NATIONAL LABORATORY HANDBOOK

TORCH Testing in Obstetrics and Neonatology V2

Document reference number	**CSP030/2019**	**Document developed by:-**	National Clinical Programme for Pathology
Revision number	Version 2	**Document approved by:-**	National Clinical Programme for Pathology. Clinical Advisory Group for Pathology. National Clinical Advisor and Group Lead.
Approval date	09/2019	**Responsibility for implementation:-**	Acute Hospital Division
Next Revision date	09/2022	**Responsibility for review and audit:-**	National Clinical Programme for Pathology

National Clinical & Integrated Care Programmes
Person-centred, co-ordinated care

PATHOLOGY

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Contents

Authors

Cillian De Gascun, Consultant Virologist & Laboratory Director, UCD National Virus Reference Laboratory, Dublin 4.

Susan Knowles, Consultant Microbiologist, National Maternity Hospital, Holles Street, Dublin 2.

Revision Date

September 2019

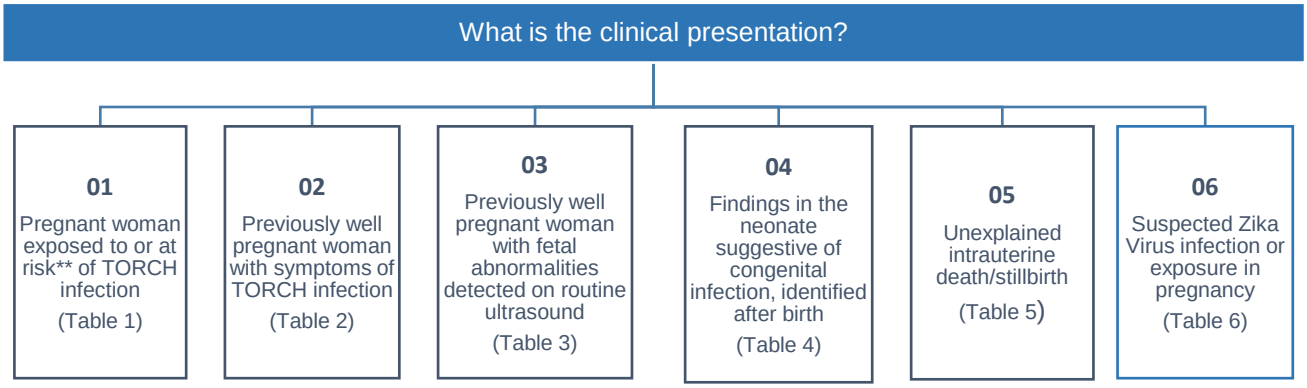
Next Revision Date

September 2022

Document History

Version Number	Location	Amendment
2.0	Graphic. Page 3	Addition of Suspected Zika Virus infection or exposure in pregnancy within graphic.
	Table 3. Page 9	Addition of Suspected Zika Virus infection or exposure in pregnancy within table.
	Table 4. Page 10	Addition of Suspected Zika Virus infection or exposure in pregnancy within table.
	Table 6. Page 12	Addition of Suspected Zika Virus infection or exposure in pregnancy table.

TORCH* Testing Algorithms in Obstetrics and Neonatology



Guidance notes for the use of this document

1. *TORCH is a non-exhaustive acronym used to refer to the main pathogens that may cause congenital infection in the fetus and newborn (Toxoplasma, Other [such as parvovirus, syphilis, varicella-zoster virus], Rubella, Cytomegalovirus, Herpes Simplex Virus).
2. **Pregnant women presenting with test results or an existing diagnosis from their GP or overseas should have their serology repeated to confirm the diagnosis before any intervention is considered.
3. This document is not a treatment guideline: it is intended to facilitate the prompt appropriate investigation of common infection-related issues in pregnancy.
4. Positive or unusual results should be discussed promptly with your local infection specialist (Clinical Microbiologist, Infectious Disease Physician (Adult or Paediatric), Clinical Virologist) & maternal-fetal medicine specialist.
5. Infection in the pregnant woman does not necessarily mean that the baby will be infected or affected: therefore, all babies born to mothers with evidence of infection during pregnancy should be screened at birth to confirm or exclude infection in the infant.
6. False positive IgM results are not uncommon in pregnancy: however, no IgM result should be assumed to be a false positive in the absence of confirmatory testing.
7. In the absence of a documented antibody response, a history of immunization against Measles or Varicella does not alter the advice presented below.

