Flu, RSV and Strep A Update: Why Molecular is the Right Method for Testing

Gregory J. Berry, Ph.D., D(ABMM)

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Director of Molecular Diagnostics and Microbiology
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Assistant Director, Infectious Disease Diagnostics
Northwell Health Labs
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The information presented is consistent with applicable FDA guidelines.
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Disclosures

• Provided educational talks and received honoraria from Abbott, BioFire, Cardinal health, Cepheid, Hologic, Luminex, Quidel
Learning Objectives

• Discuss the current state of influenza, RSV and Group A Strep (GAS) in the U.S.

• Review latest guidelines and recommendations for influenza and GAS

• Describe rapid CLIA-waived influenza and GAS diagnostic tests, including lateral flow, readers and molecular

• Assess the benefits of molecular testing in CLIA waived settings
Influenza, RSV and Group A Strep: Disease Overview
Influenza A&B in the U.S.

An average of 8% of the population gets sick from flu each season (ranging from 3-11%)\(^1\)

Most deaths are in elderly but can also occur in healthy individuals\(^3\)

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\(1\) https://www.cdc.gov/flu/about/keyfacts.htm
\(2\) https://www.cdc.gov/flu/about/burden/index.html
\(3\) https://www.cdc.gov/flu/weekly/#ClinicalLaboratories

*The top range of these burden estimates are from the 2017-2018 flu season. These are preliminary and may change as data are finalized.*

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[Image of pyramid diagram showing:
- Illnesses: 9,000,000 – 45,000,000*
- Hospitalizations: 140,000 – 810,000*
- Deaths: 12,000 – 61,000*]
Symptoms of influenza

Central
- Headache

Systemic
- Fever
  (usually high)

Muscular
- (Extreme) tiredness

Joints
- Aches

Nasopharynx
- Runny or stuffy nose
- Sore throat
- Aches

Respiratory
- Coughing

Gastric
- Vomiting
2019 - 2020
Flu Season, So Far...
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, 2019-2020 Season

Respiratory Syncytial Virus (RSV)

• One of the most common causes of childhood illness
  • Most common cause of bronchiolitis (inflammation of the small airways in the lung) and pneumonia (infection of the lungs) in children younger than 1 year of age in the United States.

• Significant cause of respiratory illness in older adults

• Symptoms heavily overlap with flu, but treatment is different
Spread of influenza and RSV

• Spread person-to-person
• Droplets spread when coughing, sneezing, talking
  • Can spread about 6 feet away
• Touching contaminated surfaces and then touching nose, mouth
• Avoiding spread of influenza/RSV
  • Wash hands!, Surgical mask, vaccination (flu)

Remember:
You can spread flu one day before you are symptomatic!

Streptococcus pyogenes (Group A Strep- GAS)

- Lancefield Group A serogrouping: “group A strep”

- Beta hemolytic (complete hemolysis) on blood agar plate: “β strep”

- Responsible for a wide range of human infections
  - Some individuals are carriers

https://www.slideshare.net/AshleyHamilton11/clinical-microbiology-53574911

Gram+ cocci, pairs and chains
GAS pharyngitis

• Most common bacterial cause of pharyngitis
• Seasonality: winter and early spring
• Clinical manifestation
  • Rapid onset sore throat
  • Painful swallowing
  • Red, swollen tonsils
  • White patches/streaks of pus
  • Petechiae on roof of mouth
  • Swollen lymph nodes
  • Fever
  • Headache, abdominal pain, nausea, vomiting

20-30% of all sore throat cases in children
5-15% of all sore throat cases in adults

How do you get infected?

- GAS resides in the nose and throat of infected individuals
- Typically spread through person-to-person contact
  - Daycare centers, schools, military training facilities
- Bacteria can travel in respiratory droplets and nasal secretions that get expelled during coughing, sneezing, etc.

