childbearing age, there may be an increase in CRS cases in the same area in the following months, typically 6–8 months later).

USING DATA FOR DECISION-MAKING
» Isolate infants in healthcare settings with CRS to prevent further spread of rubella.

» Document the burden of CRS prior to rubella vaccine introduction.

» Monitor the impact of rubella vaccine introduction in reducing the incidence of CRS.

» Understand the epidemiology of CRS and its burden in the population in order to guide rubella immunization strategies, including the need to fill immunity gaps in adolescents and young adults.

» Determine risk factors for CRS, such as mothers who may have migrated from a country where rubella vaccine is not yet introduced or recently introduced.

» In conjunction with rubella surveillance data, help demonstrate the status of achieving or maintaining rubella elimination goals.
CRS surveillance systems should be evaluated annually to assess completeness of CRS reporting at surveillance sites. This should include hospital record review to identify any missed cases. Missed cases can be identified by comparing the list of reported CRS cases with the list of all cases that meet the suspected CRS case definition. Review the indicators below at least annually. Data gathered from CRS surveillance system evaluations should be included in National Verification Committee (NVC) reports for measles/rubella/CRS.

### Surveillance Performance Indicators

<table>
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<tr>
<th>Surveillance Attribute</th>
<th>Indicator</th>
<th>Target</th>
<th>How to Calculate (Numerator / Denominator)</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td><strong>Timeliness of Reporting</strong></td>
<td>Percentage of designated units reporting to the national level on time, even in the absence of cases</td>
<td>≥ 80%</td>
<td># of designated reporting units in the country reporting by the deadline / # of designated reporting units in the country x 100</td>
<td>At each level reports should be received on or before the requested date.</td>
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<td><strong>Completeness of Reporting</strong></td>
<td>Percentage of designated units submitting 12 monthly reports per year, even in the absence of cases</td>
<td>≥ 80%</td>
<td># of designated reporting units in the country submitting 12 reports in the last year / # of designated reporting units in the country x 100</td>
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<tr>
<td><strong>Adequacy of Investigation</strong></td>
<td>Percentage of all suspected CRS that have had an adequate investigation initiated within 48 hours of notification</td>
<td>≥ 80%</td>
<td># of suspected cases of CRS for which an adequate investigation was initiated within 48 hours of notification / # of suspected CRS cases x 100</td>
<td>An adequate CRS case investigation includes collection of all the following data elements: name and/or unique identifier, place of residence, date of birth, sex, date of notification, date of investigation, date of specimen collection, history of rash illness of mother, travel history of mother, vaccination history of mother, age of mother, clinical examinations for hearing impairment, cataract, and congenital cardiac (heart) defects and clinical outcome (alive/dead) at time of investigation.</td>
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<td><strong>Sensitivity</strong></td>
<td>National annual rate of suspected CRS cases</td>
<td>≥ 1/10 000 live births</td>
<td># of suspected CRS cases / live births x 10 000</td>
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<tr>
<td><strong>Specimen Collection and Testing Adequacy</strong></td>
<td>Percentage of suspected cases with adequate blood specimens for detecting rubella infection collected and tested in a proficient laboratory</td>
<td>≥ 80%</td>
<td># of suspected cases with an adequate specimen tested in a proficient laboratory / # of suspected cases x 100</td>
<td>Note 1: An adequate specimen is a blood sample by venipuncture in a sterile tube with a volume of at least 0.5 mL. Note 2: A proficient laboratory is one that is WHO accredited or has established a recognized quality assurance programme such as International Organization for Standards (ISO) or Clinical Laboratory Improvement Amendments (CLIA) certification.</td>
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**TABLE 1**

Surveillance performance indicators for CRS
CLINICAL CASE MANAGEMENT

No current treatment is available for CRS beyond clinical management of related congenital abnormalities. Infants with CRS and CRI shed live rubella virus for long periods (60% shed for the first four months of life), therefore appropriate infection control measures should be applied. In health care settings, contact precautions should be implemented for every detected CRS and CRI case. Infants should be considered infectious until two clinical specimens, obtained one month apart, are negative for rubella virus detection/isolation. Pregnant women should not be exposed to infants with CRS or CRI; if exposed, pregnant contacts should be tested for rubella. In areas where follow-up testing of confirmed CRS and CRI cases is not feasible, emphasis must be placed on ensuring close contacts and health care workers are vaccinated for rubella.

Note: Infants with confirmed CRS or CRI should be followed by public health until two consecutive clinical specimens, obtained one month apart, are negative for rubella virus detection/isolation.
CONTACT TRACING AND MANAGEMENT

Contact tracing is recommended among mothers of infants with CRS or CRI to identify the source of the rubella virus in the mother. Infants with CRS or CRI shed rubella virus for long periods (60% for the first four months of life), and appropriate infection control measures should be applied. It is particularly important that pregnant women who are not rubella-immune should not be exposed to infants with CRS or CRI. To prevent further infection with rubella virus and further transmission, protective immunity should be assured among contacts of CRS cases, including health care workers and family members. Persons in contact with the infant should be immune to rubella either through vaccination or natural infection (serological evidence of immunity). Non-pregnant persons who lack documentation of immunity should be vaccinated. Pregnant contacts should be tested as outlined in the rubella surveillance chapter.

SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

An increase in CRS cases generally occurs six to eight months after outbreaks of rubella infection. Detecting an increase in CRS cases can be a signal for wider rubella virus circulation in the population, indicating the possible occurrence of a past or current rubella outbreak.

During rubella outbreaks, CRS surveillance should be established or strengthened in maternity hospitals, paediatric hospitals, neonatal intensive care units and amongst specialists who treat infants with cardiac, hearing or eye deficits. If not already a sentinel site, hospitals located in the area where the outbreak is occurring should become a sentinel site. If a passive surveillance system for CRS is in place, it should be enhanced with active case finding in facilities located in outbreak areas. This can help identify infants with CRS or CRI who are shedding live rubella virus and prolonging the outbreak. CRS surveillance should continue for a minimum of nine months after the last rubella case.

During rubella outbreaks, a pregnancy registry should be established, if not already in place, to document all pregnancy outcomes of infected and exposed women. Outcomes include miscarriages, fetal deaths, CRS cases, infants with congenital rubella infection, and unaffected infants.
SPECIAL CONSIDERATIONS FOR CRS SURVEILLANCE

RETROSPECTIVE REVIEW OF MEDICAL RECORDS
Retrospective medical record review should be used to monitor the sensitivity of CRS surveillance systems annually. For countries unable to establish or maintain CRS surveillance, retrospective record review can be conducted to identify CRS cases. Medical records review in itself is not considered surveillance, but can inform disease burden estimates or provide baseline data for measuring the impact of vaccine introduction for a country. It also can be used in special circumstances (for example, countries with a small population) where it is believed that CRS elimination has already been achieved. However, a limitation of this approach is that retrospectively identified cases usually lack laboratory confirmation, and therefore lack a definitive diagnosis. Details can be found in the Introducing Rubella Vaccine Into National Immunization Programmes: A Step-by-Step Guide (2).

SEROLOGICAL SURVEYS OF REPRODUCTIVE-AGE WOMEN
Serological assessments of rubella IgG antibody levels among reproductive-age women in a survey setting may help evaluate population immunity against rubella and protection against CRS in newborns. Rubella IgG can be acquired through both vaccination and natural infection, therefore serosurveys are not purely a reflection of vaccination coverage. A serological survey is not a substitute for conducting CRS surveillance, but can provide complimentary information.

REFERENCES

REFERENCES CITED

ADDITIONAL REFERENCES