Rapid Response™

TORCH IgG/IgM Test Cassette
(Whole Blood/Serum/Plasma)

REF TORCH-12C25 Product Insert

For professional *in vitro* diagnostic use only.

Intended Use

The Rapid Response™ TORCH IgG/IgM Test Cassette is a lateral flow chromatographic immunoassay for the simultaneous detection and differentiation of IgG and IgM antibodies to Toxoplasma gondii (TOXO), Cytomegalovirus (CMV), Rubella virus (RV), Herpes simplex virus (HSV) in human whole blood, serum or plasma samples. The kit is intended to be used as a screening test and as an aid in the diagnosis of infections with TOXO, CMV, RV and HSV. Any reactive specimen with the Rapid Response™ TORCH IgG/IgM Test Cassette must be confirmed with alternative testing method(s) and clinical findings. The test is for professional use only.

Introduction

The acronym TORCH was introduced in 1971 by Nahmias et al. to group pathogens known to cause hazardous congenital infections, namely Toxoplasma gondii, Rubella, Cytomegalovirus, and Herpes simplex virus.

T. gondii is a ubiquitous intracellular parasite that can affect virtually all warm-blooded vertebrates[1]. The primary hazard connected with Toxoplasma infections is the vertical transmission of the pathogen by a pregnant woman with primary infection. In infants, HIV/AIDS patients, and others with weakened immunity, infection can cause serious and occasionally fatal illness[2]. Even if children are born without apparent symptoms, they may still develop chorioretinitis or retard mentally in childhood or young adulthood.

Rubella, also known as German measles, is the disease caused by Rubella virus which is the only known Rubivirus species and belongs to the Togaviridae family[3]. Rubella is a typical childhood infection, usually with a mild course. By contrast, primary infection of a pregnant women during the first half of pregnancy and subsequent vertical transmission of the virus is a serious event, often leading to miscarriages or congenital rubella syndrome (CRS)[4].

Cytomegalovirus, also known as human herpes virus 5, belongs to the family of Herpesviridae. It is one of the world's most widespread viruses. The most sinister consequence can result after a primary infection of a pregnant woman with vertical virus transmission to the unborn child. Between 22-38% of infected fetuses are then born with symptoms[5], which may include pneumonia, gastrointestinal, retinal and neurological disease[6].

Herpes simplex virus 1 (HSV-1) and Herpes simplex virus 2 (HSV-2) are two closely related viruses, belonging to the family of Herpesviridae[7]. HSV-1 is mainly transmitted via social contacts during childhood, but also sexually later in life. HSV-2 is usually transmitted sexually by asymptomatic shedding. Both viruses can also be transmitted vertically before birth or perinatally during delivery. Such infections may have severe, if not fatal, consequences for the fetus or newborn.

The goals of TORCH testing are to determine the mother's immune status and to help differentiate between acute and past infection in pregnancy. Preconception and antenatal screening play an important role in the prevention of vertically transmitted infections.

A variety of serological tests for antibodies to TORCH pathogens have been used as an aid in diagnosis of acute infection and to assess previous exposure to the organisms. These tests include latex agglutination, indirect immunofluorescence and ELISA. Recently, lateral flow chromatographic immunoassay, such as the Rapid Response™ TORCH IgG/IgM Test Cassette has been introduced to the clinic for the instant detection of TORCH infections at the very early stages or acute infections.

Principle

The Rapid Response™ TORCH IgG/IgM Test Cassette is a lateral flow chromatographic immunoassay. Recombinant antigens of the five pathogens (TOXO, RV, CMV, HSV-1 and HSV-2), anti-human IgG and anti-human IgM antibodies are used respectively to detect the specific TORCH-IgG and TORCH-IgM antibodies in the human whole blood, serum or plasma samples.

When an adequate volume of test specimen is added to the sample well, the specific TORCH-IgG/IgM antibody, say TOXO-IgM antibody if present, will react with the TOXO antigen conjugated with colloidal gold. Then the complexes move forward chromatographically to the test region (IgM), where the complexes will be captured by anti-human IgM antibodies immobilized at the detection zone.