Good hygiene is the best way to prevent infection
GAS pharyngitis

• Can be accompanied by scarlatiniform rash - scarlet fever or scarlatina.
  • “Strawberry tongue”

• Incubation period: 2-5 days

• Most common in children 5-15 years of age, uncommon under age 3

• Costs to US economy- $224-$539 million/yr

Why is it critical to know if it is GAS vs. viral pharyngitis:

• Serious secondary complications of GAS pharyngitis include rheumatic fever (in children) and post-streptococcal glomerulonephritis

• Proper treatment can reduce the risk of rheumatic fever in children.
# Treatment for GAS pharyngitis

## Table 2. Antibiotic Regimens Recommended for Group A Streptococcal Pharyngitis

<table>
<thead>
<tr>
<th>Drug, Route</th>
<th>Dose or Dosage</th>
<th>Duration or Quantity</th>
<th>Recommendation Strength, Quality&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For individuals without penicillin allergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin V, oral</td>
<td>Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily</td>
<td>10 d</td>
<td>Strong, high</td>
<td>[125, 126]</td>
</tr>
<tr>
<td>Amoxicillin, oral</td>
<td>50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily</td>
<td>10 d</td>
<td>Strong, high</td>
<td>[88–92]</td>
</tr>
<tr>
<td>Benzathine penicillin G, intramuscular</td>
<td>&lt;27 kg: 600 000 U; ≥27 kg: 1 200 000 U</td>
<td>1 dose</td>
<td>Strong, high</td>
<td>[53, 125, 127]</td>
</tr>
<tr>
<td>For individuals with penicillin allergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalexin,&lt;sup&gt;b&lt;/sup&gt; oral</td>
<td>20 mg/kg/dose twice daily (max = 500 mg/dose)</td>
<td>10 d</td>
<td>Strong, high</td>
<td>[128–131]</td>
</tr>
<tr>
<td>Cefadroxil,&lt;sup&gt;b&lt;/sup&gt; oral</td>
<td>30 mg/kg once daily (max = 1 g)</td>
<td>10 d</td>
<td>Strong, high</td>
<td>[132]</td>
</tr>
<tr>
<td>Clindamycin, oral</td>
<td>7 mg/kg/dose 3 times daily (max = 300 mg/dose)</td>
<td>10 d</td>
<td>Strong, moderate</td>
<td>[133]</td>
</tr>
<tr>
<td>Azithromycin,&lt;sup&gt;c&lt;/sup&gt; oral</td>
<td>12 mg/kg once daily (max = 500 mg)</td>
<td>5 d</td>
<td>Strong, moderate</td>
<td>[97]</td>
</tr>
<tr>
<td>Clarithromycin,&lt;sup&gt;c&lt;/sup&gt; oral</td>
<td>7.5 mg/kg/dose twice daily (max = 250 mg/dose)</td>
<td>10 d</td>
<td>Strong, moderate</td>
<td>[134]</td>
</tr>
</tbody>
</table>

<sup>a</sup> See Table 1 for a description.

<sup>b</sup> Avoid in individuals with immediate type hypersensitivity to penicillin.

<sup>c</sup> Resistance of GAS to these agents is well-known and varies geographically and temporally.

Influenza, RSV and Group A Strep: Test Methods
Testing for these pathogens:

<table>
<thead>
<tr>
<th>Testing in Clinic (Point of Care)</th>
<th>Laboratory Testing</th>
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<tr>
<td>• Rapid antigen tests</td>
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<tr>
<td>• Molecular nucleic acid amplification</td>
<td>• Molecular nucleic acid amplification</td>
</tr>
<tr>
<td>testing (POCT)</td>
<td></td>
</tr>
</tbody>
</table>
Is your facility currently using one or more molecular technology (including POC & Non-Waived) for respiratory testing?

1. Yes, using molecular testing for respiratory

2. No, not using molecular testing for respiratory
Point-of-care testing (POCT)

- Testing performed while patient care is occurring
- Main advantage is time gained
- Therapeutic choices in real time
  - Identify treatment to administer
  - Avoid unnecessary drugs/treatments
- Requires simple platforms with accurate results
Rapid antigen tests

• Available since the 1980s

• Most common first line of testing at clinic

• Immunoassays: detect pathogen-specific antigens

• Qualitative resulting

• Vary greatly in their sensitivity
  • Negative GAS results need culture confirmation
Rapid antigen detection test for group A streptococcus in children with pharyngitis

