Maternal Perinatal Infection Screening

Introduction

The TORCH acronym is a prompt to remember key infections in a pregnant woman and neonate. Untargeted TORCH serology testing has been repeatedly demonstrated to have very low utility. Consequently, the request "TORCH screen" is no longer provided at PathWest laboratories.

It is recommended that the clinical pattern of disease be used as a guide to specific testing (see table 1 and 2). This document is intended to guide appropriate microbiological diagnostic sampling. Due to their breadth, additional investigations such as liver function tests, coagulation profiles and radiological imaging that may aid in establishing a diagnosis are not included.

Of note, maternal booking bloods are stored in the laboratory for at least one-year post receipt. Dependent on the provider of antenatal care, these samples may be stored at PathWest or an external pathology provider. This can be used as an additional time point to confirm seroconversion when required.

Polymerase chain reaction (PCR) is a nucleic acid amplification test that detects DNA or RNA of the targeted pathogen.

A Clinical Microbiologist can guide test result interpretation, where required.

Guide

Table 1: Infection Differential Guided by Maternal and Fetal Presentation

Table 2: Maternal Test Selection by Potential Aetiology

Table 3: Test Sample Type and Volume

Table 1: Infection Differential Guided by Maternal and Fetal Presentation

Signs	CMV	Enterovirus	HSV	Parvovirus B19	Rubella[&]	*Toxoplasma*	*T. pallidum (Syphilis)*	Varicella (Primary)	Zika virus
Fetal Cranial abnormalities									
Microcephaly/ Macrocephaly	+				+	+		+ ^	+[*]
Intracranial calcification	+				+	+			+[*]
Ventriculomegaly	+					+		+ ^	+[*]
Fetal cardiac abnormalities									
Structural heart defect					+				
Fetal size									
Hydrops fetalis				+			+		
Intra-uterine growth retardation	+				+	+	+	+^	+[*]
Fetal limb abnormalities									
Limb hypoplasia or shortening								+^	
Maternal Rash									
Non-vesicular	+	+[=]		+	+		+		+[*]
Vesicular		+[=]	+					+[%]	

Table 1: Maternal screening during pregnancy. [&] Congenital rubella is highly unlikely in the setting of demonstrated maternal immunity; check maternal prior to consideration of testing of the neonate. **^**May be relevant in the setting of maternal infection consistent with primary varicella infection (chickenpox) during the first two trimesters of pregnancy. **[%]** Primary varicella infection can present as a vesicular rash affecting multiple dermatomes, with lesions occurring in crops at different stages (nodular to vesicular). Varicella reactivation (shingles) can occur in pregnancy, typically restricted to one dermatome and is negligible risk to the in-utero fetus. [*] A clinically compatible illness and exposure history required. This includes travel to an area with known Zika activity or sex without a condom with someone who lives or travelled in an area with Zika activity**.** [=] Enterovirus may present with rash on the palms of hands and soles of the feet.

Table 2: Maternal Test Selection by Potential Aetiology

Aetiology	Maternal Test Selection
Cytomegalovirus	**Preferred test: CMV serology (IgG and IgM)** • If IgG positive, CMV IgG Avidity testing should be requested. Low avidity is suggestive of recent infection. **Amniotic fluid[&] CMV PCR:** Increased accuracy if performed at > 21/40 gestation and > 6 weeks after maternal infection.
Enterovirus	**Active:** Throat/ rectal swab Lesion: enteroviral PCR
Herpes simplex virus (HSV-1 and HSV-2)	**Active:** Lesion/ vesicle HSV PCR **To confirm previous infection:** HSV IgG serology
Human immunodeficiency virus	**HIV serology**
Parvovirus B19	**Parvovirus serology (IgG and IgM)-** preferred initial screen **Parvovirus PCR:** On EDTA whole blood
Rubella	**Rubella serology (IgG and IgM)** **Amniotic fluid[&] Rubella PCR:** Increased accuracy if performed at > 21/40 gestation and > 6 weeks after maternal infection
Toxoplasma gondii	***Toxoplasma* serology (IgG and IgM)** • **If IgG positive, *Toxoplasma* IgG Avidity:** Low avidity is suggestive of recent infection **Amniotic fluid[&] *Toxoplasma* PCR:** Increased accuracy if performed at 18-20 /40 gestation or > 4 weeks after maternal infection
***Treponema pallidum* (syphilis)**	**Syphilis serology** **Active:** lesion PCR
Varicella Zoster Virus (VZV)	**Active:** Lesion/ vesicle VZV PCR +/- VZV Serology (IgG and IgM) if uncertainty exists as to whether infection is primary or secondary **To confirm previous infection:** VZV IgG serology (perform urgently in the setting of antenatal exposure as VZIG should be offered to seronegative women). **Amniotic fluid[&] VZV PCR:** May be considered at least one month after maternal infection in conjunction with fetal imaging (ultrasound and/or MRI) findings.

