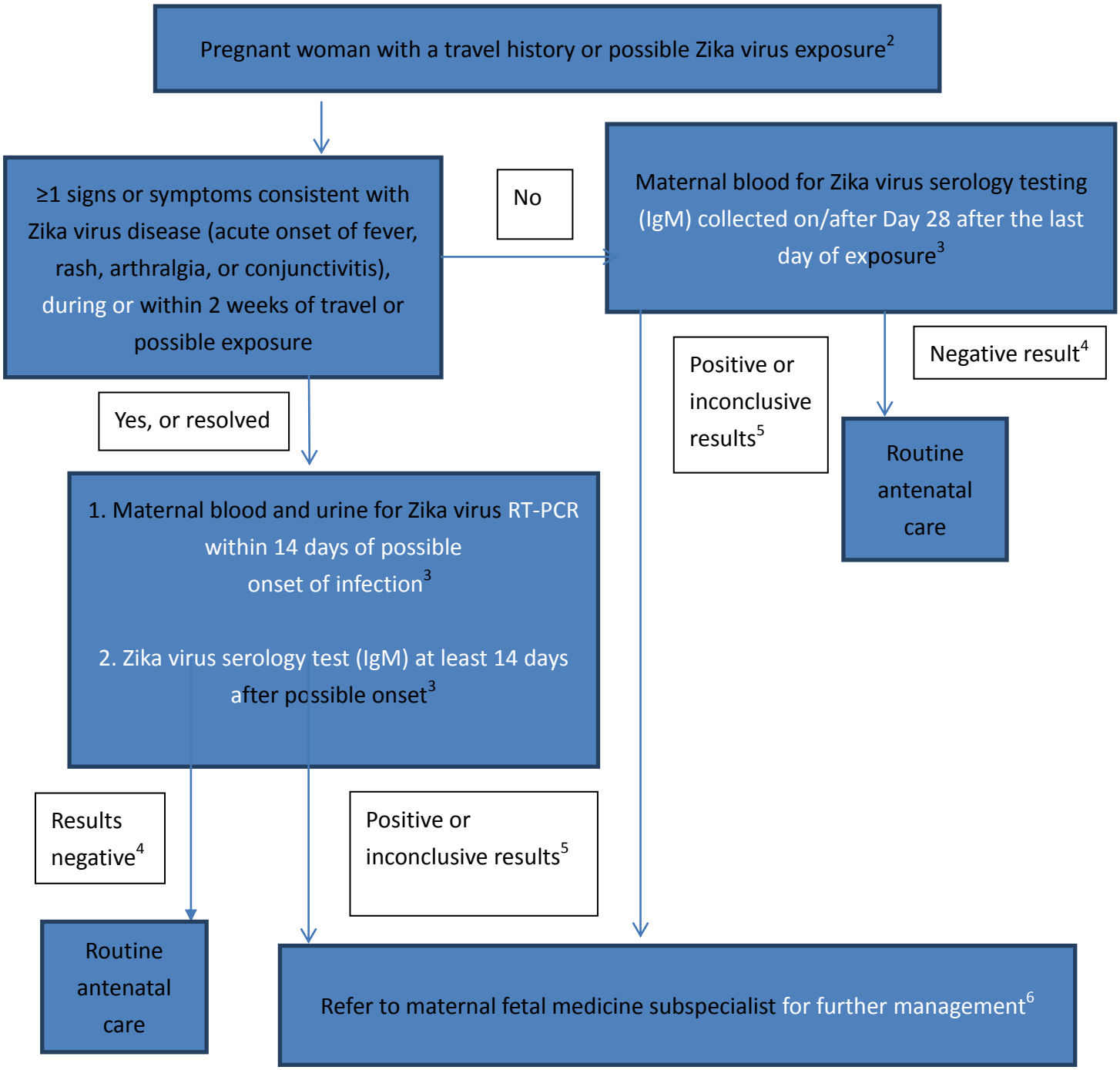
Interim guidelines[1] on the management of a pregnant woman with possible Zika virus exposure[2]

Endorsed by the Hospital Authority Coordinating Committee in Obstetrics & Gynaecology and Hong Kong College of Obstetricians and Gynaecologists

with effect from 26 September 2016



Remarks:

1. This is an **interim guidelines** update prepared by local O&G and microbiology experts after making references to the updated CDC, RCOG, ACOG and Singapore guidelines on Zika virus to replace the interim guideline published on 11 February 2016:
   - Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016. http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e
   - Interim RCOG/RCM/PHE/HPS clinical guidelines: Zika Virus Infection and Pregnancy Information for Healthcare Professionals: Updated 05/08/16 (Previous guidance published on 17/06/16). https://www.rcog.org.uk/en/news/interim-clinical-guidelines-on-zika-virus-infection-and-pregnancy/
   - Revised algorithm for assessing pregnant women with a history of travel during pregnancy to areas with active Zika virus transmission (12 August 2016). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/545782/Zika_algorithm_for_assessing_pregnant_women_with_a_history_of_travel.pdf
   - Practice Advisory on Zika Virus. http://www.acog.org/About-ACOG/News-Room/Practice-Advisories/Practice-Advisory-Interim-Guidance-for-Care-of-Obstetric-Patients-During-a-Zika-Virus-Outbreak.
   - Zika in Singapore https://www.moh.gov.sg/content/moh_web/home/diseases_and_conditions/z/zika.html#4
   - This interim guideline will be further updated when more understanding of the disease becomes available.