This document should be used in conjunction with existing national guidelines:

Immunisation Guidelines for Ireland – *www.immunisation.ie*
Rainbow Clinic guidelines – *www.ssstdi.ie*
HSE/RCPI National Clinical Programme for Obstetrics and Gynaecology Clinical Practice Guidelines, see: *http://www.hse.ie/eng/about/Who/clinical/natclinprog/obsandgynaeprogramme/guidelines/*

Please note: positive results suggesting recent or active infection should be discussed with your local Infection Specialist

Table 1: Otherwise well pregnant woman exposed to potential TORCH infection

1.1. Varicella Zoster Virus (Chickenpox/Shingles)

Ask about chickenpox or shingles history

→ **CONFIRMED HISTORY or Documented Prior Vaccination**:
No further testing required

NO HISTORY:
Draw blood (or test stored booking blood) for VZV IgG

→ **IgG DETECTED**:
No further testing required

IgG NOT DETECTED:
Administer VZIG
within 10 days (but ASAP)
Refer to Fetal Medicine

IgG EQUIVOCAL:
Administer VZIG
within 10 days (but ASAP)

NOTES: **VZIG is only 50% effective; Consider post-partum vaccination against VZV in non-immune women of childbearing age**

1.2 Parvovirus B19 (Slapped Cheek Syndrome)

Draw blood for Parvovirus B19 IgG & IgM; or test stored blood for IgG

→ **IgG DETECTED in BOOKING BLOOD**:
No further testing required; consider patient immune

IgG NOT DETECTED in BOOKING BLOOD:
Draw blood for Parvovirus B19 IgG & IgM

→ **IgG DETECTED;**
IgM NOT DETECTED:
No further testing required; consider patient immune

→ **IgM DETECTED**;
Repeat serology and request Parvovirus B19 DNA testing (regardless of IgG result).

Presence of DNA confirms recent infection
Refer to Fetal Medicine if IgM & DNA detected

IgG & IgM NOT DETECTED:
Repeat blood test in 4 weeks to test for a seroconversion

If ongoing exposure to circulating Parvovirus (e.g. a pregnant teacher with documented B19 activity in school), then repeat serology at 4 weekly intervals until delivery

NOTES: **All pregnant women with recent B19 infection should be referred to fetal medicine unit for further assessment**

1.3 Measles

Draw blood (or test stored booking blood) for Measles IgG

IgG DETECTED*:
No further intervention required

**Documentation of prior receipt of 2 doses of MMR vaccine at least 1 month apart can be considered presumptive evidence of immunity to measles*

IgG EQUIVOCAL:
Administer Human Normal Immunoglobulin (HNIG) within 6 days.

Please refer to Immunisation Guidelines for Ireland at www.immunisation.ie for additional information

IgG NOT DETECTED:
Administer Human Normal Immunoglobulin (HNIG) within 6 days.

Please refer to Immunisation Guidelines for Ireland at www.immunisation.ie for additional information

NOTES:

1. Measles does not cause a congenital syndrome, but is associated with an increased risk of premature delivery and spontaneous abortion;
2. Morbidity and mortality are increased in pregnant women with measles due to an increased risk of measles pneumonia during the third trimester and peripartum period;
3. Oral fluid should be obtained from the index case and tested for Measles IgM and RNA to confirm the diagnosis;
4. Pregnant women who are not immune to measles should be offered the MMR vaccine after delivery, and at least 3 months after receiving HNIG.

1.4 Rubella

Draw blood for Rubella IgG (if not already performed on booking blood)

IgG DETECTED*

No further intervention required

**Documentation of prior receipt of 1 dose of a rubella-containing vaccine can be considered presumptive evidence of immunity to rubella*

IgG EQUIVOCAL:
Immune globulin is NOT recommended for routine post-exposure prophylaxis of rubella in pregnancy.

Oral fluid & blood should be obtained from the index case to confirm the diagnosis and inform further management.