Zika Virus	A clinically compatible illness (fever, rash and arthralgia) and compatible exposure history required before further testing. This includes travel to an area with known Zika activity or sex without a condom with someone who lives or travelled in an area with Zika activity. **If symptom onset <2 weeks** - Baseline serology (IgM and IgG) - Blood and urine PCR - Repeat serology in two weeks **If symptom onset >2 weeks** - Serology (IgM and IgG)

Table 2: Maternal test selection by potential aetiology (see here for neonatal test selection). [&] Amniotic fluid testing can be used to confirm congenital infection. However, the risks and benefits of obtaining this sample should be considered and other diagnostic approaches utilised first, where possible. Guidance can be sought from a Clinical Microbiologist.

Table 3: Test Sample Type and Volume

Aetiology	Serology* Gold top tube preferred		PCR#		
	IgM	**IgG**	**Blood** (EDTA tube)	**Other fluid including amniotic fluid**	**Swab type% and site**
Cytomegalovirus	325 µL	325 µL	-	200 µL	X
Enterovirus	X	X	X	X	Dry swab: throat and rectal swab, lesion
Herpes simplex virus (HSV-1 and HSV-2)	X	325 µL	X	X	Dry swab: lesions
Human immunodeficiency virus	325 µL		X	X	X
Parvovirus B19	325 µL	325 µL	500 µL	200 µL	X
Rubella	200 µL	300 µL	500 µL	200 µL	X
Toxoplasma gondii	300 µL	300 µL	X	200 µL	X
***Treponema pallidum* (syphilis)**	650µL		X	X	Dry swab: lesion
Varicella (VZV)	380 µL	380 µL	X	X	Dry swab: lesion
Zika Virus	50 µL	150 µL	500 µL	200 µL	X

Table 3: Test sample type and volume. * For serology tests (IgG and IgM), the minimum stated volumes are per specific test and should be added to calculate the required volume for collection. For example, if both CMV IgG and IgM are required, the minimum serum volume is 650 µL. Sample volumes in this guide are expressed in whole blood volume based on a haematocrit of 55%. # For PCR, a single sample can be used to process multiple tests. % Any dry swab type is acceptable. Swabs in charcoal or amies are not acceptable

Bibliography

CMV

- The "Silent" Global Burden of Congenital Cytomegalovirus. CMR 2013; Jan 26(1)86 –102 doi.org/10.1128/CMR.00062-12

Enterovirus

- Neonatal enterovirus infections: emphasis on risk factors of severe and fatal infections. PIDJ: Oct 2003 - 22 (10)889-895 doi: 10.1097/01.inf.0000091294.63706.f3

HSV

- See KEMH maternal and neonatal guidelines
- Mother-to-Child Transmission of Herpes Simplex Virus. J Pediatric Infect Dis Soc. 2014 Sep; 3(Suppl 1): S19–S23. doi: 10.1093/jpids/piu050

Parvovirus

- Parvovirus B19 during pregnancy: a review. J Prenat Med. 2010 Oct-Dec; 4(4): 63–66.
- Parvovirus B19 Infection in Pregnancy. JOGC 2014, 36(12)1107-1116 doi.org/10.1016/S1701-2163(15)30390-X
- Parvovirus B19 infection in human pregnancy. BJOG 2011(118)175–186. Doi: 10.1111/j.1471-0528.2010.02749.x

Rubella

- Chapter 15: Congenital Rubella Syndrome. Manual for the Surveillance of Vaccine-Preventable Diseases. Date accessed 19th April 2021 Link
- Progress Toward Rubella and Congenital Rubella Syndrome Control and Elimination — Worldwide, 2000–2018. MMWR Morb Mortal Wkly Rep. 2019 Oct 4; 68(39): 855–859. doi: 10.15585/mmwr.mm6839a5

Toxoplasma

- Epidemiology of and Diagnostic Strategies for Toxoplasmosis. Clinical Microbiology Reviews Apr 2012, 25 (2) 264-296; DOI: 10.1128/CMR.05013-11
- Congenital Toxoplasmosis. J Pediatric Infect Dis Soc. 2014 Sep; 3(Suppl 1): S30–S35. doi: 10.1093/jpids/piu077

Syphilis testing

- See KEMH maternal and CAHS neonatal guidelines

Varicella

- Congenital varicella syndrome: A systematic review. J Obstet Gynaecol. 2016 Jul;36(5):563-6. doi: 10.3109/01443615.2015.1127905
- Management of varicella in neonates and infants. BMJ Paediatrics Open. 2019;3:e000433. doi: 10.1136/bmjpo-2019-000433

Zika virus

- Zika virus - information for clinicians and public health practitioners. The Department of Health. Australian Government. Date accessed 19th April 2021 Link
- Response to Zika; Implementing CDC guidance. Centre for Disease Control and Prevention. Date accessed 19th April 2021 Link

Feedback:	David.foley@health.wa.gov.au		
Document Owner:	Head of Department – Microbiology		
Reviewer / Team:	The PK Microbiology team		
Date First Issued:	February 2022	Last Reviewed:	February 2022
Amendment Dates:	-	Next Review Date:	February 2025
Approved by:	Clinical Microbiology, PathWest QEII	Date:	September 2021
Endorsed by:	Paediatric Infectious Diseases, Perth Children's Hospital; King Edward Memorial Hospital Maternal-Fetal Medicine	Date:	August 2021
Printed or personally saved electronic copies of this document are considered uncontrolled			