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¹Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Centre de Recherche Épidémiologie et Statistique Sorbonne Paris Cité (CRESS), Inserm UMR1153, Paris Descartes University, Paris, France. ²Department of Pediatrics, Necker Hospital, AP-HP and Paris Descartes University, Paris, France. ³Association Clinique et Thérapeutique Infantile du Val-de-Marne (ACTIV), Saint-Maur-des-Fossés, France. ⁴Department of Microbiology, Centre Hospitalier Intercommunal de Créteil (CHIC), Créteil, France

Contact address: Martin Chalumeau, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Centre de Recherche Épidémiologie et Statistique Sorbonne Paris Cité (CRESS), Inserm UMR1153, Paris Descartes University, Paris, France. martin.chalumeau@gmail.com, martin.chalumeau@nck.aphp.fr.

Editorial group: Cochrane Acute Respiratory Infections Group.
Review content assessed as up-to-date: .


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ABSTRACT

Background

Group A streptococcus (GAS) accounts for 20% to 40% of cases of pharyngitis in children; the remaining cases are caused by viruses. Compared with throat culture, rapid antigen detection tests (RADTs) offer diagnosis at the point of care (within five to 10 minutes).

Objectives

To determine the diagnostic accuracy of RADTs for diagnosing GAS in children with pharyngitis. To assess the relative diagnostic accuracy of the two major types of RADTs (enzyme immunoassays (EIA) and optical immunoassays (OIA)) by indirect and direct comparison.

Search methods

We searched CENTRAL, MEDLINE, EMBASE, Web of Science, CDSR, DARE, MEDION and TRIP (January 1980 to July 2015). We also conducted related citations tracking via PubMed, handsearched reference lists of included studies and relevant review articles, and screened all articles citing included studies via Google Scholar.

Selection criteria

We included studies that compared RADT for GAS pharyngitis with throat culture on a blood agar plate in a microbiology laboratory in children seen in ambulatory care.

Data collection and analysis

Two review authors independently screened titles and abstracts for relevance, assessed full texts for inclusion, and carried out data extraction and quality assessment using the QUADAS-2 tool. We used bivariate meta-analysis to estimate summary sensitivity and specificity, and to investigate heterogeneity across studies. We compared the accuracy of EIA and OIA tests using indirect and direct evidence.
Study characteristics

We searched for studies published in any language from January 1980 to July 2015. We found 98 unique studies, for a total of 116 test evaluations, involving 101,121 children. The number of participants ranged from 42 to 11,644 across test evaluations. The proportion of children with strep throat ranged from 9.5% to 66.6% across test evaluations.

Quality of the evidence

Important study design features were frequently not reported. The overall methodological quality of included studies was poor. For most studies, we had concerns about the ways in which participants were selected.
Key results

On average, rapid tests for strep throat had a sensitivity (ability to correctly detect people with the disease) of 86% and a specificity (ability to correctly identify people who do not have the disease) of 95%. There was substantial variability in rapid test performance across studies, which was not explained by study characteristics, including methodological quality. The two types of rapid tests under evaluation seemed to have comparable sensitivity (85.4% versus 86.2% for enzyme immunoassays and optical immunoassays, respectively). Based on these results, we would expect that amongst 100 children with strep throat, 86 would be correctly detected with the rapid test while 14 would be missed and not receive antibiotic treatment. Of 100 children with non-streptococcal sore throat, 95 would be correctly classified as such with the rapid test while 5 would be misdiagnosed as having strep throat and receive unnecessary antibiotics.
Northwell Health
What has been our experience with rapid antigen flu testing?

July-October 2016 flu outbreak
Both rapid antigen tests were performed on saved specimens after BioFire RVP testing

Quidel QuickVue®
Influenza A+B

BD Directigen™ EZ Flu A+B

Berry et al., Poster presentation at ASM Microbe 2017.
Summer 2016 Influenza Outbreak - NYC

Berry et al., Poster presentation at ASM Microbe 2017.
Rapid antigen flu testing at Northwell

Table 1: Performance of Quidel QuickVue® and BD Directigen™ rapid antigen tests in the H3N2 outbreak of July-October 2016