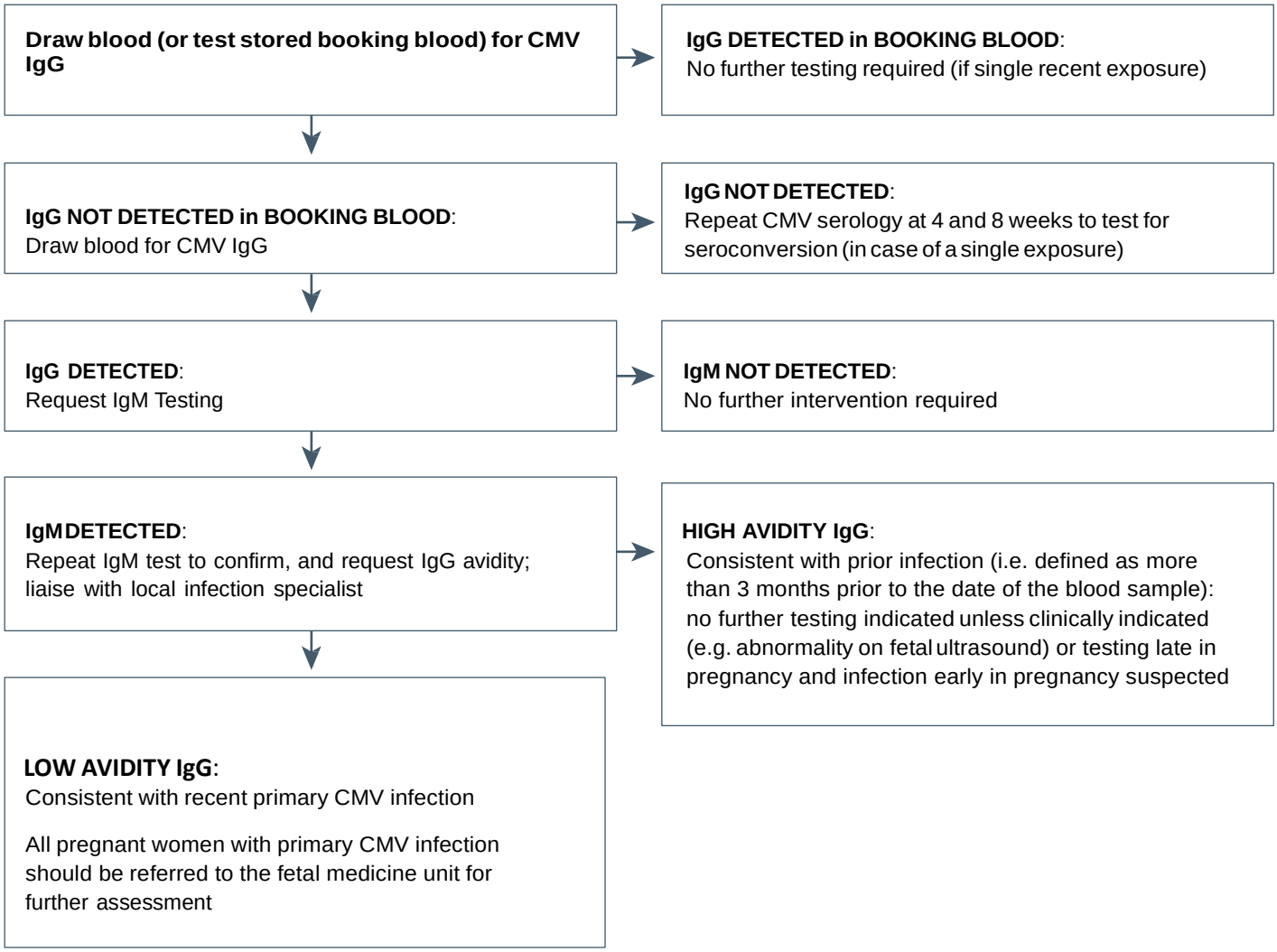
All pregnant women exposed to a case of confirmed rubella should be referred to the fetal medicine unit.

IgG NOT DETECTED:
Immune globulin is NOT recommended for routine post-exposure prophylaxis of rubella in pregnancy.

