Lecture – Rubella virus 18.2.2016

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Viruses causing rashes & skin lesions

1. Rubella virus
2. Parvovirus
3. Herpes viruses:

    HSV 1 & 2, VZV, CMV, EBV, **HHV6, HHV 7** & **HHV8**

4. Pox virus
5. Measles virus
6. Papovaviruses / Papilloma viruses

Rubella virus & Parvovirus B19

- Both viruses cause really trivial childhood infections; similar, mild rash diseases BUT they all have interesting complications.
- arthritis is a common complication of both.
- Both may endanger the foetus if the mother is infected in pregnancy, but in very different ways.
- For both of these viral infections, man is the only natural host and reservoir, so that the viruses must keep circulating in human populations, and tend to occur in small epidemics.
- However, because of long-lasting immunity, these infections usually occur only once in one person's lifetime
- Note that the person is infectious for about a week before the onset of symptoms, and then for a few days from the onset of symptoms.

Lecture outline : RUBELLA VIRUS 18.2.2016

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RUBELLA VIRUS

Family Togaviridae.

Genus Rubivirus.

Positive sense ss RNA.

Icosohedral.

Enveloped.

Sphericle.

60-70 nm in size.

Only one serotype.

Other properties

Haemagglutinates birds' RBC

Causes multi-system infection. Main impact on the foetus.

Transmitted by droplet infection.

Contagiousness;

Measles > Rubella > Mumps

Clinical Features :

Mild disease;

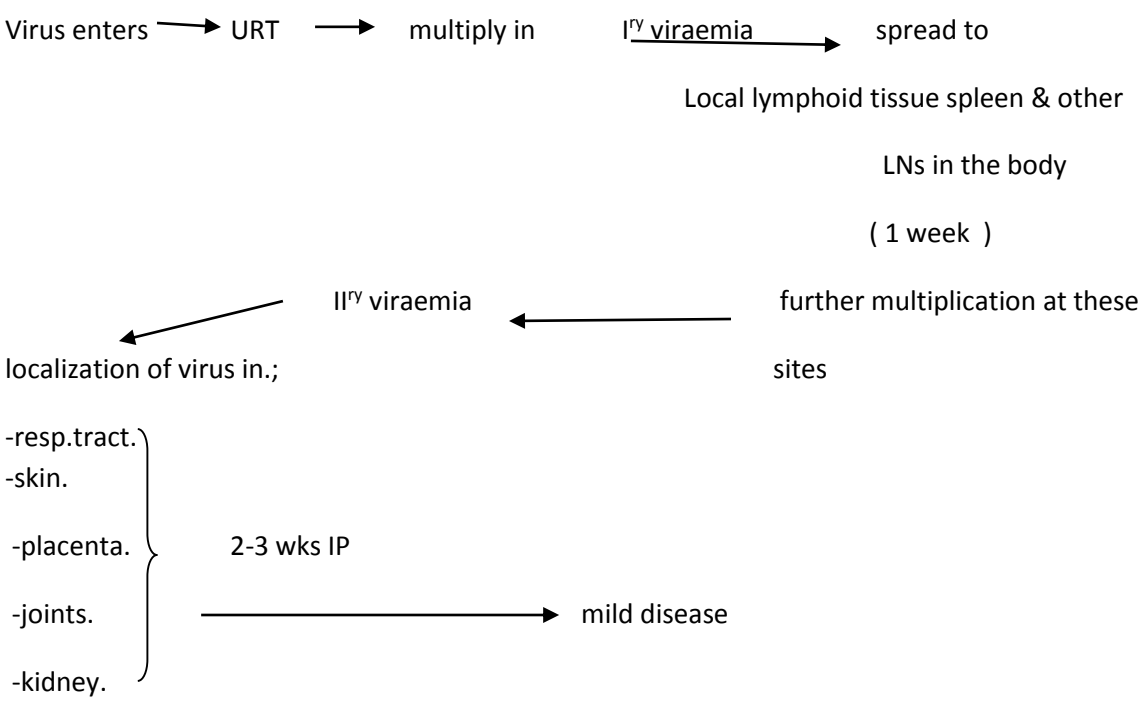
- Most common in children of 4-9 yrs

- fever, malaise, irregular macular papular rash lasting for 3 days.

- enlarged LNs seen behind the ear (post auricular & sub-occipital).

- infection often sub-clinical.

Pathogenesis



Respiratory tract;

Virus shedding but symptoms minimal (mild sore throat, coryza, cough).

Skin;

Results in rash, often transient atypical. Immunopathology involved.

(Ag - Ab complexes)

Lymphnodes;

Causes lymphadenopathy.

Common in posterior triangle of neck or behind the ear.

Joints;

Causes mild arthralgia, arthritis.

Immunopathology involved (circulating immune complexes.)

Placenta / Foetus;

Causes placentitis & foetal damage.

So causing **CONGENITAL RUBELLA**.

Infectiousness of rubella:

Virus can be isolated by 5^{th}-6^{th} day of infection.

Rash appears in 15-21^{st} day of infection

Patient is infectious 9 days before rash (5^{th} -6^{th} day of infection to 22^{nd} day of infection. (1 week before and 4 days after rash)

Immunity

IgM appears when rash appears on day 15. Detectable in significant amounts for the next 4-8 weeks. Then IgG which is life long.

