CONGENITAL INFECTIONS

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TORCH Infections

What are the Expanded TORCHES infection?

Toxoplasmosis, Treponema pallidum, cytomegalovirus (CMV), herpes simples virus (HSV) rubella, HIV, hepatitis B, hepatitis C. Others includes – varicella and parvovirus B19.

What are the forms of toxoplasmosis parasites?

The forms of toxoplasmosis parasites are oocytes which contains sporozoites. Sporozoites become tachyzoites (localised in neural and muscle tissue) and then become brachyzoites (which congregate into tissue cyst). Cysts remains in skeletal and heart muscle, brain, retinal and lymph node tissue.

What tissue do the tachyzoites invade and form tissues?

The tachyzoites invade the neural (including retinal) and the muscle tissue, and lymph nodes, where they congregate in tissue cysts.

Can infection with toxoplasmosis progress after birth?

Yes it can. Newborns who are asymptomatic have a high risk of developing late manifestation and sequelae of the disease. These include CHORIORETINITIS in which up to 90% of infected untreated infant can develop it later in adulthood, although only 20% of infants will have retinal lesions at birth. The sequelae also include MOTOR and CEREBELLAR lesions and developmental anomalies – leading to microcephaly, seizures, intellectual disability (mental retardation) and sensory-neural hearing loss. Although the cystic lesions are present at birth, the developmental manifestations will often only become fully apparent in later infancy.

What is the treatment for toxoplasmosis for both mother and infant?

Maternal Treatment – (maternal diagnosis before 18 weeks) – Spriramycin until PCR or ultrasonography is available, and if foetal infection confirmed – pyrimethamine sulfadiazine, folic acid (to minimise pyrimethamine-associated haematological toxicity) and spiramycin. Continue treatment with pyrimethamine-sulphadiazine for 12 months in infants.

Describe the clinical features of congenital syphilis?

Early signs of congenital syphilis are, maculopapular rashes (particularly on the palms and soles), hepatosplenomegalgy, snuffles (nasal secretions), lymphadenopathy, mucus membrane lesions, pneumonia, osteochondritis, and pseudo paralysis, coombs-negative haemolytic anaemia and thrombocytopenia. Late manifestation involves the CNS, bone and joints, teeth eyes and skin.

What does the VDRL and RPR test detect and explain why they are non-specific?

Venereal Disease Research Laboratory (VDRL) and Rapid Plasma Regain (RPR) Test are non-treponemal test which test antibodies to the cardiolipin and they are non-specific and can be false negative because of high titre (called the “prozone effect”), thus sample should be diluted before testing.

What is more specific test?
More specific test includes Treponema-specific test - Fluorescent antibody absorption, microhaemagglutination test for antibodies (T pallidum, T pallidum immunoassay or T pallidum particle agglutination test)

What is prozone effect?

The prozone effect is false negative results for high titre in samples collected for congenital syphilis

What are the two highest risk of foetus developing CRS?

1. First trimester of pregnancy, they have a risk of 80 to 100%
2. At term - 60% risk
(There is lower risk to the foetus of congenital infection in the second trimester)

What cardiac lesion are seen in CRS?

1. Patent Ductus Arteriosus (PDA)
2. Pulmonary Arterial Stenosis (PAS)
3. Coarctation of the Aorta (CoA)
(The lesions of CRS result from a progressive necrotising vasculitis and focal inflammation from intracellular invasion of the virus)

What other TORCHES infection can lead to Cardiac Lesions?

1. Congenital Rubella Syndrome (structural cardiac anomalies)
2. Herpes Simplex Virus (myocarditis)
3. Parvovirus B19 (can cause a myocarditis directly from parvovirus infection).

For how long is an infant with CRS considered as infectious?

Infants are considered infectious until at least one year of age (unless 2 negative cultures of clinical specimens are obtained 1 month apart are negative after 3 months of age, but in PNG such lab infestations are not available).

What are the clinical features of Parvovirus B19 infection?

Facial rash (slapped check), pruritic lactic form macular rash on trunk which can spread to extremities and associated with polyarthritis. Fever, malaise, myalgia, headache.

Foetal anomalies

- Foetal demise
- Severe anaemia
- Non-immune hydrops foetalis, from foetal heart failure
  - High output cardiac failure from anaemia
  - Myocardial failure attributable directly to Parvovirus infection
- Thrombocytopenia
- “Maternal mirror syndrome” (an odd name, which merely refers to the combination of maternal pre-eclampsia with oedema, and foetal and infant hydrops – i.e. both mother and baby have oedema).
- Meningoencephalitis (rare)

Why is anaemia so common?
The reason being Parvovirus B19 has high affinity towards erythroid progenitor cells. Cellular receptors including the blood group P antigen are present in the erythroid precursor cells. This results in direct toxic cell injury by viral protein, apoptosis (cell injury and cell death), manifesting in anaemia (and myocarditis). Persistent congenital infection is manifest as red cell aplasia.

**What factors increase the risk of Perinatal HIV transmission?**

1. Maternal plasma viral load
2. Low maternal CD4 count
3. More advance WHO clinical disease staging in the mother
4. Breastfeeding and mastitis
5. Acute maternal infection
6. Other maternal STIs

**At what age should HIV – exposed infants to be tested with and HIV nucleic acid test (e.g.: DNA PCR) to be reliably negative?**

At 4 months of age

**What stage in pregnancy does most HBV transmission during pregnancy?**

Most transmission of HBV occurs during delivery. In utero the risk of transmission is <2-4%.

**What proportion of infants infected with Hepatitis B prenatally develop chronic hepatitis B?**

About 90% of infants infected perinatally or in the first year of life develop chronic hepatitis B (compared with much lower rates of chronicity if infection occurs in later childhood or adult life).