Oral fluid & blood should be obtained from the index case to confirm the diagnosis and inform further management.

All pregnant women exposed to a case of confirmed rubella should be referred to the fetal medicine unit.

1.5 Cytomegalovirus (CMV)

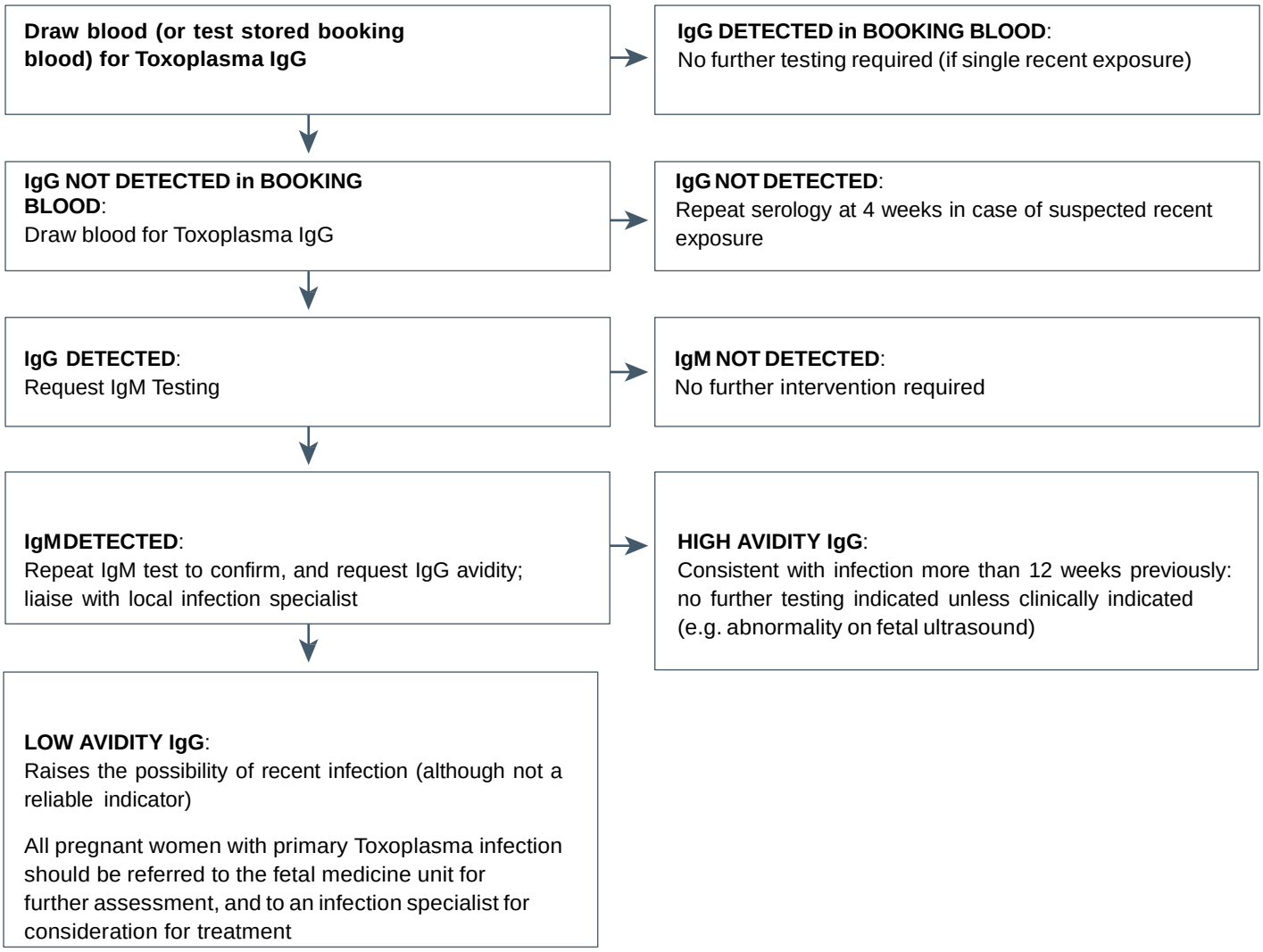


NOTES:

1. All children born to women with CMV infection in pregnancy should be screened for congenital infection at delivery.

2. Congenital infection occurs in ~40% of infants following a primary CMV infection during pregnancy. Please note that congenital CMV infection can also occur when the mother is CMV positive prior to pregnancy (secondary infection) although transmission to the fetus is less common (<2%). The purpose of the algorithm above is to detect recent primary CMV infection only.

