The acronym TORCH refers to Toxoplasmosis, Others, Rubella, Cytomegalovirus and Herpes are chronic infections that are transmitted vertically from the mother to the baby. The O in TORCH which initially stood for syphilis and hepatitis has expanded to include infections like HIV, Parvo B19 and varicella. These antenatally or perinatally transmitted infections have minimal effects on the mother but can have devastating effects on the fetus. Their diagnosis is important for therapeutic and preventive reasons but unfortunately, the tests are difficult to interpret. Over the years, TORCH serological tests have not just been used, but misused and confused, both in the mother and in the baby.

Demonstration of IgM antibody titres or rising titers of IgG antibody suggests acute infection in pregnancy but do not tell us if the infection has crossed the placenta and infected the fetus. To confirm this requires invasive tests on amniotic fluid or fetal blood which are usually not available. In most situations infection is suspected retrospectively depending on the clinical findings of the baby. Interpretation of serological titres in the baby are difficult because pathogen-specific IgM serologic tests are notoriously unreliable due to cross reactivity and neonatal IgG titers are difficult to interpret because of transplacental passage of antibodies. Culture positivity rates are low but PCR tests are helpful if available.

Toxoplasmosis

Routine Toxoplasma IgM kits are not standardized and hence are extremely unreliable. In most developed countries multiple antibody tests (eg Sabin Feldman, ISAGA, HI, IFA) are done and interpreted only in a reference laboratory. ELISA kits are commonly used today but the reliability depends on the make. The test is not indicated for recurrent fetal loss (Toxoplasma never causes recurrent abortions) or unexplained mental retardation/hepatosplenomegaly. However, its use is justified in a pregnant female with lymphadenopathy or infectious mononucleosis-like illness or for investigations of unexplained nonrecurrent, non immune hydrops or a first episode of fetal loss. Most fetal infections (>75%) occur if infection occurs in the latter part of pregnancy. If a high-risk pregnant woman (immune compromised or HIV positive) has a positive Toxoplasma serology (Four fold rise in IgG in 3 weeks with IgM or IgA positivity), fetal infection is determined by a PCR of the amniotic fluid and USG (hydrocephalus). Further management decisions, termination of pregnancy or specific drug therapy is taken based on these results.

If a pregnant mother has had a previous documented toxoplasma infection she does not require treatment during a subsequent pregnancy. However in an immune compromised state she should be investigated for reactivation. Involvement of the fetus in reactivation cases is very rare. Treatment of the mother is to be considered only if there is an acute infection during pregnancy and the pregnancy is to be continued.

A neonate or young infant may need toxoplasma serology in the following situations:
(a) Baby having chorioretinitis, hydrocephalus, intracranial calcification or unexplained jaundice, purpura or hepatosplenomegaly, irrespective of maternal tests.

(b) Mother having a confirmed infection in pregnancy.

Treatment of an acutely infected neonate with sulphadiazine and trimethoprim alternating with Spiromycin for a period of 1 year may decrease CNS sequelae but has side effects.

Rubella

Immunization or natural infection in childhood protects women from significant infection. The former has resulted in a dramatic decline in the incidence of congenital rubella syndrome the world over. A woman who is negative for IgG should be vaccinated at least 3 months before conception. Rubella immunization is contraindicated in pregnancy. Infection during pregnancy can occur but the risk to the fetus is extremely low. Congenital Rubella syndrome occurs only if primary infection occurs before 20 weeks gestation.

Obstetricians should not ask for rubella serology for recurrent fetal losses/abortions. However, if a serologically negative mother develops features of rubella, particularly in early pregnancy, (fever, maculopapular rash and occipital and epitrochlear lymph nodes) the tests are justified. Infection is likely if IgM is +ve and IgG is +ve with rising titer 3 wks later. H/o exposure may not be available in most cases. Confirmation of fetal infection is possible with amniotic fluid PCR. However, it the mother is definitely positive in the first 20 weeks abortion could be considered even without this test as no treatment is available and consequences to the fetus are devastating.