<table>
<thead>
<tr>
<th>Assay</th>
<th>+/+</th>
<th>+/-</th>
<th>-/+</th>
<th>-/-</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quidel</td>
<td>93</td>
<td>14</td>
<td>31</td>
<td>157</td>
<td>295</td>
<td>75.0%</td>
<td>91.8%</td>
</tr>
<tr>
<td>BD</td>
<td>88</td>
<td>2</td>
<td>36</td>
<td>169</td>
<td>295</td>
<td>71.0%</td>
<td>98.8%</td>
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Berry et al., Poster presentation at ASM Microbe 2017.
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<td>88</td>
<td>2</td>
<td>36</td>
<td>169</td>
<td>295</td>
<td>71.0%</td>
<td>98.8%</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>Quidel</td>
<td>17</td>
<td>2</td>
<td>20</td>
<td>55</td>
<td>94</td>
<td>45.9%</td>
<td>96.5%</td>
</tr>
<tr>
<td></td>
<td>BD</td>
<td>16</td>
<td>0</td>
<td>21</td>
<td>57</td>
<td>94</td>
<td>43.2%</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Pediatrics</strong></td>
<td>Quidel</td>
<td>76</td>
<td>12</td>
<td>11</td>
<td>102</td>
<td>201</td>
<td>87.4%</td>
<td>89.5%</td>
</tr>
<tr>
<td></td>
<td>BD</td>
<td>72</td>
<td>2</td>
<td>15</td>
<td>112</td>
<td>201</td>
<td>82.8%</td>
<td>98.2%</td>
</tr>
</tbody>
</table>
Table 2: Performance of Quidel QuickVue® and BD Directigen™ rapid antigen tests during routine H1N1 influenza testing during the 2015-2016 flu season

<table>
<thead>
<tr>
<th></th>
<th>Assay</th>
<th>+/+</th>
<th>+/−</th>
<th>−/+</th>
<th>−/−</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>Quidel</td>
<td>63</td>
<td>8</td>
<td>95</td>
<td>866</td>
<td>1032</td>
<td>39.9%</td>
<td>99.1%</td>
<td>15.3%</td>
</tr>
<tr>
<td></td>
<td>BD</td>
<td>75</td>
<td>7</td>
<td>137</td>
<td>918</td>
<td>1137</td>
<td>35.4%</td>
<td>99.2%</td>
<td>18.6%</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>Quidel</td>
<td>57</td>
<td>8</td>
<td>90</td>
<td>858</td>
<td>1013</td>
<td>38.8%</td>
<td>99.1%</td>
<td>14.5%</td>
</tr>
<tr>
<td></td>
<td>BD</td>
<td>49</td>
<td>4</td>
<td>120</td>
<td>724</td>
<td>897</td>
<td>29.0%</td>
<td>99.5%</td>
<td>18.8%</td>
</tr>
<tr>
<td><strong>Pediatrics</strong></td>
<td>Quidel</td>
<td>6</td>
<td>0</td>
<td>5</td>
<td>8</td>
<td>19</td>
<td>54.5%</td>
<td>100.0%</td>
<td>57.9%</td>
</tr>
<tr>
<td></td>
<td>BD</td>
<td>26</td>
<td>3</td>
<td>17</td>
<td>194</td>
<td>240</td>
<td>60.5%</td>
<td>98.5%</td>
<td>17.9%</td>
</tr>
</tbody>
</table>

Berry et al., Poster presentation at ASM Microbe 2017.
## Testing for these pathogens:

<table>
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<tr>
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</tr>
<tr>
<td>• Molecular nucleic acid amplification testing (POCT)</td>
<td>• Molecular nucleic acid amplification</td>
</tr>
</tbody>
</table>
Laboratory testing

• Testing performed in centralized location

• Lab is licensed and accredited to perform patient testing

• Licensed laboratory personnel perform testing
Identification of GAS by culture

• Throat swab is collected and inoculated onto plates
  • Most laboratories are routinely identifying only GAS
    • Agar selective for strep, or BAP can be used with a Bacitracin (A) disk
      • GAS is SUSCEPTIBLE
    • Additional workup can be done if other pathogens suspected
      • e.g. blood agar for other streptococci (B, C, F, G) and A. haemolyticum, or modified Thayer-Martin for N. gonorrhoeae isolation

• Incubate in aerobic incubator with 5% CO₂

• Result: 24-48 hours
Beta hemolysis

Photo courtesy of Dr. Lesley McGee, CDC
Influenza, RSV and Group A Strep: Molecular Testing
Is your facility evaluating or planning to adopt POC molecular test platforms for respiratory testing and/or strep A?