1.6 Toxoplasma gondii



NOTES:

1. All children born to women with Toxoplasma infection in pregnancy should be screened for congenital infection at delivery
2. Toxoplasma gondii is a protozoan parasite for which cats are the definitive hosts, but which can infect most species of mammal. Humans usually become infected by consumption of raw or undercooked meat (that contains cysts) or by accidental ingestion of sporulated oocysts from soil or in contaminated food or water.

1.7. Hand, foot and mouth disease (Coxsackie A/Enterovirus)

- There is no evidence that Enterovirus (EV) infections in pregnancy cause any congenital syndrome: however
  - Infection in early pregnancy can be associated with increased risk of miscarriage
  - Infection near time of delivery may result in transmission of virus to the neonate
- There is no serological test available to confirm prior EV exposure (although the majority of adults are likely to be immune)
- There is no role for post-exposure prophylaxis following EV exposure
  - Pregnant women should be reassured that the risk to the fetus is low

NOTES: Positive results suggesting recent or active infection should be discussed with your local Infection Specialist

Table 2: Previously well pregnant woman with symptoms suggestive of TORCH infection

Previously well pregnant woman with clinical symptoms

2.1. Generalised Rash Illness

Is the rash vesicular?

YES:
Most likely diagnosis is Varicella Zoster Virus infection (chickenpox)

Send vesicular fluid for VZV DNA testing to confirm. VZV IgM testing may also be performed, but vesicular fluid is the preferred sample type.

NO:
Consider Measles, Enterovirus, Rubella, and Parvovirus (MERP)

1. Draw blood for Measles, Rubella, and Parvovirus IgM
2. Send oral fluid for Measles & Rubella IgM & RNA
3. Send nose & throat swab, and stool sample for Enterovirus RNA and culture

MERP Notes:

1. There is no specific antiviral treatment for Measles, but be aware of the increased risk for viral pneumonia in the third trimester.
2. There is no specific antiviral therapy for Enterovirus, nor is treatment typically required.
3. There is no specific antiviral treatment for Rubella, but all confirmed cases should be referred to the fetal medicine unit for further assessment.
4. Parvovirus B19 infection rarely requires treatment for the mother, but all confirmed cases should be referred to the fetal medicine unit for further assessment & monitoring for hydrops fetalis.

NOTES:

1. Antiviral therapy (acyclovir) may be indicated, especially after 20 weeks gestation, or if the pregnant woman is immunosuppressed, but should always be considered in accordance with local guidelines and advice of Consultant Microbiologist or Infectious Diseases physician.
2. Adults are at an increased risk of VZV complications (e.g. pneumonia, with risk greater in later gestations.
3. All women with confirmed VZV infection in pregnancy should be referred to the fetal medicine unit for further assessment.
4. The greatest risk of congenital varicella syndrome is in the first or early second trimester: incidence is approximately 1-2% when infection occurs before 20 weeks.
5. There is no role for VZIG in the treatment of maternal VZV infection in pregnancy.

2.2 Hepatitis

- Draw blood for viral hepatitis screen (Hepatitis A, B, C, E, CMV, & EBV)
  Additional investigations guided by results
  - All primary CMV infections should be referred to fetal medicine unit for further assessment
  - All Hepatitis B & C infections should be referred to hepatology for assessment
  - There is no specific antiviral therapy for Hepatitis A or Hepatitis E, but Hepatitis E is associated with increased mortality in pregnant women (especially in the third trimester) so confirmed cases should be closely monitored
  - There are no specific concerns relating to EBV in pregnancy: severe primary EBV cases should be reviewed by a Clinical Microbiologist, or a consultant in Infectious Diseases (ID) or Haematology

NOTES: Positive results suggesting recent or active infection should be discussed with your local Infection Specialist