2. **Possible Zika virus exposure**
   - includes travel (within 4 weeks before conception) to or residence in an area with active Zika virus transmission, or have sexual contact (vaginal, oral, anal or sex toys) without a barrier contraception with a partner who has symptoms compatible with Zika virus infection and travelled (within prior 6 months) to, or lives in an area with active Zika virus transmission.
   - Countries and areas with active Zika virus transmission can be found in the Centre of Health Protection (CHP) website at http://www.chp.gov.hk/

3. **Laboratory Test for Zika virus**

   The testing strategy depends on the gestational age, dates of potential exposure or

symptom onset, and the date of specimen collection. The general principles are:

- Laboratory testing for dengue should be considered where necessary.
- The incubation period of the infection needs to be taken into account and may range from a few days to over a week.
- For pregnant women considered to be within 14 days of onset of symptom, send blood and urine specimens for Zika virus reverse transcriptase-PCR (RT-PCR).
- For pregnant women considered to be 14 days or more after onset of symptom, send blood for Zika virus serology testing (IgM).
- As symptoms of Zika virus infection are non-specific and many infected persons may not have symptom, Zika virus serology testing (IgM) can be offered to asymptomatic pregnant women with a possible Zika virus exposure. To avoid a false negative result, collect blood sample for IgM serology at least 28 days after the last exposure (incubation up to 14 days plus development of antibodies by 7-10 days after onset of infection).
- In special circumstance such as pregnant woman presents shortly before 24-week gestation with no symptom but history of exposure, RT-PCR as well as serology may be offered after consulting the microbiologist.
- If a pregnant woman seeks care > 12 weeks after the latest possible symptom onset date (taking into account the incubation period), there is currently no reliable serology to diagnose recent Zika virus infection, and laboratory testing generally should not be offered.
- Serological assays are subject to cross-reactivity especially in patients with prior flavivirus infection such as denque or immunization history (e.g. yellow fever vaccination). The results should be interpreted with the involvement of the microbiologist and further testing may be required depending on the circumstances.
- CHP laboratory will support the testing and retesting, advice on specimen collection and result interpretation.
- Appropriate samples should be collected, and appropriate forms completed with adequate information including gestation/ expected date of confinement/ last menstrual period, travel history with dates, symptoms and their onset dates.

4. Negative test results

- If Zika virus IgM result is negative in a serum sample collected between 4 and 12 weeks after the latest possible symptom onset date (taking into account the incubation period), recent Zika virus infection is excluded. Routine antenatal care can be provided.

5. Confirmed or suspected Zika virus infection

- Any confirmed or suspected recent Zika virus infection case is required to stay during viraemic phase in a mosquito free environment but not in a strict isolation ward. These cases should not be admitted to an obstetric ward even if they are pregnant because their admission is not for an obstetric reason and may cause panic to other pregnant women.

6. Maternal Fetal Medicine subspecialist involvement

- Given the uncertainties about Zika virus biology and the challenges in the management and counseling, it is advisable to refer pregnant ladies with confirmed or presumptive Zika virus infection to Maternal Fetal Medicine (MFM) subspecialist for further management. A MFM subspecialist may be able to detect subtle fetal abnormalities in earlier gestation before the late signs including calcification and small head manifest.

Role of serial fetal scan

- In confirmed or presumptive recent Zika virus infection, a mid-trimester anomaly scan and a follow up scan in the third trimester to assess fetal anatomy, particular neuroanatomy and growth can be offered. Microcephaly and intracranial calcifications may exhibit in late pregnancy, and fetal growth restriction may be present.
- Fetal microcephaly is suspected when the head circumference is <= mean -2SD with corresponding gestational age or below the 2.5^{th} centile.
- The sensitivity of prenatal ultrasound for detection of microcephaly depends on many factors including the timing of maternal infection relative to the timing of screening, severity of microcephaly, patient factors, and gestation age.
- There were other reported abnormalities including corpus callosal and vermian dysgenesis, enlarged cisterna magna, severe unilateral ventriculomegaly, agenesis of the thalami, arthrogryposis, cataracts, intracranial and intraocular calcifications.

Role of amniocentesis

- In confirmed or presumptive recent Zika virus infection, amniocentesis might be considered after taking into individual clinical circumstance.
- Discuss with the microbiologist before performing amniocentesis to test for Zika virus via RT-PCR.
- The sensitivity and specificity of detecting Zika virus RNA in amniotic fluid in diagnosing intrauterine infection is unclear. Zika virus load in the amniotic fluid is expected to be low before 20 weeks' gestation as fetal urination is not well

established until then.

- A positive Zika virus RT-PCR result from amniotic fluid is suggestive of intrauterine infection. The positive predictive value of a positive result for fetal abnormality is not known.
- A negative Zika virus RT-PCR result from amniotic fluid may prompt a work up for other causes of microcephaly (e.g. other infections like toxoplasma, rubella, parvovirus and CMV, genetic disorders).

After birth

- Paediatric consultation after delivery is recommended.
- To evaluate possible congenital Zika virus infection in newborns of mothers with confirmed or presumptive recent Zika virus infection, Zika virus identification can be performed on infant serum, umbilical cord and placenta after delivery or on fetal tissue after fetal loss. Please discuss with a hospital microbiologist or relevant laboratory for arrangement.