**What is the ideal preventative treatment for newborn known to be Hepatitis B exposed?**

Newborns of Hepatitis B Antigen positive mother should receive: Hepatitis B immunoglobulin, and single vaccine Hepatitis B Vaccine *within 12 hours of delivery* (followed by a full course of HBV vaccine as routine). Follow-up testing should occur at 9-18 months.

**The “Silent” Global Burden of Congenital CMV**


It used to be thought that only mothers with primary CMV are at the risk of having a newborn with congenital CMV. Is it true? And what implications does it this have on countries like PNG?

No it not true. The sero-prevalence of CMV in adults and the incidence of CMV infection are highest in developing countries (1 to 5%) and are most likely driven by non-primary maternal infection.

In PNG, the burden of CMV in unknown as a result of lack of awareness among clinicians and general population. This leads to lack of identifying probable cases and further investigating them appropriately. There is no vaccine for CMV which means that there is no protection or herd immunity. Some populations, for example those with HIV are prone to getting CMV. Because there is lack of awareness in identifying the cases we are mostly likely missing out cases of possible patients with squealed from CMV, the commonest of which is sensorial deafness.
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What Clinical Features would make you suspect maternal primary CMV Infection (Primary infection in mothers)?

This includes glandular fever or flu-like illness
Routine USS of abnormalities suggestive of CMV that lack other apparent cause

What is the commonest complication of CMV? What are the clinical features?

- Hearing impairment (sensory-neural hearing loss)
- Microcephaly
- Petechiae and thrombocytopenia
- Chorioretinitis and visual impartment is thought to occur in 22 to 58% of symptomatic infants

What are the risk factors of CMV transmission in pregnancy?

There is a higher risk of CRS in foetuses of mothers with primary infection, but the risk still exists for foetuses of mothers with non-primary infection. HIV is a risk factor for vertical transmission, but most CRS is not related to HIV. Cerebral ultrasound abnormalities inutero indicate a poor prognosis for microcephaly and developmental problems.

What is the treatment for symptomatic CMV in newborn? What are the benefits and the side effects for this treatment?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Benefits</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valaciclovir (oral)</td>
<td>Safe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decrease circulating-foetal viral load</td>
<td></td>
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<tr>
<td>CMV hyper-immune globulin (HIG)</td>
<td>Inhibits viral spread in vitro</td>
<td></td>
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<tr>
<td></td>
<td>Restore placental health in mothers</td>
<td></td>
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<tr>
<td></td>
<td>Leads to regression of cerebral USS abnormalities</td>
<td></td>
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<tr>
<td>Ganciclovir</td>
<td></td>
<td>Shown to have mutagenic potential in animal</td>
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</tbody>
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Zika virus – a review for clinicians

When Zika virus was first discovered?
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It was first discovered in 1947 in Rhesus monkey during experiments conducted to study the vectors responsible for yellow fever in Zika Forest, Uganda.

What are the vectors of Zika and what other viruses share these vector?

Vector for Zika virus are the Aedes genus of mosquitoes predominately *Aedes aegypti* and *Aedes albopictus*. The other viruses that share the same vector includes Chikungunya and Dengue.

What Countries in Oceania are known to have Zika Virus?


What are the modes of Transmissions of Zika Virus?

Transmission of Zika Virus can be

- Mosquito borne (*A. aegypti* or *A. albopictus*)
- Sexual transmission
- Animal contact transmission (confirmed transmission from a monkey bite in Indonesia)
- Blood transfusion
- By canoe! (this is how it is believed that Zika first went from Pacific islands to Brazil, in mosquito eggs in canoes or other containers around the time of the Va’s World canoe sprint championship)

What are the clinical features of Zika Virus infection?

- Maculopapular rash, fever, arthralgia’s, conjunctivitis, headache and myalgia.
- 80% remain asymptomatic
- Course of illness self-limiting and last 4 to 7 days

And how do these clinical features differ from those caused by other viruses carried by the same vector?

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Zika virus</th>
<th>Dengue fever</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maculopapular rash</td>
<td>Descending rash , starts from the face&amp; spreads throughout the body within 6 days</td>
<td>Generalised and confluent with islands of sparing</td>
<td></td>
</tr>
<tr>
<td>Non-purulent conjunctivitis</td>
<td>60%</td>
<td>15-30%</td>
<td></td>
</tr>
<tr>
<td>Fevers</td>
<td>Short course of low grade fevers</td>
<td>High fevers</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Arthralgia and myalgia</td>
<td></td>
<td>Bilateral migratory arthralgia affecting small joints of the extremities</td>
</tr>
</tbody>
</table>
Beside microcephaly identified in Brazil, what are the other neurological manifestation of Zika virus infection?

Guillain-Barre syndrome, meningitis, encephalitis, myelitis

What are the diagnostic test for Zika virus and what are the problems of these test?

The methods used include

- **Reverse Transcriptase- Polymerase Chain Reaction – (RT-PCR)**
  - Can be done on serum, urine, saliva, amniotic and semen samples.
  - Because of the of the period of viraemia which last for 4 to 8 days after the onset of symptoms— CDC recommends 5 day cut off for performing RT – PCR and the virus is more isolated on saliva samples compared to serum.
  - Also urine samples have a viral load and it carries the virus for more than 10 to 20 days compared to serum samples.

- **Serology / antibody Testing**
  - Zika virus IgM is usually present in serum 4 days to 2 weeks after symptom onset, and may last for 6 months post-infection.
  - Serological tests of Zika or Dengue IgM lacks some diagnostic precision because of cross reactivity between Zika virus and other Flavovirus (Dengue)
  - Confirmatory neutralising antibody testing can help differentiate Zika from other viruses.