In the neonate the tests should only be done if there are definite features of congenital rubella (triad of deafness, microcephaly and PDA) and not for unspecified Intrauterine Growth Restriction (IUGR) or microcephaly. False negative results can occur due to competing antibodies. Rubella infection can be long-standing and smoldering in the neonate and young infant but there is no specific treatment presently known for this disease.

CMV Infection

IgM for acute infection is unreliable because of technical difficulty in doing the assay. Specific ELISA tests available are more reliable with specificity of > 95% specificity. IgG only confirms past infection unless there is a 4-fold rise in titres.

Obstetricians often request this test after a single or recurrent abortion. Though CMV infection can theoretically cause abortion in early pregnancy it never causes recurrent abortion. Only the primary infection in mother leads to fetal manifestation severe enough to cause abortion. Subsequent infection in the mother during her next pregnancy is either reactivation infection or reinfection, both of which lead to milder manifestations in the fetus because of the protective role of maternal IgG antibodies. 95% of primary infections are asymptomatic and only 5% have an ‘infectious mononucleosis like’ illness in the first trimester. Primary CMV infection is suspected when IgM is +ve and recurrent infection is suspected if there is a 4 fold rise in IgG titres. If a pregnant female gives a
past h/o primary CMV or is IgG positive then the risk to the fetus is minimal and no active intervention is required. Fetal infection is ruled out in a high risk mother with IgM +ve serology by amniotic fluid PCR at > 20 weeks (100% sensitivity and 90% specificity).

In the neonate features of congenital infection (jaundice, organomegaly, purpura, microcephaly, persistent diffuse pneumonia) within 2 weeks of life warrants CMV serology. IgM is +ve. Infection is confirmed by PCR studies or urine culture for CMV. After the first 2 weeks it is difficult to differentiate between congenital and acquired infection.

Outcome of CMV infection in pregnancy

<table>
<thead>
<tr>
<th>Pregnant Women</th>
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<tbody>
<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>95% - 98% Immune (Prior infection)</td>
<td>2% - 5% Nonimmune</td>
</tr>
<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>0.15% Congenital Infection</td>
<td>1% - 4% Primary infection</td>
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<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>0%-1% Symptomatic with sequelae</td>
<td>40% fetal infection</td>
</tr>
<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>10%-15% Symptomatic</td>
<td>85% - 90% Asymptomatic</td>
</tr>
<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>90% - 95% sequelae</td>
<td>95% normal</td>
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</tbody>
</table>

Herpes Simplex

Infection is almost always acquired perinatally. Risk to newborn after primary infection in the mother at the time of labor is 33-50%. Reactivation infection at the time of labor decreases the risk to newborn to 3-5%. There is no reliable way to distinguish primary and reactivation infection. In 80% of neonatal herpes, the mother is asymptomatic. Serology for diagnosis of herpes is difficult as the sensitivity and specificity of the tests are low. Newer ELISA Ag kits claim to have better results. MSAFP is raised and maternal cervical secretions may show +ve PCR. Diagnosis of fetal infection is by amniotic fluid PCR and culture. Diagnosis of neonatal herpes can be done by following tests:

1. Tzanck smear
2. PCR of CSF, Blood
3. EEG / CT / MRI

Acyclovir is the drug of choice for both the mother and baby
Parvo B19 infection

This infection has become more frequent diagnosed in the recent past. It typically presents as a non-specific fever with arthritis in a pregnant woman whose fetus can then develops hydrops secondary to progressive anemia. The workup is usually that for the hydrops. The fetus is managed by titres and by MCA velocity to decide intrauterine transfusion. Pregnant women exposed to, or who develop symptoms of, parvovirus B19 infection should be assessed to determine if they are susceptible to infection (nonimmune) or if they have a current infection, by determining their parvovirus B19 IgG and IgM status. If parvovirus B19 IgG is present and IgM is negative, the woman is immune and can be reassured that she will not develop infection and that the virus will not adversely affect her pregnancy. If both parvovirus B19 IgG and IgM are negative and the incubation period has passed, the woman is not immune and has not developed the infection. If infected the woman should be counselled regarding risks of fetal transmission, fetal loss, and hydrops. Serial ultrasounds should be performed up to 8 to 12 weeks after infection to detect the development of hydrops. If hydrops develops consideration should be given to fetal blood sampling and intravascular transfusion.

References: