GUIDELINE

Microbiological Diagnostic Testing for Infections in Neonates (previously TORCH)

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

Aim

Outline testing recommendations for key infections in neonates, previously referred to as TORCH screening

Risk

Delayed or inaccurate testing may result in delayed diagnosis and treatment.

Background

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.

Table 1: Neonatal signs and symptoms.

Signs & symptoms	CMV	Enterovirus	HSV	Parvovirus B19	Rubella[&]	*Toxoplasma*	*T. pallidum (Syphilis)*	Varicella (VZV) ^	Zika virus[#]
Cranial/ eye abnormalities/ hearing									
Microcephaly	+				+	+		+	+
Hydrocephalus	+					+		+	+
Intracranial calcifications	+				+	+		+	+
Cataracts or microphthalmia					+			+	+
Chorioretinitis	+					+	+	+	+
Failed newborn hearing screen	+				+				+
Liver									
Hepatomegaly/ Jaundice/ hepatitis	+	+	+	+	+	+	+		
Haematological abnormality									
Anaemia	+	+	+	+			+		
Thrombocytopaenia	+	+	+	+			+		
Skin/ limbs									
Vesicles or blisters		+	+				+		
Rash (non-vesicular)	+	+	+		+		+	+ ^	
Limb hypoplasia or								+	

shortening									
Arthrogryposis									+
Neonate size									
Hydrops foetalis				+			+		
IUGR	+				+		+	+	+
Cardiac									
Myocarditis	+	+	+	+	+				
Structural abnormalities					+%				+
Other									
Unexplained sepsis		+	+				+		

& Congenital rubella is highly unlikely in the setting of demonstrated maternal immunity; check maternal results 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. Skin thickening and scarring, particularly in a dermatomal distribution is characteristic. May be associated with limb malformation or atrophy.

Compatible exposure history required. This includes maternal 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.

% Although a variety of abnormalities may be produced, the most frequently include pulmonary artery stenosis and patent ductus arteriosus.

Table 2: Test selection by potential aetiology

Aetiology	Test selection
Cytomegalovirus	**1 X urine CMV PCR** If positive, see Congenital Cytomegalovirus CMV pathway for interpretation and management
Enterovirus	Throat and rectal swab for Enterovirus PCR CSF testing and blood PCR can be considered
Herpes simplex virus (HSV-1 and HSV-2)	Testing guided by risk assessment and symptoms. See Herpes Simplex in Pregnancy (WNHS Guideline) for risk assessment and management. Note that HSV serology is not useful in the diagnosis of neonatal infection. **Low risk, asymptomatic:** Surface swabs of eye, throat, umbilicus and rectum for HSV PCR, collected 24hrs post delivery **High risk or symptomatic infant**: Surface swabs of eye, throat, umbilicus, rectum and any skin lesions if present for HSV PCR **+** HSV PCR on blood **+** CSF HSV PCR (if no contraindications for lumbar puncture).
Human immunodeficiency virus	Neonates born to mothers with known HIV infection will have an action plan. Discuss testing with Perth Children's Hospital Infectious Diseases service. In other cases, maternal serology testing is the preferred method of screening. If maternal screening is not possible, serology testing on an infant sample can be performed.
Parvovirus B19	Neonatal testing rarely indicated. Consider: **Parvovirus serology**: for initial testing**,** maternal screening preferred **Parvovirus PCR:** On EDTA whole blood
Rubella	**Highly unlikely in the setting of demonstrated maternal immunity to rubella. Check maternal results prior to consideration of testing of the neonate.** **Rubella PCR:** Urine

Toxoplasma gondii	Confirm maternal history of infection (IgG positivity) ***Toxoplasma* Serology (IgG and IgM):** Measure IgG in parallel with maternal sample (collect maternal sample at time of testing neonate) **+** ***Toxoplasma* PCR:** Perform on**:** • Placental tissue • Whole blood (EDTA) +/- CSF

***Treponema pallidum* (syphilis)**	Confirm maternal history of infection- syphilis serology test
	If positive, approach based on risk assessment (see KEMH neonatal guideline)
	Serology (RPR performed <u>in parallel with maternal sample</u> and IgM): Do not use cord blood.
	***T. pallidum* PCR**:
	Perform on:
	• Placental tissue
	• In the high-risk setting:
	  ○ Nasal swab
	  ○ Skin lesions (if present)
	CSF: sampling can be considered in high risk neonate and should be discussed with clinical microbiologist and/ or Perth Children's hospital Infectious disease team prior to collection to guide appropriateness and test selection.

Varicella Zoster Virus (VZV)	**Congenital Varicella Syndrome:** Diagnosis in the neonate is largely dependent on the diagnosis of maternal infection during pregnancy and consistent clinical findings in the neonate. In some settings serial VZV IgG measurement may be indicated to demonstrate persistence. **Perinatal Varicella Infection (**where primary maternal VZV infection occurs less than 7 days prior to delivery): **Lesion/vesicle** VZV PCR
Zika virus	Confirm maternal exposure history and serology results before testing neonate. If interpreted as consistent with possible recent infection- **Placenta, blood and urine Zika PCR:** If very high clinical suspicion and other PCRs/ serology not diagnostic, CSF PCR recommended **+** **Serology:** IgM and IgG

Table 3: Test sample type and volume

Aetiology	Serology* Gold top tube preferred		PCR[#]		
	IgM	**IgG**	**Blood** (EDTA tube)	**CSF and Other fluid**	**Swab type[%] and site**
Cytomegalovirus	X	X	500 µL	200 µL	X
Enterovirus	X	X	500 µL	200 µL	Dry swab: throat and rectal swab
Herpes simplex virus (HSV-1 and HSV-2)	X	X	500 µL	200 µL	Dry swab: swabs of eye, throat, umbilicus and rectum for HSV PCR, collected 24hrs post delivery
Human immunodeficiency virus	X		See neonatal plan	X	X
Parvovirus B19	325 µL	325 µL	500 µL	200 µL	X
Rubella	X	X	X	200 µL	X
Toxoplasma gondii	300 µL	300 µL	500 µL	200 µL	X
***Treponema pallidum* (syphilis)**	650µL		X	X[S]	Dry swab: nasal +/- lesion
Varicella (VZV)	X	X	500 µL	X	Dry swab: lesion
Zika Virus	50 µL	150 µL	500 µL	200 µL	X

* 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 neonate with 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.

[S] CSF sampling can be considered in high risk neonate and should be discussed with clinical microbiologist and/ or Perth Children's hospital Infectious disease team prior to collection to guide appropriateness and test selection

Related CAHS internal policies, procedures and guidelines

Neonatology

Cytomegalovirus CMV Neonatal Pathway

Herpes Simplex Virus (HSV): management of neonates born to HSV positive women

WNHS

Herpes simplex in pregnancy

Neonatal Viral Infections

Syphilis in pregnancy

Varicella Zoster Virus (VZV)

References and related external legislation, policies, and guidelines

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

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

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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

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.

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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

This document can be made available in alternative formats on request.

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