Rubella (German Measles, Three Day Measles) and Congenital Rubella Syndrome
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Rubella and Congenital Rubella Syndrome

Overview
Rubella is a viral illness caused by a togavirus of the genus *Rubivirus* and may be prevented through vaccination. Rubella is characterized by a mild, maculopapular rash; however up to 50% of rubella infections are subclinical and are sometimes misdiagnosed as measles or scarlet fever. Rubella may be transmitted by persons with subclinical or asymptomatic infections. Children usually develop few or no constitutional symptoms, but adults may experience a 1–5 day prodrome of low-grade fever, headache, malaise, mild coryza, and conjunctivitis. Postauricular, occipital and posterior cervical lymphadenopathy is characteristic and precedes the rash by 5–10 days. Arthralgia or arthritis may occur in up to 70% of adult women with rubella. Rare complications include thrombocytopenic purpura and encephalitis. Rubella is transmitted through direct or droplet contact from nasopharyngeal secretions and has an average incubation period of 16 to 18 days (range: 12 – 23 days). Persons with rubella are most infectious when rash is erupting, but they can shed virus from 7 days before to 7 days after rash onset. A small number of infants with congenital rubella syndrome (CRS) may shed virus for one year or more after birth.

NOTE: If a pregnant woman is exposed to rubella, she should call her healthcare provider immediately; particularly if she does not know whether she is immune (has had rubella disease or vaccine in the past).

When rubella infection occurs during pregnancy, especially during the first trimester, serious consequences can result. These include miscarriages, fetal deaths/stillbirths, and a constellation of severe birth defects known as CRS. The most common congenital defects are cataracts, heart defects, and hearing impairment. In addition, infants with CRS frequently exhibit both intrauterine and postnatal growth retardation. Infants who are moderately or severely affected by CRS are readily recognizable at birth, but mild CRS (e.g., slight cardiac involvement or deafness) might not be detected for months or years after birth or not at all. The risk for congenital infection and defects is highest during the first 12 weeks of gestation, and the risk for any defect decreases after the 12th week of gestation. Defects are rare when infection occurs after the 20th week. Subclinical maternal rubella infection also can cause congenital malformations.

Approximately 95% of susceptible persons aged ≥12 months developed serologic evidence of immunity to rubella after vaccination with a single dose of rubella vaccine. After a second dose of MMR vaccine, approximately 99% had detectable rubella antibody. However, rubella reinfection can occur and has been reported after both wild type rubella infection and after receiving 1 dose of rubella vaccine.

For a complete description of rubella, refer to the following texts:
2013 Case Definition - Rubella

**Case Classification**

**Confirmed**
A case with or without symptoms who has laboratory evidence of rubella infection confirmed by one or more of the following laboratory tests:
- Isolation of rubella virus; or
- Detection of rubella-virus specific nucleic acid by polymerase chain reaction; or
- IgG seroconversion† or a significant rise between acute- and convalescent-phase titers in serum rubella IgG antibody level by any standard serologic assay; or
- Positive serologic test for rubella IgM antibody†*

**OR**
An illness characterized by all of the following:
- Acute onset of generalized maculopapular rash; and
- Temperature greater than 99.0°F or 37.2°C; and
- Arthralgia, arthritis, lymphadenopathy, or conjunctivitis; and
- Epidemiologic linkage to a laboratory-confirmed case of rubella.
† Not explained by MMR vaccination during the previous 6-45 days.
*Not otherwise ruled out by more specific testing in a public health laboratory.

**Probable**
In the absence of a more likely diagnosis, an illness characterized by all of the following:
- Acute onset of generalized maculopapular rash; and
- Temperature greater than 99.0°F or 37.2°C, if measured; and
- Arthralgia, arthritis, lymphadenopathy, or conjunctivitis; and
- Lack of epidemiologic linkage to a laboratory-confirmed case of rubella; and
- Noncontributory or no serologic or virologic testing.

**Suspected**
Any generalized rash illness of acute onset that does not meet the criteria for probable or confirmed rubella or any other illness.