The presence of red or pink line(s) indicates a positive result. The unbounded complex moves on to the control region (C) and a red line will appear, indicating the assay is a valid one. So the control line provides an inner quality control mechanism. The test principle of RV, CMV, HSV-1 and HSV-2 antibodies is the same as that of the TOXO IgM testing.

Precautions

- For professional *in vitro* diagnostic use only.
- Do not use after expiration date indicated on the package. Do not use the test if its foil pouch is damaged. Do not reuse tests.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore, recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest or inhale).
- Avoid cross-contamination of specimens by using a new specimen collection container for each specimen obtained.
- Read the entire procedure carefully prior to performing any tests.
- Do not eat, drink or smoke in the area where the specimens and kits are handled. Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- Humidity and temperature can adversely affect results.
- The used testing materials should be discarded in accordance with local, state and/or federal regulations.

Materials

Materials provided

- Test cassette
- Disposable specimen dropper
- Buffer
- Product insert

Materials required but not provided

- Centrifuge
- Specimen collection container
- Timer

Storage and Stability

- The kit should be stored at 35.6-86°F (2-30°C) until the expiry date.
- The test must remain in the sealed pouch until use.
- **Do not freeze the kit.**
- Care should be taken to protect the components of the kit from contamination. Do not use if there is evidence of microbial contamination or precipitation. Biological contamination of dispensing equipments, containers or reagents can lead to false results.

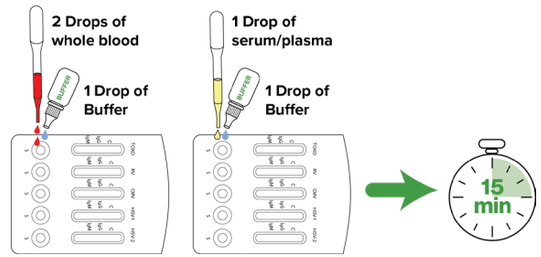
Collection and Storage of Specimens

- The Rapid Response™ TORCH IgG/IgM Test Cassette can be performed using human whole blood, serum or plasma specimens.
- Only clear, non-hemolyzed specimens are recommended for use with this test. Serum or plasma should be separated as soon as possible to avoid hemolysis.
- Perform testing immediately after specimen collection. Do not leave specimens at room temperature for prolonged periods.
- Serum and plasma specimens may be stored at 35.6-46.4°F (2-8°C) for up to 7 days. For long term storage, specimens should be kept below -4°F (-20°C). Whole blood collected by venipuncture should be stored at 35.6-46.4°F (2-8°C) if the test is to be run within 3 days of collection. Do not freeze whole blood specimens. Whole blood collected by finger stick should be tested immediately.
- Containers containing anticoagulants such as EDTA, citrate, or heparin should be used for whole blood storage.
- Bring specimens to room temperature prior to testing. Frozen serum or plasma specimens must be completely thawed and mixed well prior to testing. Avoid repeated freezing and thawing of serum or plasma specimens.
- If specimens are to be shipped, pack them in compliance with all applicable regulations for transportation of etiological agents.
- Icteric, lipemic, hemolysed, heat treated and contaminated specimens may cause erroneous results.
- Pack the specimens in compliance with applicable regulations for transportation of etiological agents, in case they need to be shipped.

Test Procedure

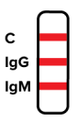
Bring tests, specimens, buffer and/or controls to room temperature (59-86°F; 15-30°C) before use.

1. Remove the test from its sealed pouch, and place it on a clean, level surface. Label the cassette with patient or control identification. For best results, the assay should be performed within an hour.
2. **For serum/plasma specimens:**
   Using the provided dropper, carefully transfer 1 drop (25 µL) of serum or plasma to the sample well (S), and then add 1 drop of buffer to the sample well (S).
   For whole blood specimens:
   Using the provided dropper, carefully transfer 2 drops (50 µL) of whole blood to the sample well (S), and then add 1 drop of buffer to the sample well (S).
   Avoid trapping air bubbles in the specimen well (S), and do not add any solution to the result area.
   As the test begins to work, sample will migrate across the membrane.
3. Read the result at 15 minutes. Do not interpret the result after 30 minutes.



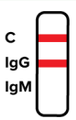
Results Interpretation

Positive



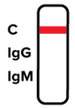
IgG+IgM Positive: One red line appears in the control region (C), and two other red lines appear in both IgG region and IgM region. The shade of color may vary from pink to purple, but it indicates a positive result even with a faint line.

IgM Positive: One red line appears in the control region (C), and another red line in the IgM region. The shade of color may vary from pink to purple, but it indicates a positive result even with a faint line.



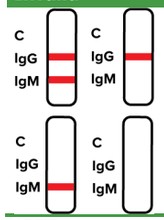
IgG Positive: One red line appears in the control region (C), and another red line in the IgG region. The shade of color may vary from pink to purple, but it indicates a positive result even with a faint line.

Negative



Negative: Only one red line appears in the control region (C), and no band appears either in the IgG region or IgM region.

Invalid



Invalid: No red line appears in the control region (C), whether a test band(s) is present or not. Repeat invalid tests with a new sample, new test cassette and reagent. Insufficient sample volume, inaccurate operating procedure or expired tests may yield an invalid result. Contact your local distributor if the problem continues.

NOTE:

1. The intensity of color in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of color in the test region should be considered positive. Note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

Quality Control

- Internal procedural controls are included in the test. A colored band appearing in the control region (C) is considered an internal positive procedural control, confirming correct procedural technique.
- External controls are not supplied with this kit. It is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

Limitations

1. The Rapid Response™ TORCH IgG/IgM Test Cassette is for professional *in vitro* diagnostic use, and should only be used for the qualitative detection of IgG and IgM to TORCH. The intensity of color in a positive band should not be evaluated as "quantitative or semi-quantitative".
2. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
3. Failure to follow the TEST PROCEDURE and RESULTS INTERPRETATION may adversely affect test performance and/or invalidate the test result.
4. Results obtained with this assay, particularly in the case of weak test lines that are difficult to interpret, should be used in conjunction with other clinical information available to the physician.

Performance Characteristics

Clinical sensitivity and specificity

The performances of the Rapid Response™ TORCH IgG/IgM Rapid Test Cassette (Whole Blood/Serum/Plasma) have been established in comparison with ELISA. The testing results were shown in the table below:

For TOXO IgG Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. TOXO IgG ELISA

Relative Sensitivity: >99.9% (87.9%-100%)*
Relative Specificity: 99.1% (95.2%-99.8%)*
Overall Agreement: 99.3% (96.1%-99.9%)*
*95% Confidence Interval

		TOXO IgG ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	28	1	29
	-	0	114	114
	Total	28	115	143

For TOXO IgM Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. TOXO IgM ELISA

Relative Sensitivity: >99.9% (83.2%-100%)*
Relative Specificity: 99.2% (95.6%-99.9%)*
Overall Agreement: 99.3% (96.1%-99.9%)*
*95% Confidence Interval

		TOXO IgM ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	19	1	20
	-	0	123	123
	Total	19	124	143

For RV IgG Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. RV IgG ELISA

Relative Sensitivity: 99.0% (94.5%-99.8%)*
Relative Specificity: >99.9% (91.6%-100%)*
Overall Agreement: 99.3% (96.1%-99.9%)*
*95% Confidence Interval

		RV IgG ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	98	0	98
	-	1	42	43
	Total	99	42	141

For RV IgM Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. RV IgM ELISA

Relative Sensitivity: >99.9% (79.6%-100%)*
Relative Specificity: 99.2% (95.6%-99.9%)*
Overall Agreement: 99.3% (96.1%-99.9%)*
*95% Confidence Interval

		RV IgM ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	15	1	16
	-	0	125	125
	Total	15	126	141

For CMV IgG Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. CMV IgG ELISA

Relative Sensitivity: >99.9% (84.5%-100%)*
Relative Specificity: 98.9% (94.2%-99.8%)*
Overall Agreement: 99.1% (95.2%-99.8%)*
*95% Confidence Interval

		CMV IgG ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	21	1	22
	-	0	92	92
	Total	21	93	114

For CMV IgM Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. ELISA

Relative Sensitivity: >99.9% (82.4%-100%)*
Relative Specificity: 99.0% (94.3%-99.8%)*
Overall Agreement: 99.1% (95.2%-99.8%)*
*95% Confidence Interval

		CMV IgM ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	18	1	19
	-	0	95	95
	Total	18	96	114

For HSV-1 IgG Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. HSV-1 IgG ELISA

Relative Sensitivity: 98.8% (93.6%-99.8%)*
Relative Specificity: >99.9% (93.1%-100%)*
Overall Agreement: 99.3% (96.0%-99.9%)*
*95% Confidence Interval

		HSV-1 IgG ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	84	0	84
	-	1	52	53
	Total	85	52	137

For HSV-1 IgM Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. ELISA

Relative Sensitivity: >99.9% (84.5%-100%)*
Relative Specificity: 99.1% (95.3%-99.8%)*
Overall Agreement: 99.3% (96.0%-99.9%)*
*95% Confidence Interval

		HSV-1 IgM ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	21	1	22
	-	0	115	115
	Total	21	116	137

For HSV-2 IgG Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. HSV-2 IgG ELISA

Relative Sensitivity: >99.9% (85.7%-100%)*
Relative Specificity: 98.1% (93.4%-99.5%)*
Overall Agreement: 98.4% (94.5%-99.6%)*
*95% Confidence Interval

		HSV-2 IgG ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	23	2	25
	-	0	104	104
	Total	23	106	129

For HSV-2 IgM Test

Table: Rapid Response™ TORCH IgG/IgM Test Cassette vs. HSV-2 IgM ELISA

Relative Sensitivity: >99.9% (83.9%-100%)*
Relative Specificity: 99.1% (95.0%-99.8%)*
Overall Agreement: 99.2% (95.7%-99.9%)*
*95% Confidence Interval

		HSV-2 IgM ELISA		
		+	-	Total
Rapid Response™ TORCH IgG/IgM Test Cassette	+	20	1	21
	-	0	108	108
	Total	20	109	129

Bibliography

1. Ryan KJ, Ray CG (editors) (2004). Sherris Medical Microbiology (4th ed.). McGraw Hill. pp. 556; 566–9.
2. Munro SC, Hall B, Whybin LR, Leader L, Robertson P, Maine GT, Rawlinson WD. Diagnosis of and screening for cytomegalovirus infection in pregnant women. J ClinMicobiol. 2005 Sep;43(9):4713-4718.
3. Cannon MJ, Davis KF. Washing our hands of the congenital cytomegalovirus disease epidemic BMC Public Health. 2005 Jun 20;5:70.
4. Hecker M, Qui D, Marquardt K, Bein G, Hackstein H. Continuous cytomegalovirus seroconversion in a large group of healthy blood donors. Vox Sang. 2004 Jan;86(1):41-44.
5. Lerner CW, Tapper ML. Opportunistic infection complicating acquired immune deficiency syndrome. Clinical features of 25 cases. Medicine (Baltimore) 1984; 63:155-64.
6. Marsano L, Perrillo R P, Flye M W, Hanto D W, Spitzer E D, Thomas J R, Murray P R, Windus D W, Brunt E M, Storch G A. Comparison of culture and serology for the diagnosis of cytomegalovirus infection in kidney and liver transplant recipients. J Infect Dis. 1990;161:454-461.

Glossary of Symbols

Consult instructions for use
Test per Kit
Do Not Reuse
Store between 35.6°F to 86°F
Use by
REF Catalogue #
LOT Lot Number
IVD For *in vitro* diagnostic use only

BTNX Inc.
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