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EVALUATION

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**Group A streptococcus rapid antigen
detection test kits:
A review of evaluation literature**



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Group A streptococcus rapid antigen detection test kits: A review of evaluation literature

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Background

Group A streptococcus (GAS) is a common cause of throat infection worldwide and is one of the most common respiratory infections of children. The infection is usually self-limiting; however a small number of cases can be associated with serious complications such as rheumatic fever and glomerulonephritis. Consequently it is extremely important that an accurate diagnosis is made and appropriate treatment given.

The symptoms of bacterial and viral pharyngitis overlap to such an extent that they are clinically difficult to distinguish. Some countries have addressed this by using GAS rapid antigen detection tests (RADT). In the UK, GAS-RADTs are hardly used, and only a small proportion of sore throats are swabbed for investigation at a microbiology laboratory. Since 90-95% of adult pharyngitis is of viral aetiology, antibiotic administration is mostly ineffective, wasteful, and leads to increased antibiotic resistance for the patient and within the community. Effective usage of proven RADTs is likely to reduce antibiotic prescribing by GPs.

Currently, diagnosis of group A streptococcal infection is made by employing bacterial culture alone or by using a rapid antigen detection test (RADT). Presently the consensus opinion is that it is necessary to perform culture confirmation of a negative RADT since the sensitivities of these tests are still unacceptable.

Scope of review

This review covers 27 peer-reviewed papers published between 1985 and 2003, and from these the sensitivities and specificities of 16 different GAS RADTs have been recorded ([Appendix](#)). The names of the tests and their manufacturers are shown in table 1.

The papers reviewed were retrieved from PubMed and Medline using the keywords; point of care, rapid test device, rapid antigen detection and latex agglutination. It was clear from the start there is no agreement over which description should be used for the tests. Authors also used different terms to describe the bacteria eg group A streptococcus, β -haemolytic streptococci or *Streptococcus pyogenes*. These factors made searching for papers difficult and could mean that some papers are still to be discovered. In addition, it is likely that some evaluations were presented as conference posters but the data from these are less easy to trace.

Table 1: Manufacturers and availability of the 16 GAS RADTs evaluated.

Test name	Company	Evaluations	Available?
Signify Strep A	Abbott	1	Yes
Test Pack PLUS	Abbott	4	No
Test Pack Strep A	Abbott	4	No
Directigen 1, 2, 3	Beckton Dickinson	3	Yes
Visuwell	Dynatech Labs	1	No
OSOM Strep A test	Genzyme	1	No
OSOM Ultra Strep A	Genzyme	3	Yes
Tandem	Hybritech	1	No
Culturette Brand 10 minute GAS ID	Marion Scientific Corp	2	No
Respirastick	Orion Diagnostica	1	No
Card OS	Pacific Biotech	1	No
Quicvue In-line Strep A test	Quidel	1	Yes
Direct Strep EIA	Roche	1	No
Strep A OIA	Thermo Biostar	11	No
Strep A OIA MAX	Thermo Biostar	1	Yes
Reveal	Wellcome	1	No

Findings

Of the 16 RADTs that have been evaluated, sensitivities ranged from 48% to 98.9%. The specificities were generally higher ranging from 62% to 100%. A number of factors were found to affect the sensitivity and specificity. These included the use of antibiotics prior to testing which could lead to false results. The manufacturers of the Strep A OIA (Thermo Biostar) do not recommend the use of the OIA RADT for patients previously treated with antibiotics or for those reinfected with GAS; this is because the test detects both viable and non-viable antigen which could result in false positive results (1).

RADTs are designed for use in a GP surgery. However, the majority of evaluations (67%) were carried out in a microbiology laboratory. This results in a number of variables that potentially affect the performance of the kit. Delays in transport between the doctor's surgery and the laboratory could result in a decrease in the number of viable organisms on the swabs and therefore decreased sensitivity. While laboratory staff would be expected to be more experienced and better trained to interpret these types of tests, Bodino *et al.*, and Giesker *et al.*, both found very little difference in the sensitivities between RADTs carried out in a laboratory and those performed at the doctor's surgery (2;3).

The number of organisms present on the swab is likely to affect the outcome of the test. Most of the evaluations describe plating the swab for bacterial culture before performing the rapid test. By using the same swab there is the possibility of a reduction in organisms from the swab during this procedure. This could result in a false negative result on the RADT. Anhalt *et al.*, tested this hypothesis by carrying out a sequential plating experiment. They used the same swab to inoculate five plates and found no significant difference between the numbers of organisms recovered on each plate (4); therefore this should not affect the result of the RADT. However, Schwartz (5) showed that the result of the RADT was directly related to the number of colonies on the plate. So if a swab does not contain many organisms in the first place, then this is more likely to equate to a false negative result with the rapid test. Kurtz *et al.*, investigated this phenomenon further and showed that testing the extract of two combined swabs was more sensitive than testing either swab alone. However, an increase in sensitivity resulted in decreased specificity in this case (6). It is thought that the type of swab used can also affect the result of a test.

