Clinical Evaluation of the 3M™ Rapid Detection Flu A+B Test

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Background and Aims of Study

Background: Easy to use immunochromatographic methods for the detection of influenza A and influenza B can provide clinicians with rapid results. The specificities of the assays are generally good when used during influenza season, but the tests often lack sufficient sensitivity. Therefore, continued improvement of these test methods are desirable. The new investigational 3M™ Rapid Detection Flu A+B Test (3M Medical Diagnostics, St. Paul, MN) is a qualitative immunochromatographic cartridge assay. The assay utilizes fluorescent-dyed latex particles coated with anti-Influenza A and anti-Influenza B antibodies that bind to Influenza A or B antigens, respectively, if present in the sample. Detection is performed using the 3M™ Rapid Detection™ Reader.

The aims of this study were:

1) To evaluate the investigational 3M Rapid Detection Flu A+B Test for the direct detection of influenza A and influenza B in clinical respiratory samples.

2) To compare the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the 3M assay to direct fluorescent antibody staining (DFA), rapid cell culture (R-Mix) (Diagnostic Hybrids, Inc., OH) and to the BinaxNOW Influenza A+B test (Binax, Inc., ME).

Materials and Methods

Specimens: A total of 500 fresh respiratory specimens (nasopharyngeal (NP) aspirates, NP washings, NP swabs in viral transport media) submitted for routine viral culture and DFA were included in this study. The samples were from both out-patients and in-patients and ages ranged from 2 weeks to 95 yr.

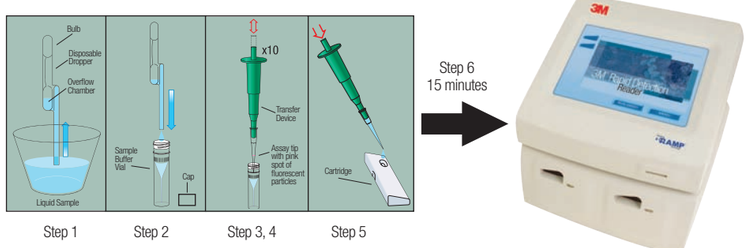
Methods:

1) Neat sample was used to perform both the 3M and Binax assays, according to the respective manufacturer's instructions.

2) Each specimen was then centrifuged to obtain NP cells to perform DFA for influenza A, B, RSV, adenovirus, parainfluenza 1, 2, 3, and hMPV.

3) The supernatants were micro-filtered and used to inoculate R-Mix trays. R-Mix cultures were performed according to validated laboratory procedures.

3M Influenza A and B Test Format



1) Place the disposable dropper in the liquid sample. Squeeze and release the bulb such that a visible amount of sample flows into the overflow chamber.
2) Remove the cap from the sample buffer vial and dispense the sample into the sample buffer vial. Sample will remain in the overflow chamber.
3) Place a new assay tip on the transfer device.
4) Insert the assay tip into the sample buffer vial and slowly press and depress the transfer device 10 times to mix in the fluorescent particles.
5) Transfer the mixture of sample and fluorescent particles into the cartridge well.
6) Insert the cartridge into the reader.

Results: Influenza A and Influenza B

Influenza A Test	Sens (%)	Spec (%)	PPV (%)	NPV (%)
DFA	80.90	98.67	93.51	95.61
R-Mix	98.88	100	100	99.73
BinaxNOW	46.07	100	100	88.65
3M	70.79	99.73	98.44	93.50

Sensitivity (Sens), specificity (Spec), positive predictive value (PPV) and negative predictive value (PPV) for both influenza A and influenza B tests were based on 464 samples with valid results for all 4 tests.

Influenza A		3M +	3M –	3M Total
R-Mix Culture	+	66	27	93
	–	2	405	407
	Total	68	432	500

Influenza A		3M +	3M –	3M Total
DFA	+	59	18	77
	–	5	382	387
	Total	64	400	464

Influenza A		3M +	3M –	3M Total
BinaxNOW A+B	+	43	0	43
	–	25	432	457
	Total	68	432	500

Influenza A		3M +	3M –	3M Total
DFA + QNS Samples*	+	59	18	77
	–	9	414	423
	Total	68	432	500

Comparison of 3M results to individual assays. DFA results are presented in two ways: Top panel does not include samples with insufficient cells (QNS) for appropriate DFA analysis. Bottom panel includes QNS samples that were scored as negative, since no result was obtained for DFA. Four (4) samples reported as QNS for DFA were positive for Influenza A by 3M Test. **3M test was significantly more sensitive than the Binax assay (p=0.008).**

Influenza B Test	Sens (%)	Spec (%)	PPV (%)	NPV (%)
DFA	73.58	100	100	96.71
R-Mix	100	100	100	100
BinaxNOW	37.74	100	100	92.57
3M	86.79	98.54	88.46	98.30

Influenza B		3M +	3M –	3M Total
R-Mix Culture	+	46	8	54
	–	6	440	446
	Total	52	448	500

Influenza B		3M +	3M –	3M Total
DFA	+	37	2	39
	–	15	410	425
	Total	52	412	464

Influenza B		3M +	3M –	3M Total
BinaxNOW A+B	+	20	0	20
	–	32	448	480
	Total	52	448	500

Influenza B		3M +	3M –	3M Total
DFA + QNS Samples*	+	37	2	39
	–	15	446	461
	Total	52	448	500

3M test was significantly more sensitive than the Binax assay (p=<0.0001).

Results: Comparison of 3M/Binax Assay Sensitivities

	Influenza A Dilution Tested													
	1:10		1:20		1:50		1:100		1:200		1:300		1:400	
	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos
3M	Pos	NA	Pos	NA	Pos	NA	Pos	NA	5/5	100	3/5	60	0/5	0
Binax	5/5 w*	100	5/5 vw*	100	0/5	0	NA	NA	NA	NA	NA	NA	NA	NA

	Influenza B Dilution Tested													
	1:10		1:20		1:50		1:100		1:200		1:300		1:400	
	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos	Pos/ Test	% Pos
3M	Pos	NA	Pos	NA	Pos	NA	5/5	100	4/5	80	0/5	0	NA	NA
Binax	5/5 w*	100	0/5	100	0/5	0	NA	NA	NA	NA	NA	NA	NA	NA

Replicates of serial dilutions of influenza A and influenza B clinical isolates were tested in parallel with the 3M and Binax assays. Results in red indicate last dilution with a positive result.

* w = weak reaction, vw = very weak reaction.

Summary and Conclusions

- The 3M assay demonstrated superior analytical sensitivity (>1 log) for the detection of both influenza A and B as compared to the Binax assay.
- The 3M assay demonstrated superior sensitivity (p=0.008) for the detection of influenza A as compared to the Binax assay (70.79% vs 46.07%, respectively) and was less sensitive than DFA (80.9%).
- The 3M assay demonstrated superior sensitivity for the detection of influenza B as compared to the Binax assay (p=<0.0001) and DFA (86.79% versus 37.74% and 73.58%, respectively).
- The 3M assay detected influenza A in 4 samples that did not have sufficient cells for DFA. The reporting of a positive result for these samples would have been delayed by 24-48 hours, if dependent on the R-Mix culture results.
- The easy to use reader and printer provided documentation of instrument quality control and test results.
- The automated reading of test results eliminated the potential for user misreading or misinterpretation of test results.

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