**Epidemiologic Classification**

**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 (U.S.) as evidenced by at least some of the exposure period (12–23 days before rash onset) occurring outside the U.S. and the onset of rash within 23 days of entering the U.S. and no known exposure to rubella in the U.S. during that time. All other cases are considered U.S.-acquired cases.

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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 a recent measles infection, can have a false-positive serum rubella IgM test result.
**2010 Case Definition – Congenital Rubella Syndrome (CRS)**

**Case Classification**

**Confirmed**
An infant with at least one symptom (listed below) that is clinically consistent with congenital rubella syndrome; and laboratory evidence of congenital rubella infection as demonstrated by:

- isolation of rubella virus, or
- detection of rubella-specific immunoglobulin M (IgM) antibody, or
- infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month), or
- a specimen that is PCR positive for rubella virus.

**Probable**
An infant without an alternative etiology that does not have laboratory confirmation of rubella infection but has at least 2 of the following*:

- cataracts or congenital glaucoma,*
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment, or
- pigmentary retinopathy;

**OR**
An infant without an alternative etiology that does not have laboratory confirmation of rubella infection but has at least one or more of the following:

- cataracts or congenital glaucoma,*
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment, **OR**
- pigmentary retinopathy

**AND** one or more of the following:

- purpura,
- hepatosplenomegaly,
- jaundice,
- microcephaly,
- developmental delay,
- meningoencephalitis, **OR**
- radiolucent bone disease.

*In probable cases, either or both of the eye-related findings (cataracts and congenital glaucoma) count as a single complication. In cases classified as infection only, if any compatible signs or symptoms (e.g., hearing loss) are identified later, the case is reclassified as confirmed.

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Suspected
An infant that does not meet the criteria for a probable or confirmed case but who has one of more of the following clinical findings:
- cataracts or congenital glaucoma,
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment,
- pigmentary retinopathy,
- purpura,
- hepatosplenomegaly,
- jaundice,
- microcephaly,
- developmental delay,
- meningoencephalitis, or
- radiolucent bone disease.

Other Criteria
Infection only
An infant without any clinical symptoms or signs but with laboratory evidence of infection as demonstrated by:
- isolation of rubella virus, or
- detection of rubella-specific immunoglobulin M (IgM) antibody, or
- infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a two-fold dilution per month), or
- a specimen that is PCR positive for rubella virus.

Epidemiologic Classification
Congenital rubella syndrome (CRS) cases will be classified epidemiologically as internationally imported or U.S.-acquired, according to the source of infection in the mother, using the definitions below, which parallel the classifications for rubella cases.

Internationally imported case: To be classified as an internationally imported CRS case, the mother must have acquired rubella infection outside the United States or in the absence of documented rubella infection, the mother was outside the U.S. during the period when she may have had exposure to rubella that affected her pregnancy (from 21 days before conception and through the first 24 weeks of pregnancy).
U.S.-acquired case: A US-acquired case is one in which the mother acquired rubella from an exposure in 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.
- **Import-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.

**COMMENTS**: 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 US-acquired.

**Information Needed for Investigation**

**Establish a diagnosis of rubella**: Confirm a diagnosis of rubella. Clinical diagnosis of rubella is unreliable, therefore, cases must be laboratory confirmed, especially if the reported cases are not epidemiologically linked to a laboratory-confirmed case. Laboratory testing should be conducted for all suspected cases of rubella as soon as possible. Detection of rubella immunoglobulin IgM antibody in a serum specimen usually indicates recent infection, but false-negative and false-positive results occur. Other laboratory tests are available such as enzyme immunoassays and latex agglutination tests. Laboratory confirmation of rubella infection may be difficult in pregnant women with unknown immune status who experience a rash illness or who are exposed to rubella. Obtain demographic, clinical and laboratory information on the case from the attending physician, hospital, and/or laboratory. Obtain the other epidemiological information necessary to complete the Disease Case Report (CD-1) and Rash Investigation Form (IMMP-4) from the patient or a knowledgeable family member. **NOTE**: Consider a single case of rubella a potential outbreak because rubella has been eliminated in the United States.
Additionally, rubella is an infectious disease for which up to 50% of cases are asymptomatic and investigation of an apparently isolated case could reveal additional cases.

