
بسم الله الرحمن الرحيم

Rubella in pregnancy

- Maryam Afrakhteh.MD
- Shahid Beheshti Medical University
- 2019 Shiraz Iran

Rubella in pregnancy

- a member of the togavirus family,
- genus Rubivirus, humans are the only reservoir for rubella infection.
- Transmitted by direct droplet contact from nasopharyngeal secretions, replicates in the lymph tissue of the upper respiratory tract, spreads hematogenously.
- Congenital infection occurs when maternal viremia allows hematogenous spread of the virus across the placenta.

Congenital rubella syndrome

Congenital rubella syndrome (CRS) refers to variable constellations of birth defects

hearing impairment,

congenital heart defects,

cataracts

congenital glaucoma

pigmentary retinopathy

congenital rubella syndrome (CRS)

- congenital rubella syndrome (CRS) have largely been eliminated in the United States.
- incidence of rubella has declined from
- 0.45 per 100,000 in 1990 to 0.1 per 100,000 in 1999
- rubella outbreaks continue to occur in other parts of the world, and CRS remains a concern.

- rubella vaccine in 1969
- epidemics of rubella occurred in six to nine year cycles, usually in the late winter and early spring.
- rubella susceptible women of childbearing age varies
- 15 percent of women between the ages of 20 and 29 lack antibodies to rubella in Turkey

- 23 percent in Nigeria lack antibodies Russian Federation, 16.5 percent
-

Rubella

CRS

- Even in countries where rubella vaccination programs are available, the extent of vaccination is not always optimal
- Unvaccinated susceptibles can be a source of many preventable cases of CRS

CLINICAL MANIFESTATIONS

Rubella

- Acquired rubella is generally a mild, self-limited disease associated with a characteristic exanthem
- Symptoms appear approximately 14 to 21 days after inoculation with the virus.
- Though asymptomatic in 25 to 50 percent of cases, affected individuals may experience mild, prodromal symptoms consisting of low-grade fever, conjunctivitis, coryza, sore throat, cough,
- headache ; malaise.
- These symptoms usually last one to five days before the onset of the rash.

CLINICAL MANIFESTATIONS
Rubella

- Rubella may also be associated with generalized, tender lymphadenopathy, particularly involving suboccipital, postauricular, and cervical nodes, which often becomes pronounced during the rash.
- Just prior to the onset of the rash, approximately 20 percent of those infected will develop discrete rose spots on the soft palat
- (Forchheimer spots) that may later expand and coalesce.
- Polyarthritis and polyarthralgia are potential sequelae.

Congenital rubella syndrome

- catastrophic effects on the developing fetus,
- spontaneous abortion,
- fetal infection,
- stillbirth,
- or intrauterine growth restriction

Congenital rubella syndrome

- Maternal-fetal transmission occurs via hematogenous spread and varies with gestational age.
- There is considerable pathologic evidence that suggests that the rubella virus spreads through the vascular system of the developing fetus after infecting the placenta.

- The resulting defects stem from cytopathic damage to blood vessels and ischemia in affected organs

Congenital rubella syndrome

- first trimester, fetal infection rates 81 percent
- 25 percent in the late second trimester
- third trimester from 35 percent at

  27 to 30 weeks
- 100 percent for fetuses exposed beyond 36 weeks
- , the risk of congenital defects after maternal infection is essentially limited to maternal infection in the first 16 weeks of pregnancy

Congenital rubella syndrome

- infection after 20 weeks' gestation, intrauterine growth retardation may be the only sequelae of third trimester infection

no evidence that rubella infection immediately prior to pregnancy increases the risk of congenital infection

DIAGNOSIS

Acute rubella syndrome

- Most laboratories use ELISA due to its convenience, sensitivity, and accuracy.
- ●A fourfold rise in IgG titer between acute and convalescent serum specimens
- ●The presence of rubella specific IgM
- ●A positive rubella culture

Congenital rubella syndrome

- Serum should be obtained within 7 to 10 days after the onset of the rash
- and repeated two to three weeks later. Rubella virus may be isolated from
- nasal, blood, throat, urine, or cerebrospinal fluid (CSF) specimens
- . The virus is generally isolated from the pharynx one week before to two weeks after the rash.

Congenital rubella syndrome

- . In persons with no or low risk of exposure to rubella, the reactive IgM is likely falsely positive due to rheumatoid factor
- or other antibodies to infection which can cross react with the assay.
- Use of rubella specific avidity assay may be useful in these situations.

Prenatal diagnosis

- Polymerase chain reaction (PCR) is another option for providing presumptive diagnosis of rubella infection.
- A reverse transcription-nested PCR assay has been used in small studies where it detects rubella virus in chorionic villous samples (CVS) and amniotic fluid samples of affected pregnancies.

