Evaluation of the Abbott ARCHITECT CMV Panel in Pregnant Women with Primary CMV Infection

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Abstract

Background
What serologic tests should be used to screen pregnant women for CMV infection.

Objectives
Evaluate the performance of the ARCHITECT CMV IgM, IgG, and IgG avidity assays in women with documented seroconversion for CMV during gestation.

Methods
The three CMV assays for the ARCHITECT instrument are two-step immunoassays utilizing CMV virus lysate coated paramagnetic microparticles for the capture of human anti-CMV antibodies. The CMV IgM assay also contains both viral lysate and the recombinant protein CKS-pp150, pp52 (UL32, UL44) coated onto paramagnetic particles. Samples (n=136) from 31 pregnant women with documented recent seroconversion were tested on the Abbott ARCHITECT CMV assays and the results were compared to the Abbott AxSYM CMV IgG, AxSYM or IMx CMV IgM assays, and a modified Dade Behring CMV IgG avidity assay.

Results
The seroconversion sensitivity of the ARCHITECT CMV IgM assay was approximately equivalent to the AxSYM and IMx CMV IgM assays with the ARCHITECT assay detecting the same bleed as positive relative to IMx (n=19) and one bleed earlier than AxSYM (n=13). The seroconversion sensitivity of the ARCHITECT CMV IgG assay was slightly greater than the AxSYM CMV IgG assay as shown by detection of the first bleed as CMV IgG positive by ARCHITECT in 2/31 patients before AxSYM. Detection of CMV-specific IgM before CMV IgG also occurred in 6/31 patients (19%) with a window period of approximately 8-13 days. The clinical sensitivity of the ARCHITECT CMV IgG avidity assay using a cutoff of 4 months post-seronegative bleed was (62/64) = 96.9% (95% CI = 89.2-99.6%). The relative agreement between the ARCHITECT and modified Dade CMV IgG avidity assays was (71/80) = 88.8% (95% CI = 79.7-94.7%).

Conclusion
The performance of the three fully automated Abbott ARCHITECT CMV immunoassays, including the reflex CMV IgG avidity assay, was equivalent to the reference assays. The observation that detection of CMV-specific IgM before IgG occurred in 19% of the patients tested emphasizes the importance of testing pregnant women with both a sensitive CMV IgM and IgG test at the same time to avoid false negative results during early seroconversion.

Introduction

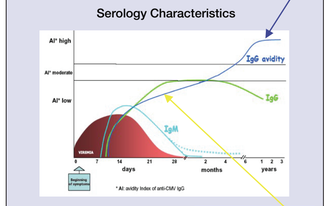
Human Cytomegalovirus (CMV) is a herpesvirus that commonly infects the human population. CMV is the most common congenital infection, occurring in approximately 1% of all live births. Intrauterine transmission of primary CMV infection, especially during the first trimester, is the second leading cause of mental retardation after Down's syndrome. Since CMV IgM antibodies can be produced during primary and non-primary CMV infections, CMV IgG avidity tests have been found useful at the diagnostic level to discriminate between primary and non-primary CMV infections in pregnant women with CMV IgM positive serology.

The objective of this study was to evaluate the performance of the fully-automated ARCHITECT CMV serology panel (CMV IgG, CMV IgM, CMV IgG avidity) in pregnant women with primary CMV infection.

Methods and Procedures

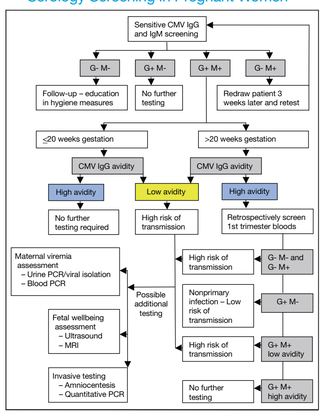
Typical Time Course of CMV Seroconversion in Immunocompetent Individuals

- IgG antibody of high avidity is detected in subjects with non-primary CMV infection.
- The maturation of antibody avidity over time can be used at the diagnostic level to discriminate between primary and non-primary infection.
- Avidity testing should be performed in pregnant women early in gestation (i.e., within the first trimester), as a high avidity result later in gestation cannot rule out a primary infection earlier in gestation when low avidity IgG may have been present.



Low to moderate IgG avidity is a marker of CMV primary infection for 18-20 weeks after seroconversion.

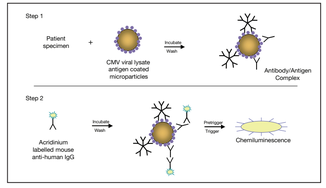
Proposed Diagnostic Algorithm for CMV Serology Screening in Pregnant Women*



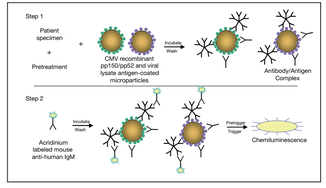
[1]Munro, S.C., et al. (2005) *J. Clin. Microbiol.* 43: 4713-4718.

Samples (n=136) were selected from 31 pregnant women with documented recent CMV seroconversion. These archived samples were selected from the time period 1996-2006 and were tested on the Abbott ARCHITECT CMV IgG, IgM, and IgG avidity assays and the results compared to the Abbott AxSYM CMV IgG, AxSYM or IMx CMV IgM, and a modified Dade Behring CMV IgG avidity assay. The days post-seroconversion for each serial bleed series was calculated from the midpoint of the seroconversion interval in each patient. In this patient population (n=31) the mean days from last seronegative bleed to first seropositive bleed was 43 days and the mean days calculated from the midpoint was 21 days.

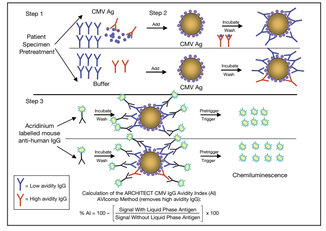
ARCHITECT CMV IgG Assay



ARCHITECT CMV IgM Assay



ARCHITECT CMV IgG Avidity Assay Using AVIcomp Technology



Results

ARCHITECT CMV IgG Avidity Clinical Sensitivity

Samples from Pregnant Women (n=136)		Time Post-Seroconversion		
		<4 Months	≥4 Months	Total
ARCHITECT CMV IgG Avidity	Low	62	21	83
	Eqv	4	6	10
	High	2	41	43
	Total	68	68	136

ARCHITECT Clinical Sensitivity: 62/64 = 96.9%* (95% CI = 89.2-99.6%)

*Equivocal results excluded from calculation

ARCHITECT and Modified Dade Behring CMV IgG Avidity Assay Comparison

Samples from Pregnant Women (n=89)		Behring CMV IgG Avidity		
		Low	High	Total
ARCHITECT CMV IgG Avidity	Low	60	2	62
	Eqv	8	1	9
	High	7	11	18
	Total	75	14	89

Relative Agreement: 71/80 = 88.8%* (95% CI = 79.7-94.7%)

*Equivocal results excluded from calculation

Relative Detection of CMV IgM by ARCHITECT, AxSYM, and IMx

	No. First Antibody Positive Samples CMV IgM Detected by ARCHITECT and AxSYM or IMx	No. First Antibody Positive Samples CMV IgM Detected by ARCHITECT Earlier than IMx	No. First Antibody Samples CMV IgM Detected by ARCHITECT Earlier than AxSYM	No. First Antibody Positive Samples CMV IgM Detected by AxSYM or IMx Earlier than ARCHITECT
Total (n=27)	26	0	1	0

Relative Detection of CMV IgG by ARCHITECT and AxSYM

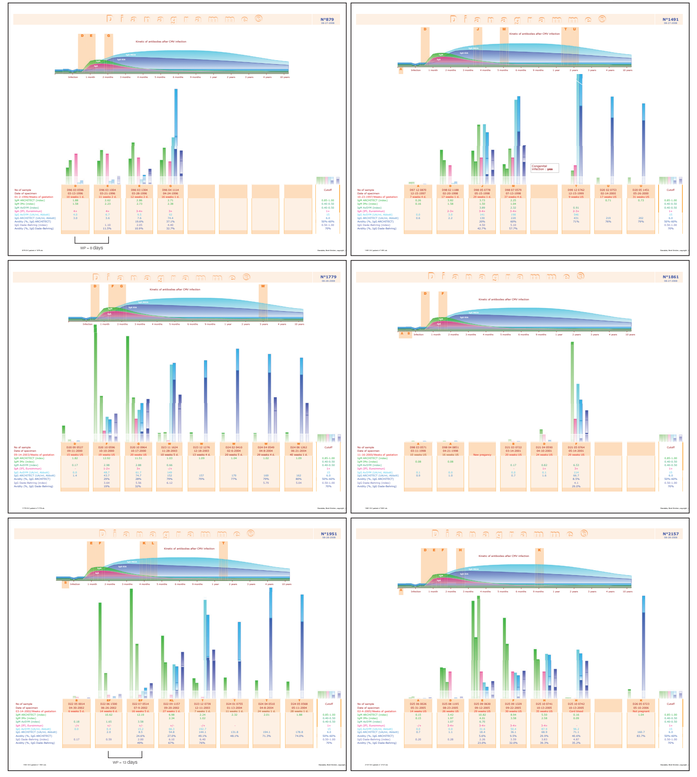
	No. First Antibody Positive Samples CMV IgG Detected by ARCHITECT and AxSYM	No. First Antibody Positive Samples CMV IgG Detected by ARCHITECT Earlier than AxSYM	No. First Antibody Positive Samples CMV IgG Detected by AxSYM Earlier than ARCHITECT
Total (n=31)	29	2	0

Relative Detection of CMV IgM and IgG by ARCHITECT, AxSYM, and IMx

	No. First Antibody Positive Samples CMV IgM Detected at the Same Time as CMV IgG	No. First Antibody Positive Samples CMV IgM Detected Before CMV IgG*	No. First Antibody Positive Samples CMV IgG Detected Before CMV IgM
Total (n=31)	25	6	0

*Window period of approximately 8-13 days

Seroconversion Profiles of Patients Where CMV IgM was Detected Before CMV IgG



Conclusion

The performance of the three fully automated Abbott ARCHITECT CMV immunoassays, including the reflex CMV IgG avidity assay, was equivalent to the reference assays. The observation that detection of CMV-specific IgM before IgG occurred in 19% (6/31) of the patients tested emphasizes the importance of testing pregnant women with both a sensitive CMV IgM and IgG test as published in the diagnostic algorithm of Munro, SC et al. (2005) *J. Clinical Microbiology* 43:4713-4718.