**Conduct case investigations and vaccinate contacts without evidence of immunity:**
Aggressive response to rubella cases may interrupt disease transmission and will increase vaccination coverage among persons who might otherwise not be protected. Case investigation and identification of contacts should be conducted for all suspected cases of rubella. The main strategies are to define populations at risk, to ensure that persons without evidence of immunity are rapidly vaccinated (or excluded from exposure if a contraindication to vaccination exists) and to maintain active surveillance to permit modification of control measures if the situation changes. **Contraindications for MMR and MMRV vaccines include** history of anaphylactic reactions to neomycin, history of severe allergic reaction to any component of the vaccine, pregnancy, and immunosuppression. For additional information see Morbidity and Mortality Weekly Report (MMWR), Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP), Recommendations and Reports, June 14, 2013 / 62(RR04);1-34. **NOTE:** It is essential that exposed pregnant women be identified, evaluated, and counseled. If a pregnant woman is infected with rubella, immediate medical consultation is necessary.

**Conduct laboratory evaluation of exposed pregnant women:**
The goal of rubella case investigation is to identify rubella infections, particularly infection in pregnant women, and to prevent exposure of susceptible pregnant women, and thereby prevent cases of CRS. Exposed pregnant women should be tested for the presence of rubella IgG and IgM antibodies as outlined in Figure 1 below, regardless of symptom history. A blood specimen should be taken as soon as possible and tested for rubella IgG and IgM antibody and stored for possible retesting. **NOTE:** Particular care should be taken when rubella IgM is detected in a pregnant woman with no history of illness or contact with a rubella-like illness. Although this is not recommended, many pregnant women with no known exposure to rubella are tested for rubella IgM as part of their prenatal care. If rubella test results are IgM-positive for persons who have no or low risk of exposure to rubella, additional laboratory evaluation should be conducted.
Identify the source of infection: Efforts should be made to identify the source of infection for every confirmed case of rubella. Case-patients or their caregivers should be asked about contact with other known cases. Identify symptomatic household and other close contacts and obtain or recommend specimen collection and testing. Has the case traveled to an area where there is a known outbreak or increased rubella activity? Has the case traveled outside the immediate area during the exposure period (14 - 23 days prior to when rash first appeared)? Did the case attend any group meetings or gatherings during the exposure period (14-23 days prior to when rash first appeared)?

NOTE: Since many rubella cases are asymptomatic, identification of a source will not always be possible. When no history of contact with a known case can be elicited, opportunities for exposure to unidentified cases in populations at high risk (e.g., foreign-born persons) should be sought. Investigating sources of exposure should be directed to the place and time period in which transmission would have occurred.
Assess potential for transmission and identifying contacts: Does the case or a member of the case’s household attend a child care center, nursery school, or any other school setting? Does the case or a member of the case’s family work as a health care provider or other high-risk setting? Determine the immunization status of the case and close contacts. NOTE: It is essential that exposed pregnant women be identified, evaluated, and counseled. If a pregnant woman is infected with rubella, immediate medical consultation is necessary. COMMENT: Rubella-containing vaccines are not administered routinely in many countries, and in others, rubella-containing vaccine was only recently added to the childhood immunization schedule. Thus, many persons born outside the United States or who received childhood immunizations in other countries may have never received rubella vaccine.5

Obtain specimens for virus detection: With the successful elimination of indigenous rubella and CRS in the United States, molecular typing of viral isolates is critical in defining a source in outbreak scenarios and sporadic cases. Laboratory personnel should be notified that rubella is suspected, because specialized testing is required to detect the virus.2 Clinical specimens (throat swabs and urine) for virus detection should be obtained from all case-patients (or from at least some patients in each outbreak) at the time of the initial investigation. Cases of rubella occurring within 10 days of rubella vaccination should be investigated, and specimens should be obtained for virus isolation to determine if the rash is attributable to vaccine virus or wild virus. COMMENT: Cases in persons vaccinated within 7 days of a rubella-like illness who are IgM-positive should be classified as confirmed cases of wild-type rubella if they are epidemiologically linked to a laboratory-confirmed case.