1. No, not evaluating or planning to adopt POC molecular
2. Yes, evaluating or planning to adopt POC molecular
3. Evaluating current molecular testing methods
Molecular testing

• In general, molecular methods are the most sensitive/specific testing

• Advantage for clinician - rapid turnaround time (hours, even minutes vs. 1-3 days)

• Downstream impact:
  • More rapid answer means right therapeutic therapy chosen up-front
  • Patient satisfaction
The quality and power of sample amplification

Detection threshold

Nurse A

Amplified Sample

Nurse B

Not Amplified Sample
Traditional Laboratory testing platforms for molecular Flu/RSV and GAS detection

• TOO MANY TO LIST!!!

• There are options available for any size lab and skill level
  • Random-access single specimen testing
  • Batch testing - large batch, small batch

• General TAT is 1-2 hours (once received, if NOT batched)
  • If batched, could be 12-24 hours, depending on how often testing is performed
Testing for these pathogens:

**Testing in Clinic (Point of Care)**
- Rapid antigen tests
- **Molecular nucleic acid amplification testing (POCT)**

**Laboratory Testing**
- Throat culture (Strep)
- Molecular nucleic acid amplification
Available CLIA-waived Methods
ID NOW™ (Abbott, formerly Alere™)

5-13 minutes to result for Flu
≤13 minutes to result for RSV
2-6 minutes to result for Strep A
Isothermal Amplification
Interpreted by instrument

Flu: CLIA-waived for use with nasal or nasopharyngeal swabs (direct and eluted in viral transport medium)

For in vitro Diagnostic Use
ID NOW™ Strep A 2 clinical trial data, held on file
Cepheid Xpert® Xpress Flu/RSV & Xpert Xpress Strep A

20-30 minutes to result Flu A/B, RSV

18-24 minutes to result Strep A

RT-PCR

Interpreted by instrument

Flu/RSV: CLIA-waived for use with nasal/nasopharyngeal swabs

For in vitro Diagnostic Use

cobas® LIAT® - Lab In a Tube (Roche)

20 minutes to results Flu A/B, RSV
15 minutes to results Strep A
RT-PCR
Interpreted by instrument

Flu: CLIA-waived for use with nasopharyngeal swabs

For in vitro Diagnostic Use
Silaris™ Influenza A&B Test (Sekisui)

Flu: CLIA-waived for use with nasal swabs

30 minutes or less for flu A & B

RT-PCR amplification followed by hybridization and colorimetric visualization of amplified products on a test strip flu A & B

Results are interpreted visually by the operator
Molecular testing pros and cons

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can amplify genome</td>
<td>Typically costs more</td>
</tr>
<tr>
<td>Highly sensitive and specific</td>
<td>Takes longer</td>
</tr>
</tbody>
</table>
Another big change has happened lately....
What Test(s) Should Be Used to Diagnose Influenza?

Recommendations

10. Clinicians should use rapid molecular assays (ie, nucleic acid amplification tests) over rapid influenza diagnostic tests (RIDTs) in outpatients to improve detection of influenza virus infection (A-II) (see Table 6).

11. Clinicians should use reverse-transcription polymerase chain reaction (RT-PCR) or other molecular assays over other influenza tests in hospitalized patients to improve detection of influenza virus infection (A-II) (see Table 6).

