

RUBELLA AND CONGENITAL RUBELLA SYNDROME (CRS)



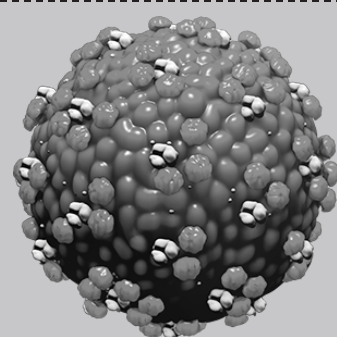
What is Rubella, what is CRS?

Rubella (German measles):

- Acute, contagious, viral exanthematous disease; usually asymptomatic or mild in children; severe for fetus if contracted during pregnancy
- Main public health concern: Risk to the unborn if the mother is infected (especially in first trimester), leading to fetal malformations and miscarriage

Congenital Rubella Syndrome (CRS):

- **Key triad:** Cataract, deafness and congenital heart defects; see details below



Microbiology & Pathogenesis

Viral Properties:

- Rubella virus: Single-stranded RNA virus, *Togaviridae* family, genus *Rubivirus*
- Only humans are hosts; only one serotype exists, with several genotypes in circulation worldwide.

Viral Entry & Spread:

- Enters via nasopharynx, replicates locally, then spreads to lymph nodes and then via viremia across organs
- Viremia and viral shedding begin 7 days before the onset of the rash, making detection before begin of transmission almost impossible

Fetal Pathogenesis:

- Transplacental infection inhibits embryonal mitosis, most severely affecting the eye (especially lens), cochlea, and brain cells
- Risk for fetal damage highest in early pregnancy (weeks 4–12), declines in later pregnancy

Epidemiology 2025

Global Distribution (read our review)

- Rubella incidence is highly variable by region; some have achieved elimination, others experience persistent outbreaks; asymptomatic cases usually not detected
- Between March 2024 and February 2025, Europe (EU/EEA) saw only 49 rubella cases (mostly Germany, Poland, Sweden, Italy); 22/30 countries reported zero cases, showing progress toward elimination
- South Africa reported 409 lab-confirmed cases Jan–July 2025
- In Latin America and Africa, outbreaks continue due to gaps in routine immunization and surveillance
- Nepal eliminated rubella in August 2025
- Outbreaks cluster in areas with vaccine coverage below 95%



Epidemiology & Surveillance:

- Epidemics often occur in 6–9-year cycles pre-vaccination, targeting children aged 4–9; teachers/adults in contact with children at higher risk today
- Routine CRS surveillance is recommended as CRS incidence correlates with rubella transmission in the population

Transmission & Clinical Disease

Transmission:

- Highest efficiency in schools, kindergartens, crowded places; direct respiratory droplet spread
- Incubation period: 14–23 days; contagious 7 days before to 7 days after rash onset

Clinical Features in Children:

- Often (up to 50%) asymptomatic or with mild fever, lymphadenopathy (posterior auricular, suboccipital), and a faint maculopapular rash, starting on the face, spreading in 24 hours, fading in 3 days
- Lymphadenopathy begins in week 2, resolves in ~1 month
- Fever is usually low-grade, sometimes mild conjunctivitis

Clinical Features in Adults:

- More pronounced symptoms; prodrome with fever, malaise, headache, then arthralgia/arthritis (up to 50% of post-pubertal females)
- Symptoms resolve in 1 week, but polyarthralgia/polyarthritis may persist longer

Complications:

- Encephalitis (1 in 5,000–6,000 cases), thrombocytopenia (1 in 3,000 cases), transient arthropathy
- CRS newborns: cataracts, deafness (70% of cases), heart defects (30–45%), CNS involvement (mental retardation, microcephaly, autism, 6–40%), hepatosplenomegaly, other ocular defects (retinitis, glaucoma) and late complications, e.g. diabetes (10–20%)
- CRS infants may shed viruses in urine for years, remaining contagious

Diagnosis:

- Laboratory confirmation essential: **IgM serology**; virus isolation, PCR from various specimens, **CRS** confirmed by isolation, genome detection, or specific IgM

Prevention

General Measures

Asymptomatic infections and early viral shedding limit the effectiveness of non-vaccine measures

Passive Immunization

Immune serum globulin occasionally used early post-exposure, but not fully protective against fetal CRS

Control Strategies

Routine immunization of boys and girls, catch-up campaigns of female adolescents



Vaccines

Technology & Strains:

- Live-attenuated rubella vaccines licensed since 1969–1970; RA27/3 strain is global standard, previously HPV-77 used in US before replacement in MMR-II
- Most vaccines given as part of MMR (measles–mumps–rubella), two-dose schedule (first at 12–15 months, second at 11–12 years or as locally recommended)

Immune Response:

- Good IgM, IgG, IgA response; circulating neutralizing antibodies indicate long-lasting protection
- Protection thought to last lifelong after vaccination (≥2 doses) or natural infection

Efficacy:

- High vaccine uptake leads to virtual elimination of rubella and CRS within a few years

Safety and Adverse Events

- Local reactions, mild transient joint pain in 15–25% of vaccinated adults (esp. women); severe adverse events (<1/100,000 doses): febrile seizure; anaphylaxis; few case reports with encephalitis (causality unknown)
- Contraindications: immunosuppression, pregnancy, severe neomycin allergy; inadvertent vaccination in pregnancy poses minimal risk to fetus (<10%)

Programmatic Successes:

- Finland (1997; first globally) and US achieved elimination with sustained high coverage; Latin America eliminated endemic rubella in 2015
- WHO-led initiatives use bivalent MR vaccine to target elimination globally

Challenges:

- Outbreaks recur if coverage drops below 95% or gaps persist among women of childbearing age
- CRS incidence remains a sentinel indicator of rubella control failure or gaps in program implementation

Reference:

- Rubella epidemiology October 2025. Internal briefing.
- Peltola H. Rubella, German Measles. In Schmitt HJ, ed. *Essentials in Vaccinology*. Singapore: Global Health Press; 2021. <https://doi.org/10.33442/vt202139>. Rubella and Congenital Rubella Syndrome

Globally Licensed Rubella Vaccines (please inform us if we missed a product)

Brand Name	Manufacturer (Country)	Strain Used	Remarks
MMR II	Merck (USA)	RA27/3	Most widely used globally; part of combined MMR vaccine; provides long-lasting immunity
Priorix	GSK (Belgium/ UK)	RA27/3	Combined MMR vaccine; also widely used in Europe, Asia, Latin America
Trimovax	Sanofi Pasteur (France)	RA27/3	MMR formulation; used in France and several other regions
Ruvax	Serum Institute of India (India)	RA27/3	Monovalent rubella vaccine; sometimes used in bivalent MR and trivalent MMR; principal option in India
M-M-RVAXPRO	MSD (various, EU/Asia)	RA27/3	Used for MMR immunization in EU and Asia; RA27/3 strain standard
Morupar	Sanofi Pasteur (France, global)	Wistar RA27/3	Discontinued in some regions due to safety preference for RA27/3
Measbio-Rub	Bio-Med Pvt Ltd (India)	RA27/3	Licensed for use in India; usually as MR or MMR formulation
Takeda Rubella	Takeda (Japan)	Takeda (Japan) strain	Only licensed/used in Japan; different local strain
Shanghai Rubella	Shanghai Institute (China)	Chinese local strain	Used only in China; not RA27/3, local strain adaptation

Note:

- Most global vaccines now use the RA27/3 strain, favored for efficacy and safety. Earlier strains (HPV-77, Cendehill) have been replaced except in limited settings
- RA27/3 strain was originally isolated from an infected fetus and is credited for robust immunogenicity and safety, fueling global elimination campaigns
- Japan and China use proprietary rubella strains and related domestically manufactured vaccines
- ProQuad and Priorix-Tetra contain MMR plus varicella-zoster virus antigens

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