Conduct enhanced surveillance: Active surveillance for rubella should be maintained for at least two incubation periods (46 days) following rash onset of the last case. Two incubation periods allow for the identification of transmission from a subclinical case.

In addition, surveillance for CRS should be implemented when confirmed or probable rubella cases are documented in a setting where pregnant women might have been exposed. Women who contract rubella infection while pregnant should be monitored for birth outcome, and appropriate testing should be performed on the infant after birth. Healthcare providers should be advised to evaluate infants born with conditions consistent with CRS and to collect specimens for virus detection and to perform a rubella-specific IgM antibody test on infants suspected of having CRS.

Report the pregnancy outcome for women diagnosed with rubella during pregnancy: All pregnant women infected with rubella during pregnancy should be followed to document the pregnancy outcome (e.g., normal infant, termination, CRS). Outcomes that are documented should be reported to CDC.
Provide information about rubella to persons at risk and/or the general public: Advise cases that while infectious, they should avoid contact with susceptible children, pregnant women, and immunosuppressed individuals.

1. Especially avoid contact with potentially susceptible women who are, or may be, pregnant.
2. Instruct contacts or parents to look for the symptoms and signs of rubella beginning 12 days after the first day of contact with a case; until 23 days after last contact.
3. *It should be highly recommended that susceptible contacts who have not received any rubella-containing vaccine avoid all public settings from 7 days after the first date of exposure until 23 days after the last date of exposure.*
4. If suggestive symptoms develop, potential cases should call their local health department for instructions.

An excellent Question-&-Answer rubella information sheet is available from the Immunization Action Coalition.

**Notification**

- If rubella is suspected, the local public health agency (LPHA) should immediately contact the District Communicable Disease Coordinator, or the Senior Epidemiology Specialist for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7).
- If a case(s) is associated with a childcare center, BCDCP or the LPHA will contact the Bureau of Environmental Health Services, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.

**Control Measures**

Control measures should be implemented as soon one case of rubella is confirmed in a community. In settings where pregnant women may be exposed, control measures should begin as soon as rubella is suspected and *should not be postponed* until laboratory confirmation. Patients with rubella should be isolated for 7 days after rash onset. All persons at risk who cannot readily provide acceptable evidence of rubella immunity should be considered susceptible and should be vaccinated. **NOTE:** *Neither rubella vaccine nor immune globulin is effective for postexposure prophylaxis of rubella and is not recommended for that purpose. Vaccination after exposure is not harmful and may possibly avert later disease.* Children with CRS should be
considered contagious until they are 1 year of age or have two negative cultures after 3 months of age.\textsuperscript{3}


Control of Outbreaks in Schools and Other Institutions\textsuperscript{5}
In schools and other educational institutions, exclusion of persons without acceptable evidence of rubella immunity may limit disease transmission and may help to rapidly raise the vaccination level in the target population. All persons who have been exempted from rubella vaccination for medical, religious, or other reasons also should be excluded from attendance. Exclusion should continue until 23 days after the onset of rash of the last reported case-patient in the outbreak setting. Unvaccinated persons who receive MMR vaccine as part of the outbreak control may be immediately readmitted to school \textit{provided all persons without documentation of immunity have been excluded}.

Control of Outbreaks in Medical Settings\textsuperscript{5}
In healthcare settings, exposed healthcare personnel without adequate presumptive evidence of immunity should be excluded from duty beginning 7 days after exposure to rubella and continuing through either 23 days after last exposure, or 7 days after rash appears. Exposed healthcare personnel who are vaccinated as part of control measures should be excluded from direct patient care for 23 days after the last exposure to rubella because effectiveness of postexposure vaccination in preventing rubella infection has not been shown. In addition, because birth before 1957 does not guarantee rubella immunity, during outbreaks in healthcare settings, healthcare facilities should recommend one dose of MMR vaccine for unvaccinated personnel born before 1957 who lack laboratory evidence of rubella immunity or laboratory confirmation of infection or disease. Serologic screening before vaccination is not recommended during outbreaks because rapid vaccination is necessary to halt disease transmission.\textsuperscript{7}

Control of Congenital Rubella Syndrome\textsuperscript{5}
\textit{Cases of U.S.-acquired CRS} are sentinel events indicating the presence of rubella infections in a community that may have been previously unrecognized. The diagnosis of a single case of U.S.-acquired CRS in a community should result in intensified rubella and CRS surveillance and an investigation to determine where the mother was exposed to rubella. If the mother was exposed in a different state, state health officials should contact the other state to alert public health officials to possible rubella circulation.
Infants with CRS may present with various manifestations of the syndrome, depending on timing of the infection in pregnancy. Infants born to women infected with rubella during pregnancy should be evaluated for infection and CRS; however, depending on the gestational age of the infant at the time of the mother’s infection, symptoms may not be apparent. After 20 weeks’ gestation, the only defect may be hearing impairment. Furthermore, some children are infected in utero but have no congenital defects. **NOTE:** Laboratory confirmation should be sought in all suspected CRS cases, regardless of signs or symptoms.

Cases of U.S.-acquired rubella have occurred among susceptible persons providing care for infants with CRS. Because infants can shed the virus for prolonged periods, (up to 1 year of age or longer) infants with CRS should be considered infectious until they are at least 1 year old or until two cultures of clinical specimens obtained one month apart after the infant is older than three months of age are negative for rubella virus. **Infants with CRS should be placed in contact isolation during any hospital admission before age one year or until the infant is no longer considered infectious.** In addition, health officials should consider **excluding infants with CRS from child care facilities until he or she is no longer considered infectious.** Persons having contact with infants with CRS should have documented evidence of immunity to rubella and caregivers of infants with CRS should be aware of the potential hazard of the infants to susceptible pregnant contacts.

**Laboratory Procedures**

For information on the collection or shipment of specimens to the Missouri State Public Health Laboratory, see their website at: [http://health.mo.gov/lab/measlesrubella.php](http://health.mo.gov/lab/measlesrubella.php).

**Reporting Requirements**

Rubella and congenital rubella syndrome are a Category 2 (A) **State Reportable Condition** reportable within one (1) calendar day of first knowledge or suspicion to the local health authority or to the Missouri Department of Health and Senior Services (MDHSS).

As a Nationally Notifiable Condition, **confirmed** rubella cases require an **IMMEDIATE, URGENT** report to the Centers for Disease Control and Prevention (CDC). **IMMEDIATE, URGENT** reporting requires MDHSS to call the CDC EOC at 770-488-7100 within 24 hours of a cases meeting the notification criteria; followed by submission of an electronic case notification via (WebSurv) in the next regularly scheduled electronic transmission.

As a Nationally Notifiable Condition, **confirmed** CRS is a **STANDARD** report to the Centers of Disease Control and Prevention (CDC). **STANDARD** reporting requires the Missouri Department of Health and Senior Services (MDHSS) to report to CDC by electronic transmission via WebSurv within the next normal reporting cycle.

1. Health care providers should report any possible case of rubella or CRS to the local public health agency of the patient’s residence or MDHSS.
2. For suspect, probable, or confirmed cases of rubella complete a Disease Case Report (CD-1) and a Rash Investigation Form (IMMP-4).

3. All women infected with rubella during pregnancy should have their pregnancy outcome documented so the information can be reported to CDC.

4. For suspect, probable, or confirmed cases of CRS complete a Disease Case Report (CD-1) and a Congenital Rubella Syndrome Case Report.

5. MDHSS will report to CDC following the above reporting criteria (see boxes).

6. Entry of the completed CD-1 into the WebSurv database negates the need for the paper CD-1 to be forwarded to the District Health Office.

7. Send the completed secondary investigation form(s) to the District Health Office.

8. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).

9. Within 90 days of the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

References


Other Sources of Information