Table 3: Pregnant woman with abnormalities detected on foetal ultrasound

Recommended investigations for the pregnant woman with abnormalities detected on foetal ultrasound						
	CMV [1]	Parvovirus B19 [2]	Rubella [3]	Toxoplasma [4]	Treponema pallidum (syphilis) [5]	Zika Virus[6]
3.1 Micro/ Macrocephaly	X		X	X		X
3.2 IUGR	X	X	X	X	X	
3.3 Intracranial calcification	X		X	X		X
3.4 Echogenic bowel	X					
3.5 Ventriculomegaly	X			X		X
3.6 Structural heart defects			X			
3.7 Hydrops		X			X	

NOTES:

1. Draw blood for CMV IgG & IgM. If both negative, consider alternative diagnosis. If IgM present, may suggest recent infection. Repeat serology to confirm, and request IgG avidity testing (if not already done): In addition, request retrospective testing (for CMV IgG and IgM) on antenatal booking bloods.
   All confirmed CMV infections in pregnancy should be referred to the fetal medicine unit for further assessment.
2. Draw blood for Parvovirus IgG & IgM. If both negative, consider alternative diagnosis. If IgM present, request Parvovirus B19 DNA testing to confirm recent infection.
   All Parvovirus infections in pregnancy should be referred to fetal medicine unit for further assessment.
3. Draw blood for Rubella IgM. If negative, consider alternative diagnosis. If IgM present, or if patient known to be IgG negative at booking visit, request IgG testing plus IgG avidity to confirm seroconversion in pregnancy and/or recent infection. All confirmed Rubella infections in pregnancy should be referred to the fetal medicine unit for further assessment, and notified to Public Health.
   PLEASE NOTE: positive results suggesting recent or active infection should be discussed with your local Infection Specialist
4. Draw blood for Toxoplasma IgG & IgM. If both negative, consider alternative diagnosis. If IgM present, may suggest recent infection. Repeat serology to confirm, and request IgG avidity testing (if not already done): In addition, request retrospective testing (for Toxoplasma IgG and IgM) on antenatal booking bloods.
   All confirmed Toxoplasma infections in pregnancy should be referred to the fetal medicine unit for further assessment.
5. Draw blood for Treponema pallidum antibodies. If both negative, consider alternative diagnosis. If positive, request RPR to confirm recent / active infection.
   All T. pallidum infections in pregnancy should be referred to consultant in Genitourinary Medicine (GUM) or Infectious Diseases for antimicrobial therapy.
6. Zika Virus testing should only be performed in those patients presenting with the appropriate travel history.

Table 4: Neonatal abnormalities at birth									
Recommended investigations for the neonate with clinical / laboratory abnormalities at birth									
	CMV [1]	HSV [2]	Parvovirus B19 [3]	Rubella [4]	Toxo [5]	T pallidum [6]	VZV [7]	Other[8]	Zika[10]
4.1 Hepatitis / Jaundice / Hepatomegaly	X	X			X	X			
4.2 Rash	X	X				X	X		
4.3 Thrombocytopenia	X		X			X			
4.4 Anaemia	X	X	X			X			
4.5 IUGR[11]	X		X	X		X			X
4.6 Microcephaly	X			X	X				X
4.7 Hydrocephalus	X				X				
4.8 Failed Newborn Hearing Test	X								X
4.9 Patient Ductus Arteriosus (at term)				X					X
4.10 Intracranial Calcification	X			X	X				X
4.11 Congenital Cataracts or Microphthalmia				X					X
4.12 Hydrops			X			X			
4.13 Culture Negative Sepsis not responding to antibiotics in the first month of life[9]		X						X	

PLEASE NOTE: Positive results suggesting recent or active infection should be discussed with your local Infection Specialist

NOTES:

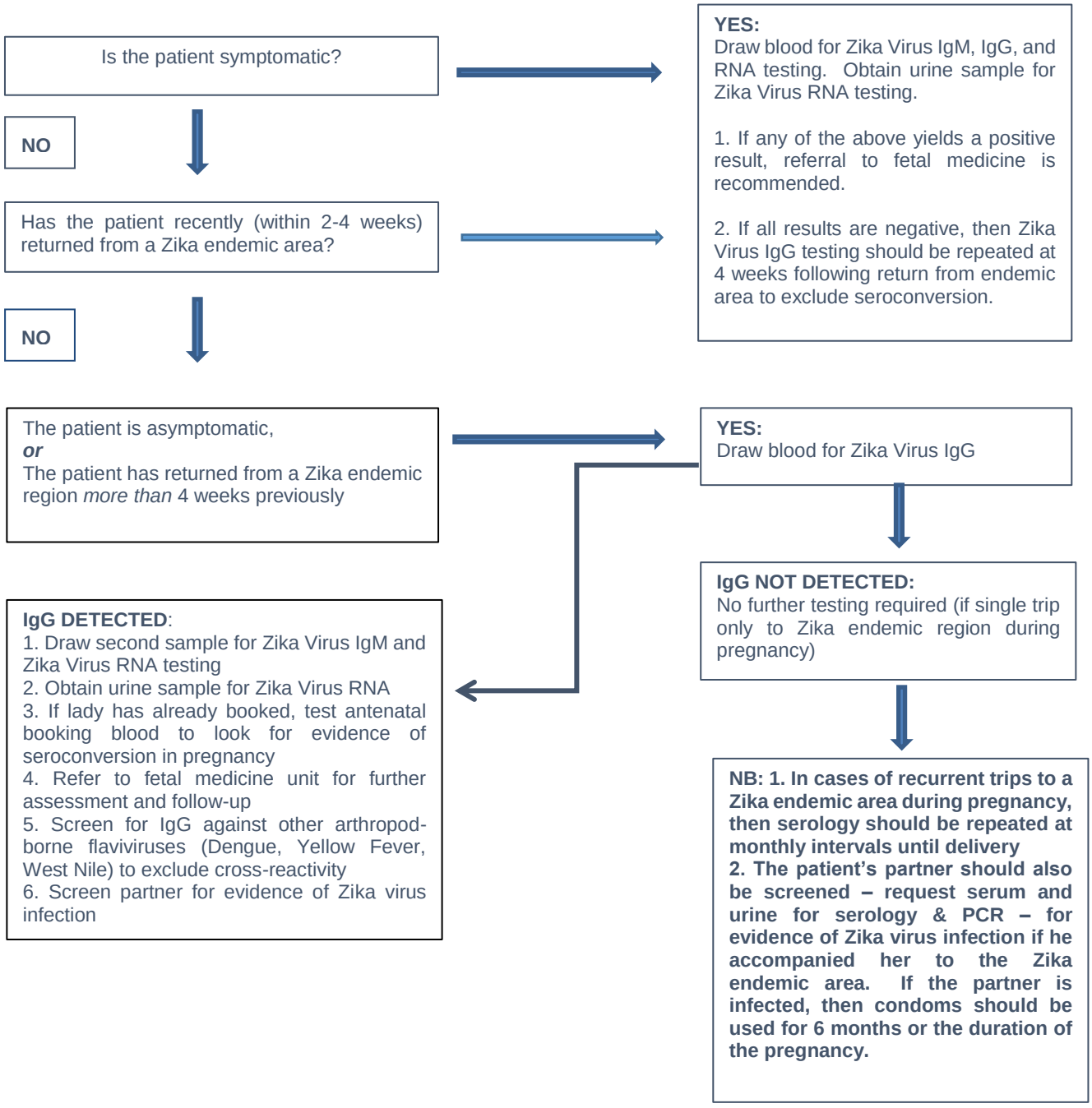
1. Send urine sample or salivary (viral) swab from the neonate for CMV DNA testing by PCR.
2. Send vesicular fluid or skin scrapings for HSV DNA testing; oral fluid, conjunctival swabs, EDTA blood, and CSF are also suitable for testing if neonatal HSV suspected.
3. Draw blood from the infant for Parvovirus B19 IgM and DNA testing.
4. Send urine sample and salivary swab from the neonate for Rubella RNA testing.
5. Draw blood from mother and infant for paired Toxoplasma IgM and IgG. If IgM present in either, request IgG avidity and discuss with Infection Specialist.
6. Draw blood from mother and infant for paired T pallidum antibody testing (including RPR). If RPR positive, discuss with Infection Specialist.
7. Send vesicular fluid or skin scrapings for VZV DNA testing.
8. Send NPA, stool, EDTA blood, +/- CSF (as clinically indicated) for Enterovirus RNA, and Adenovirus DNA testing.
9. All cases of culture negative sepsis should be discussed with Consultant Microbiologist or Infectious Diseases physician.
10. Zika Virus testing should only be performed in those patients presenting with the appropriate travel history.
11. If IUGR alone is present, without any other abnormalities, testing for CMV only is recommended.