Prenatal diagnosis

- rubella specific PCR on CVS samples may be superior to standard serologic testing on fetal blood.
- CVS sampling ideally done at 10 to 12 weeks' gestation would allow for earlier detection than other samples, such as fetal blood obtained at 18 to 20 weeks' gestation

Prenatal diagnosis

- Ultrasound diagnosis of an affected fetus would be extremely difficult given the nature of the malformations seen with CRS,
- although, the workup of any fetus with intrauterine growth restriction should include evaluation for congenital viral infections including rubella.

TREATMENT

- Treatment for acute rubella infection may include acetaminophen for symptomatic relief. Glucocorticoids, platelet transfusion

Prenatal diagnosis

- because of the potentially devastating effects on the fetus, women should be counseled about maternal-fetal transmission and offered pregnancy termination, especially prior to 16 weeks' gestation.
- After 20 weeks' gestation, management should be individualized, and parents should be counseled about the potential for delayed consequences of rubella infection

- There is no definitively beneficial in utero treatment available for exposed or affected fetuses.
- The use of immune globulin for pregnant women with acute infection is controversial.

- There are no data to suggest that IgG has a beneficial effect on the fetal response to disease.
- Thus, the Centers for Disease Control and Prevention (CDC) recommends limiting the use of immune globulin to women with known rubella exposure who decline pregnancy termination

PREVENTION

- single dose of this vaccine given at one year of age or older results in measurable antibody in almost 95 percent of susceptible persons

- Vaccination is recommended for all children at 12 to 15 months and 4 to 6 years in conjunction with measles and mumps (MMR).
- All other persons should be vaccinated unless immunity is documented by serology.

Postpartum vaccination programs

- Postpartum vaccination programs have been shown to significantly reduce rubella susceptibility in pregnant seronegative women

- Rubella vaccine virus may cross the placenta and infect the fetus.
- However, there have been no cases of CRS reported in women inadvertently vaccinated during early pregnancy

- pregnancy termination is **not** recommended for these women

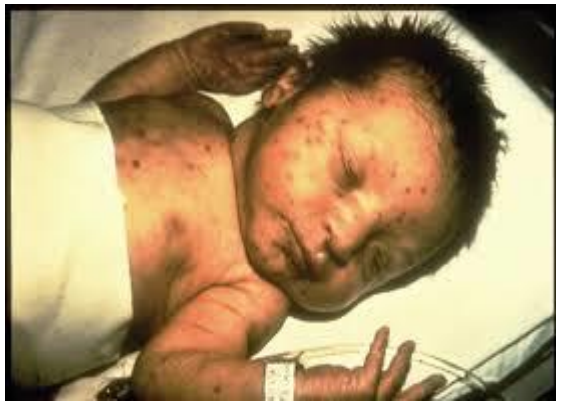
Rubella in Neonate

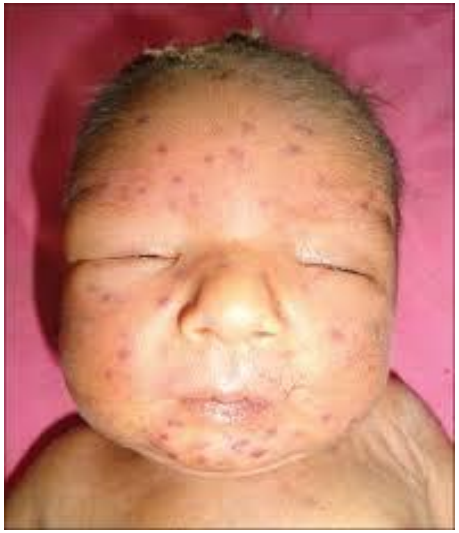
Dr. Mehrdad Rezaei

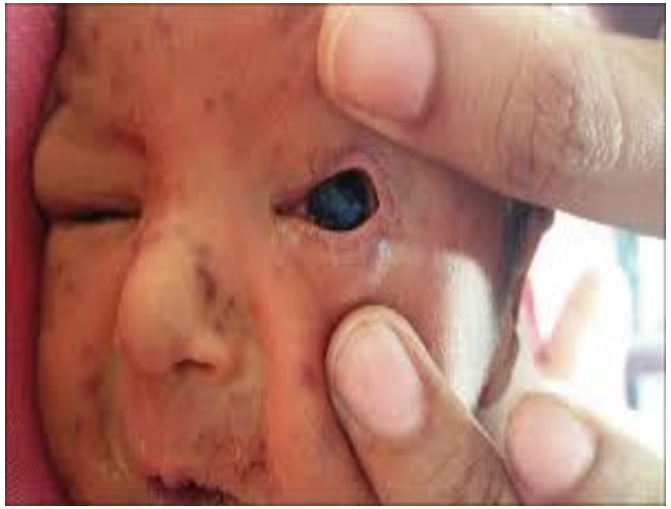
Neonatologist - SUMS

RUBELLA (CONGENITAL)

- This human-specific RNA virus is a member of the Togavirus family. It causes a mild self-limiting infection in susceptible children and adults, but its effects on the fetus can be devastating.