Diagnosis

Clinically some times possible. But unreliable (symptoms are fleeting, can be caused by other viruses , rash is not diagnotic)

Lab diagnosis; 1. Virus isolation.

2. Sero-conversion.

1. Virus isolation (rarely indicated)**;**

From throat. No CPE. Therefore, indirect methods needed to demonstrate virus.

2. SEROCONVERSION;

Rubella specific IgM Abs by ELISA OR,

Rising titre of Abs (IgG)/whole Ab equal to or more than 4 fold rise by HI, ELISA, CF, RIA (over 10 days) .

Serology is important as sub clinical infection is common and rash mimics other viruses.

Antibodies;

can be detected by HAI, ELISA, RIA, CF.

IgM 1st detectable on day 15 of infection (appearance of rash).

rapid rise of Ab in a week.

IgG remain detectable for the rest of patient's life.

How to distinguish recent /active infection from past infection ?

By measuring type of Ab.

By repeating the test after a few days.

Day 15, nearly all the Ab is IgM and detectable significant levels for 4-8 weeks further.

Gradually replaced by IgG.

Treatment & Prevention

No antiviral treatment.

Self limiting infection.

Therapeutic abortions in the 1^{st} 3- 4 months of pregnancy with confirmed lab diagnosis. (not done in Sri Lanka)

Immunization is available

Normal Immunoglobulin (750mg)

Rubella in pregnancy, prevention of clinical attack possibly, reduces the risk to the foetus.

Used when termination of pregnancy is not acceptable & is given as soon as possible after exposure & serological follow-up is essential.

Not recommended for protection of pregnant women exposed (foetus is not protected).

CONGENITAL RUBELLA SYNDROME

Maternal viraemia → infection of placenta & foetus.

Earlier the infection in pregnancy, more the damage.

Foetus susceptible when maternal infection occurs in the 1st 3 months of pregnancy.

Studies have shown defects seen in;

15% cases	1st month (foetal death common).
25% cases	2nd month.
18% cases	3rd month.
6% cases	4th month.

Birth defects are uncommon after 18^{th} week.

In-apparent maternal infections may lead to foetal death, lesions, abortion.

Primary effect of rubella virus on blood vessels of developing organs.

Brain; Small brain size (microcephaly), Mental retardation, Psychiatric disorders, Behavioural manifestation.

Eye; Cataract, Glucoma, Chorioretinitis & Blindness.

Ear; Deafness, Deaf-mutism.

Heart; PDA, VSD, ASD, PS, AS, & Myocardial necrosis.

Liver / Spleen; Hepatosplenomegaly, Thrombocytopaenia, Anaemia, Hypogammaglobulinaemia.

Dental abnormalities.

Purpura.

Bone lesions.

Interstitial pnumonitis.

Low birth weight.

Failure to thrive.

Infant mortality.

Virus mediated inhibition of mitosis → Reduce number of cells → Small size of babies

<u>Clinical Features of congenital rubella</u>

May be; Transient effects.

Permanent manifestations.

Develop abnormalities that appear progressing during childhood & adolescence.

25% congenitally infected children eventually develop IDDM (virus replicate in pancreas).

15-20% mortality in infants showing signs at birth.

<u>Diagnosis of congenital rubella</u>

Clinical; Low birth weight.

Eye lesions.

Heart lesions.

Brain / Ear - later in childhood → Deafness, mental retardation)

Lab Diagnosis;

Serology ; Foetus produce own Ab (IgM) →Can be detected in cord blood.

Maternal IgG also present.

Ab detected by CFT, RIA, ELISA, HI.

HI test is a reliable test for estimating rubella Abs.

Isolation of virus ;

Virus present in; urine, blood, throat for several months.

Synovial fluid of chronically infected joints.

Aborted foetuses in early months.

Infants born with congenital defects &

normal infants whose mothers had rubella in late pregnancy.

Use neutralization test.

If a pregnant woman is exposed;

1. Careful history on time, nature of exposure.
2. Sample of blood should be tested for rubella Abs.

Three groups of cases;

1. Patient had rubella infection in the past. →No risk.
2. Patient with active or very recent infectio → Risk

Refer to a Gynaecologist for advice on therapeutic abortion.

3. Patient with no detectable Abs. →May or may not develop rubella.

Repeat serological tests until 5weeks after the date of exposure.

If Ab appears , patient is infected. → Risk

If No Ab detected, patient is not infected. Advise to have vaccine after delivery.

Prevention

With live attenuated vaccine.

Completely preventable.

Pregnancy is a contraindication for vaccination.

Only safe time is immediate post-partum period. (for the prevention of future foetus).

Pregnancy should be avoided 4 weeks after immunization.

Refer to National Immunization revised schedule of Sri Lanka on updated for 2015

9 months of age: MMR 1st dose on completion of 9 months.

Pre-school age

3 years: MMR 2nd dose on completion of 3 years

Females in the child bearing age (15-44 ys age)

One dose of rubella vaccine (MMR) to un-immunized women of 15 -44 years age.

Pregnancy should be avoided 4 weeks after immunization.

What to do if exposed and Blood test for IgM and Ig G is one of the following?

IgM-, IgG _

IgM+, IgG-

IgM+, IgG+

IgM-, IgG+