Table 5: Intrauterine death (IUD) / stillbirth

Intrauterine death (IUD) / stillbirth

Please refer to existing HSE / RCPI National Clinical Programme for Obstetrics and Gynaecology Clinical Practice Guidelines and seek advice from Pathologist if post mortem examination is performed and findings are suggestive of infective process.

Table 6: Suspected Zika Virus Infection or Exposure in Pregnancy



NOTES

1: All women with evidence of Zika Virus infection in pregnancy should be referred to fetal medicine

2: All children born to women with evidence of Zika Virus infection in pregnancy should be screened for evidence of congenital infection at delivery

TORCH Guideline development

A group was established in 2014 including representation from the National Virus Reference Laboratory, the National Clinical Programme for Obstetrics and Gynaecology, the National Clinical Programme for Paediatrics and Neonatology, the National Clinical Programme for Pathology, the Irish Society for Clinical Microbiologists, and the HSE on foot of a request from Dr. Philip Crowley, National Director of Quality Improvement to develop National guidelines for diagnosis and management of viral infections in obstetrics & gynaeocology and neonatology. The draft guideline was developed by the National Director of the NVRL in conjunction with the President of the ICSM. The first draft was circulated to the members of the ICSM and the larger group for feedback, and suggested changes made. The final document was signed off by the group and published in 2016.

This second version was reviewed in January 2019 by the authors and the addition of testing for Zika Virus was inserted.

References

1. American Academy of Pediatrics. Red Book: 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics, 2012.

2. Royal College of Physicians of Ireland National Immunisation Advisory Committee. Immunisation Guidelines for Ireland (2013). *www.hse.ie/portal/eng/health/immunisation/hcpinfo/guidelines/immunisationguidelines.html.*

3. Department of Health, UK (2013). Immunisation against Infectious Diseases (The Green Book.) *www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book*.

4. Royal College of Obstetricians & Gynaecologists. Chickenpox in Pregnancy. RCOG Green-top Guideline No.13 (2015). *https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg13/*.

5. Health Protection Agency UK (2011). Guidance on Viral Rash in Pregnancy. *www.gov.uk/government/uploads/system/uploads/attachment_data/file/322688/Viral_rash_in_pregnancy_guidance.pdf*.

6. Society of Obstetricians and Gynaecologists of Canada Clinical Practice Guideline (2013). Toxoplasmosis in Pregnancy: Prevention, Screening, and Treatment. J Obstet Gynaecol Can 2013;35(1 eSuppl A):S1–S7.

7. Society of Obstetricians and Gynaecologists of Canada Clinical Practice Guideline (2010). Cytomegalovirus Infection in Pregnancy. J Obstet Gynaecol Can 2010;32(4):348–354.

8. Royal College of Obstetricians & Gynaecologists, and the British Association for Sexual Health and HIV (BASHH) Consensus Guideline (2014). Management of Genital Herpes in Pregnancy. *www.rcog.org.uk/en/guidelines-research-services/guidelines/genital-herpes/*.

9. Janier M, Hegyi V, Dupin N, et al. 2014 *European guideline on the management of syphilis*. J Eur Acad Dermatol Venereol. 2014 Dec;28(12):1581-93.

10. Butler K, Ferguson W, Goode M, Lyons F. Preventing Perinatal Transmission: a practical guide to the antenatal and perinatal management of HIV, Hepatitis B, Hepatitis C, Herpes Simplex, and Syphilis (June 2015 Edition). *www.ssstdi.ie* (Accessed August 14, 2015).

11. Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland Clinical Guideline No.31. Parvovirus B19 exposure/ infection during pregnancy (Version 1.0), September 2014.