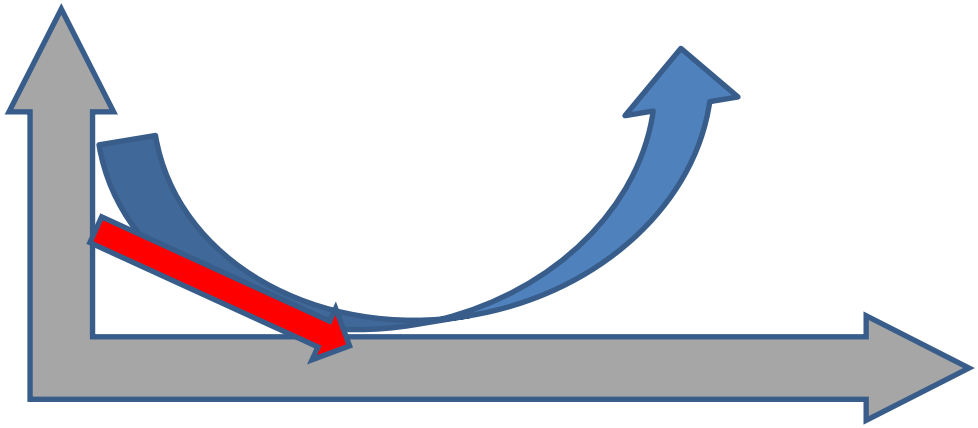




Rubella Fetal infection & damage:

- **Rate of fetal infection**

first 12 weeks of gestation	81%.
13 to 16 weeks of gestatio	54%,
17 to 22 weeks of gestation	36%,
23 to 30 weeks of gestation	30%
31 to 36 weeks of gestation	60%
>=36 weeks of gestation	100%



Early gestation infection may result in multiple organ anomalies.

- **Rate of fetal damage**

infected before **8** weeks' gestation	52%,
infected at **9 to 12** weeks' gestation	36%,
infected at 13 to 20 weeks' gestation	10%
infection **beyond 20 weeks**' gestation	**0%**

Clinical manifestations:

Congenital rubella Syndrome (CRS is not a static disease)

- **75%** infected infants show **no apparent involvement at birth**, but develop consequences years later.
- **Classically, CRS is characterized by cataracts, SNHL, cong. heart dis.**
- **IUGR** (birth weight is often <1500 g) (continue to FTT postnatally).
- These infants often have **myriad transient symptoms**, including **thrombocytopenia, petechiae, purpura, hemolytic anemia, hepatitis, jaundice, HSM, "blueberry muffin" spots** (50%)
- **myocarditis, cloudy cornea, long bone radiolucencies, interstitial pneumonia, and meningoencephalitis**, manifested by an elevated CSF protein level and pleocytosis

- **sensorineural deafness** (75%), usually **bilateral**. Deafness may be the only sequela of congenital infection and may occur with maternal infection **up to 20 weeks' gestation**.

- **Congenital heart disease** occurs only when the fetus is infected during the **first 8 weeks** of gestation.

  PDA, the most common lesion, may occur alone or in conjunction with pulmonary artery or valvular stenosis, or there may be stenoses of other vessels.

- **Microcephaly and neuropsychiatric problems**

  26% of children were severely mentally retarded, 12% had neurologic problems, 18% had behavioral abnormalities, and 6% had autism.

- **Ophthalmologic abnormalities** : **cataracts** (30%), often bilateral and occasionally accompanied by **glaucoma**. Other children may have microphthalmos or characteristic salt-and-pepper chorioretinitis. Rubella RNA can be detected and quantified in the **lens** of affected infants.

A 20-year follow-up study:

- **ocular disease** (most common disorder 78%),
- **sensorineural hearing deficits** (66%),
- psychomotor retardation (62%),
- cardiac abnormalities (58%),
- mental retardation (42%).

- **Immune globulin** is **not recommended** for prophylaxis in an exposed pregnant woman because congenital rubella has occurred despite the lack of symptoms in women given immune globulin.

- **vaccination** after exposure does **not prevent** infection from the current exposure, but might prevent exposure and infection in the future.

- The **goal** is to eliminate rubella with **vaccination.** Infants should be vaccinated at 12 to 15 months of age and again at school entry

- children with CRS: **contagious for at least 1 year**, unless repeated urine and blood cultures are negative.

- **Pregnancy women should not be vaccinated** because **3%** of fetuses may be subclinically infected, but birth defects have **not** been reported after vaccination of pregnant women, even if the fetus is infected.

- It is **acceptable to vaccinate children of pregnant women** because there is no evidence of transmission of virus after vaccination.

Congenital Rubella syndrome : Lab diagnosis in neonates

Dr Gholamreza Pouladfar

Evaluation

- The evaluation of a newborn with clinical findings compatible with intrauterine rubella infection (eg, cataract, congenital cardiac defect) is the same as the evaluation for other intrauterine infections.

Evaluation

1) Review of maternal history (evidence of rubella immunity)
2) Assessment of physical stigmata consistent with the syndrome, including complete cardiac and neurologic examinations
3) CBC & Platelet
4) LFT
5) Radiographs of long bones
6) Ophthalmologic evaluation
7) Audiologic evaluation
8) Neuroimaging (eg, ultrasonography, CT)
9) LP
10) Echocardiography: **?:** all vs +P/E

Time of evaluation

- Laboratory evaluation should be performed before the child reaches one year of age,

after which

it is difficult to establish a diagnosis of CRI

Laboratory confirmation of CRI

1) Isolation of rubella virus

2) Demonstration of rubella-specific IgM Ab

3) Demonstration of rubella-specific IgG Abs
   - Persist at a higher concentration or longer duration than expected from passive transfer of maternal antibody

4) Detection of rubella virus RNA

Virus isolation

- Confirmation of CRI
- The most frequently isolated site
  - **Nasopharyngeal secretions**
- Other sites:
  1) Blood (including cord blood)
  2) Placenta
  3) Urine
  4) CSF

Virus isolation

- Special tests:
  - Laboratory personnel should be notified that rubella virus is suspected.

- Timing:
  - As soon as CRI is suspected
  - Viral excretion wanes during infancy
  - for several years
    - Isolation of rubella virus may be possible from lens tissue in children with cataracts or CSF in children with encephalitis

Serologic confirmation of CRS: Developing countries

- Demonstration of rubella-specific IgM Abs:
  - With commercially available enzyme immunoassay kits
  - the preferred initial test
  - particularly for infants in the first 2 months of life
  - may be detectable for as long as 12 months in some infants
  - Infants with symptoms consistent with CRS who test negative soon after birth should be retested at age one month
    - Approximately 20 percent of infected infants tested for rubella IgM may not have detectable titers before age one month
    - In infants older than two months, positive IgM is helpful, but negative IgM does not exclude infection.
    - False-positive IgM
    - RF, parvovirus, and heterophile antibodies

Serologic confirmation of CRS: Developing countries

- OR
- Rubella-specific IgG
  - Most helpful in infants between 6 and 12 months of age
  - for a longer time than expected from passive transfer of maternal antibody
  - Monitoring rubella-specific IgG over time (eg, at 3, 6, and, if necessary, 12 mo of age)
  - Maternal rubella antibody has a half-life of approximately 30 days
  - Decrease by 4 to 8 fold by three months of age
  - Disappear by 6 to 12 mo of age

Rubella virus polymerase chain reaction

- Detection of rubella virus RNA by polymerase chain reaction (PCR)
- May not be available in all settings

- Samples:
  1) throat swabs
  2) Respiratory secretions
  3) Central nervous system tissues and CSF
  4) Amniotic fluid
  5) Products of conception
  6) Urine samples
  7) Lens tissue (in children with ocular anomalies)

Viral shedding

- After fetal infection, rubella virus persists throughout gestation and for months postnatally. It can be recovered from multiple sites.

- Pharyngeal shedding
  - Common
  - Prolonged
    - At one year of age, as many as 20%
    - By two years of age: rare
  - Intense during the months after delivery.

Viral shedding

- Ocular involvement (eg, cataracts)
  - Cultured from the crystalline lens in children older than one year of age
- CNS (eg. late subacute panencephalitis)
  - Cultured from cerebrospinal fluid in children older than one year of age

Retrospective diagnosis

- It is difficult to establish a diagnosis of CRI in children older than one year of age

1) Detection of persistent rubella RNA by PCR.
2) Measuring lymphocyte response to rubella in vitro
3) Measuring rubella IgG avidity (strength of antigen-antibody binding); children with intrauterine rubella infection have low rubella-specific IgG avidity
4) Measuring antibody response to rubella vaccination (in children with compatible manifestations but nondetectable antibody); children with CRS generally do not respond to rubella vaccination