Revised algorithm\(^1\) for assessing pregnant women with a history of travel during pregnancy to countries or areas with risk for Zika virus (ZIKV) transmission\(^2\)

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1. **Currently symptomatic**
   - Pregnant woman reports clinical illness consistent with ZIKV disease\(^4\) during or within two weeks of travel or sexual contact with potentially infectious partner\(^5\)
   - Submit serum for testing at RIPL. Also send urine if within 21 days of symptom onset\(^6\)
   - Offer baseline fetal ultrasound screening
   - **Positive (or inconclusive) ZIKV antibody (and PCR) test results**
     - Confirm negative ZIKV antibody test results on a further serum sample, if appropriate\(^7\)
     - Submit further samples as advised by RIPL
     - Refer to fetal medicine service for further evaluation and follow up\(^8,9\)
   - Return to normal pregnancy care

2. **Symptoms resolved**
   - Pregnant woman with history of travel during pregnancy to a country or area with risk for ZIKV transmission\(^3\)
   - Submit serum for testing at RIPL. Also send urine if within 21 days of symptom onset\(^6\)
   - Offer baseline fetal ultrasound screening
   - **Positive (or inconclusive) ZIKV antibody test results**
     - Submit further samples as advised by RIPL
     - Refer to fetal medicine service for further evaluation and follow up\(^8,9\)

3. **Pregnant woman does NOT report clinical illness consistent with ZIKV disease\(^4\) during or within two weeks of travel or sexual contact with potentially infectious partner**
   - Take and store clotted serum sample\(^10\). Offer baseline fetal ultrasound & again at 18-20 weeks or at same visit if first visit is later than 20 weeks. (If ultrasound normal, consider repeating at 28-30 weeks)\(^11\)
   - **If abnormal ultrasound findings (e.g. small head\(^12\) or intracranial calcifications)\(^13\) or additional concerns, refer to fetal medicine service**

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\(1\) Revised algorithm

\(2\) Zika virus

\(3\) Pregnant woman reports clinical illness consistent with ZIKV disease during or within two weeks of travel or sexual contact with potentially infectious partner

\(4\) Pregnant woman does NOT report clinical illness consistent with ZIKV disease during or within two weeks of travel or sexual contact with potentially infectious partner

\(5\) During or within two weeks of travel or sexual contact with potentially infectious partner

\(6\) At 21 days of symptom onset

\(7\) If appropriate

\(8\) Further evaluation and follow up

\(9\) Fetal medicine service

\(10\) Clotted serum sample

\(11\) Fetal ultrasound

\(12\) Small head

\(13\) Intracranial calcifications
Notes

1. This guidance will be updated as more information becomes available. Currently this algorithm applies to women at all stages of pregnancy although infection in early pregnancy is likely to be the greatest risk.

2. Laboratory testing is performed by the PHE Rare and Imported Pathogens Laboratory (RIPL). Given the overlap of symptoms and endemic areas with other viral and bacterial infections, RIPL will routinely test significantly symptomatic pregnant women (those hospitalised and/or acutely unwell) returning from areas with active ZIKV transmission for dengue, chikungunya and other infections as well as ZIKV.

3. Assessment of pregnant women should be based on a history of travel to countries and territories at risk for ZIKV transmission. This is not required after travel to countries at very low risk for ZIKV.

4. Clinical illness is suggestive of Zika virus disease if a combination of the following symptoms are reported: rash; itching/pruritis; fever; headache; arthralgia/arthritis; myalgia; conjunctivitis; lower back pain; retro-orbital pain.

5. A pregnant woman with typical Zika virus symptoms (as above) that began within 2 weeks of sexual contact with a male sexual partner who has recently travelled (within the previous 3 months) to a country or area with risk for ZIKV, should be tested regardless of her own travel history, due the possibility of sexual transmission.

6. Appropriate samples are a clotted blood (or serum) and, if indicated, a small volume of urine without preservative. The samples must be submitted with an appropriate RIPL request form. This form must clearly state the pregnancy gestation and both the travel history (i.e. which countries visited and the dates of the outward and return journeys) and the clinical details (i.e. the patient’s symptoms and the date of illness onset). This is so that the appropriate investigations can be performed and their results correctly interpreted. ZIKV testing will be performed using real-time PCR and serology. For more information refer to: Zika virus: sample testing advice

7. If Zika virus antibodies are not detected in a serum sample collected 4 or more weeks after the last possible travel-associated or sexual exposure, then recent Zika virus infection is highly unlikely.

8. This evaluation and follow-up is likely to include repeat fetal ultrasound and blood testing for ZIKV RNA at four weekly intervals, and consideration of fetal MRI. Abnormal fetal findings will prompt appropriate investigation including, for example, submission of booking and current serum samples for toxoplasma, rubella, parvovirus and CMV serology. Amniocentesis may be considered for ZIKV PCR.

9. Neonatologists and obstetricians should collaborate prior to delivery to agree a plan for investigations at birth. For more information refer to: Zika virus congenital infection: algorithm and interim guidance for neonatologists and paediatricians

10. For women who have not had symptoms, taking and storing a clotted serum sample locally, without immediate testing, is recommended. In the event that there is a later concern about fetal development, this sample will be available for retrospective testing, including detection of Zika virus antibodies. For more information refer to: Zika virus: sample testing advice

11. This is in line with WHO guidance on the management of asymptomatic pregnant women who have returned from Zika-affected countries

12. In this context, 'small fetal head' is defined as: Head Circumference more than 2 Standard Deviations below the mean for gestational age, i.e. below the 2.5th centile.

13. Apart from microcephaly and intracranial calcifications, other brain abnormalities that have been reported in association with ZIKV infection are ventriculomegaly, cell migration abnormalities (e.g. lissencephaly, pachygyria), and arthrogryposis (congenital contractures) secondary to central or peripheral nervous system involvement.

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