The most important factor that affected the performance of the RADT was the choice of gold standard that it was compared to. Of the papers reviewed here, nine different gold standards were used and this makes it difficult to compare the results obtained. A number of the more recent evaluations use an enhanced broth culture (Todd-Hewitt broth) and found that the RADT were more sensitive than standard culture. This means that in the evaluations where standard culture is used as a gold standard the interpretation of the RADT results may be inaccurate.

Findings

There is a generally held view that a sensitivity of 95% would be high enough for a RADT to be used reliably in a point of care setting without back-up culture. However, of the tests currently available only the Strep A OIA has exceeded

this level. The Strep A OIA was evaluated on 11 different occasions and only twice achieved sensitivities greater than 95% (range 75.5 to 98.9%). The range of sensitivities highlights the impact of using different evaluation designs.

As most of the tests do not reach the recommended 95% sensitivity the majority of researchers and the American Academy of Pediatrics recommend that culture confirmation should be carried out on negative RADT results. Performing both tests is not cost or time effective and papers by Mayes *et al.*, Needham *et al.*, and Webb., all conclude that it would be sufficient to use the RADT alone (7-9). Webb states that GAS tests that give a low rate of false negatives would lead to a very low risk of complications from GAS infection. However, he still recommends culture confirmation during outbreaks of rheumatic fever.

Conclusions

From reviewing a relatively small number of evaluations of rapid antigen detection tests for Group A streptococcus it is clear that more work needs to be done. The reasons are as follows:

The application of different gold standard methods makes it difficult to assess whether evaluation results for the different devices are comparable. Standard methods and a high-quality evaluation design needs to be applied so that accurate comparisons can be made.

Insufficient evaluations have been undertaken in a primary care setting

The UK needs to gain experience in the evaluation of GAS RADTs so that informed advice can be given to GPs. None of the evaluations reviewed were performed in the UK. More than 80% of evaluations were carried out in the United States.

There is a need to assess the attitude of GPs and Practice Nurses towards such tests. Without their co-operation these tests will not be implemented

This review included five currently available Strep A RADTs. No data was found for Aceava Strep A (Thermo Biosciences), BD Link 2 (Becton Dickinson), BD Q-test (Becton-Dickinson), Quickvue + (Quidel Corp.) and Quickvue dipstick (Quidel Corp.) which are also currently on the market.

It is therefore recommended that a thorough evaluation in near patient setting using a sensitive gold standard should be carried out to gain more accurate data on the sensitivity and specificity of GAS RADTs.

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Appendix

Author	Year	Test	Manufacturer	Sensitivity	Specificity	PPV	NPV	Gold Standard	Setting	Number Tested	Notes
Anhalt	1992	Test Pack Strep A	Abbott	68	99	nr	nr	SBA / SSA	Lab	970	
Bodino	1987	Culturette Brand 10 minute GAS ID	Marion Scientific Corp	90.6	93.6	87.5	95.2	5% SBA	Dr's Surgery	256	
			Marion Scientific Corp	91	97.2	91	97.2	5% SBA	Hospital Lab	836	
Chang	1985	Culturette Brand 10 minute GAS ID	Marion Scientific Corp	90	99.2	95.5	98.1	TSA + 5%SB	Lab	435	
Chapin	2002	Strep A OIA	Thermo Biostar	86.1	97.1	93.7	93.4	Culture and/or RTD/genprobe	Lab	520	
Clegg	2003	Test Pack PLUS	Abbott	92.3	98.5	96	97	SBA	Dr's Lab	247	* Removed by FDA in 2002
		Signify Strep A	Abbott	87.9	96.7	94.4	93.3	SBA	Dr's Lab	247	
		Directigen 1, 2, 3	Becton-Dickinson	77.9	100	100	89.4	SBA	Hospital Lab	247	
Dagnelie	1998	Directigen 1, 2, 3	Becton-Dickinson	48	98			7% SBA + Antibody titres	Lab	558	In patients with less than 2 symptoms
				75	91			7% SBA + Antibody titres	Lab	558	In patients with 3-4 symptoms
Dale	1994	Strep A OIA	Thermo Biostar	81	97.4	90.1	94.6	SBA or THB Plus Latex agg	Lab	746	
		Card OS	Pacific Biotech	74.4	99	95.4	93	SBA or THB Plus Latex agg	Lab	746	
Daly	1994	Strep A OIA	Thermo Biostar	84.2	95.7			Enhanced THB	Lab	424	
Della-Latta	1994	Strep A OIA	Thermo Biostar	97	94			SBA	Lab	690	
			Thermo Biostar	95	97			THB	Lab	690	
Drulack	1988	Visuwell	Dynatech Labs	88	92.4	70.4	97.4	5% SBA	Hospital Lab	585	
Fries	1995	Strep A OIA	Thermo Biostar	94.8	98.8			THB	Dr's Surgery	505	
				93.2	95			TSA	Dr's Surgery	505	
Gerber	1997	Strep A OIA	Thermo Biostar	84	93			THB & TSA + 5% SB	Dr's Lab	2113	
Giesker	2002	OSOM Ultra Strep A	Genzyme	92.6	92.8			Multiplate culture standard	Lab	307	
		Strep A OIA	Thermo Biostar	75.5	97.1			Multiplate culture standard	Lab	307	
Giesker	2003	OSOM Ultra Strep A	Genzyme	87.6	96.2			Culture (2 plate std)	Dr's Surgery	887	
		OSOM Ultra Strep A	Genzyme	86.2	97.2			Culture (2 plate std)	Lab	887	
				91.4	95			Culture (2 plate std)	Combination of	887	
									two results		

Key: SBA - Sheep Blood Agar, SSA - Streptococcus selective agar, THB - Todd-Hewitt Broth, TSA - Trypticase Soy Agar, PCR - Polymerase chain reaction

PPV and NPV values printed in article are incorrect

Appendix

Author	Year	Test	Manufacturer	Sensitivity	Specificity	PPV	NPV	Gold Standard	Setting	Number Tested	Notes
Harbeck	1993	Strep A OIA	Thermo Biostar	97.4	95.6			THB	Lab	475	Study 1
				98.9	98.4			THB	Lab	800	Study 2
Hart	1997	Strep A OIA	Thermo Biostar	77	62	22	95	SSA / THB	Dr's Lab	263	
Heiter	1993	Test Pack Strep A	Abbott	76.3	99.7	98.9	92.1	SSA	Lab	1103	
Hoffmann	1990	Test Pack Strep A	Abbott	79	98			5% Horse blood agar	Dr's Surgery	651	
		Direct Strep EIA	Roche	79	63			5% Horse blood agar	Dr's Surgery	446	
		Respirastick	Orion Diagnostica	55	96			5% Horse blood agar	Dr's Surgery	403	
		Reveal	Wellcome	82	83			5% Horse blood agar	Dr's Surgery	449	
		Tandem	Hybritech	78	98			5% Horse blood agar	Dr's Surgery	520	
Kaltwasser	1997	Strep A OIA	Thermo Biostar	82	87	72	93	TSA	Lab	200	
				80	89	77	91	THB	Lab	200	
				78	89	77	90	TSA + THB	Lab	200	
				80	92	85	90	PCR	Lab	200	
Kurtz	2000	Test Pack PLUS	Abbott	80	92.7			5% SBA or SSA	Lab	257	Swab A
				79.9	89.8			5% SBA or SSA	Lab	257	Swab B
				94.1	81.5			5% SBA or SSA	Lab	280	Swab A & B together
Laubscher	1995	Test Pack PLUS	Abbott	95.8	89.9			5% SBA	Lab	454	
Roddey	1995	Strep A OIA	Thermo Biostar	91.4	95.6	93	94.6	SBA	Dr's Lab	301	
				90.4	94.1	90.4	94.1	THB	Dr's Lab	301	
Santos	2003	Test Pack Strep A	Abbott	73	94	85	88	5% SBA	Lab	50	
Schwartz	1997	OSOM Strep A test	Wyntek Diagnostics	95	100			5% SBA	Lab	258	
		Quickvue In-line Stri Quidel		87	100			5% SBA	Lab	258	
Sheeler	2002	Test Pack PLUS	Abbott	91	96	96	90	TSA + 5%SBA	Lab	200	Patients who had recently been treated
				70	98	92	90	TSA + 5%SBA	Lab	200	Patients who had not been treated
Supon	1998	Strep A OIA MAX	Thermo Biostar	89	93			THB	Lab	403	
Uhl	2003	Directigen 1, 2, 3	Becton-Dickinson	55	99	97	93	SSA	Lab	384	

Key: SBA - Sheep Blood Agar, SSA - Streptococcus selective agar, THB - Todd-Hewitt Broth, TSA - Trypticase Soy Agar, PCR - Polymerase chain reaction

PPV and NPV values printed in article are incorrect