15. Clinicians should not use RIDTs in hospitalized patients except when more sensitive molecular assays are not available (A-II), and follow-up testing with RT-PCR or other molecular assays should be performed to confirm negative RIDT results (A-II).
### Table 6. Influenza Diagnostic Tests for Respiratory Specimens

<table>
<thead>
<tr>
<th>Testing Category</th>
<th>Method</th>
<th>Influenza Viruses Detected</th>
<th>Distinguishes Influenza A Virus Subtypes</th>
<th>Time to Results</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid molecular assay</td>
<td>Nucleic acid amplification</td>
<td>Influenza A or B viral RNA</td>
<td>No</td>
<td>15-30 minutes</td>
<td>High sensitivity; high specificity</td>
</tr>
<tr>
<td>Rapid influenza diagnostic test</td>
<td>Antigen detection</td>
<td>Influenza A or B virus antigens</td>
<td>No</td>
<td>10-15 minutes</td>
<td>Low to moderate sensitivity (higher with analyzer device); high specificity;</td>
</tr>
<tr>
<td>Direct and indirect immunofluorescence assays</td>
<td>Antigen detection</td>
<td>Influenza A or B virus antigens</td>
<td>No</td>
<td>1-4 hours</td>
<td>Moderate sensitivity; high specificity</td>
</tr>
<tr>
<td>Molecular assays (including RT-PCR)</td>
<td>Nucleic acid amplification</td>
<td>Influenza A or B viral RNA</td>
<td>Yes, if subtype primers are used</td>
<td>1-9 hours</td>
<td>High sensitivity; high specificity</td>
</tr>
<tr>
<td>Multiplex molecular assays</td>
<td>Nucleic acid amplification</td>
<td>Influenza A or B viral RNA; other viral or bacterial targets (RNA or DNA)</td>
<td>Yes, if subtype primers are used</td>
<td>1-2 hours</td>
<td>High sensitivity; high specificity</td>
</tr>
<tr>
<td>Rapid cell culture (shell vial and cell mixtures)</td>
<td>Virus isolation</td>
<td>Influenza A or B virus</td>
<td>Yes</td>
<td>1-3 days</td>
<td>High sensitivity; high specificity</td>
</tr>
<tr>
<td>Viral culture (tissue cell culture)</td>
<td>Virus isolation</td>
<td>Influenza A or B virus</td>
<td>Yes</td>
<td>2-10 days</td>
<td>High sensitivity; high specificity</td>
</tr>
</tbody>
</table>

Negative results may not rule out influenza. Respiratory tract specimens should be collected as close to illness onset as possible for testing. Clinicians should consult the manufacturer’s package insert for the specific test for the approved respiratory specimens. Most US Food and Drug Administration (FDA)-cleared influenza diagnostic tests are approved for upper respiratory tract specimens but not for sputum or lower respiratory tract specimens. Specificities are generally high (>90%) for all tests compared to RT-PCR. FDA-cleared rapid influenza diagnostic tests are Clinical Laboratory Improvement Amendments (CLIA)-waived; most FDA-cleared rapid influenza molecular assays are CLIA-waived, depending on the specimen.

*Abbreviation: RT-PCR, reverse-transcription polymerase chain reaction.*
During low flu activity positive RIDTs should be confirmed by molecular
During high flu activity negative RIDTs should be confirmed by molecular
## Comparison of Methods

<table>
<thead>
<tr>
<th></th>
<th>POCT Rapid Antigen</th>
<th>Culture</th>
<th>Laboratory Molecular</th>
<th>POCT Molecular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Convenient</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Actionable Results</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>POCT- Friendly</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Little/No Subjectivity</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>LIS/EMR Interfaced</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>High Sensitivity/Specificity</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Low Cost</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Is your facility attempting to standardize molecular point-of-care testing across your network including non-acute providers?

1. Yes, attempting to standardize
2. Evaluating standardization among all provider locations
3. Not at this time
Group A Streptococcus Study
GAS study goals

Compare the BD Veritor™, ID NOW™, and culture for detection of GAS

Evaluate the hypothetical impact of results on antibiotic utilization

Berry et. al, J. Clin. Microbiol., 2018
Study design

• Prospectively tested 216 clinical throat samples that were collected during the months of May and June of 2016 for routine strep throat testing from two predominantly pediatric outpatient clinics within our hospital system.

• Routine patient testing (BD Veritor™ with reflex to group A strep culture) was performed and compared to results obtained on the ID NOW™ (formerly Alere™ i) system.

• Inclusion criteria was a strep throat test ordered by a clinician. Pediatric cases (<18 years of age) accounted for 199 (92.1%) of the specimens, while adults (≥18 years of age) accounted for 17 (7.9%) of the specimens.

• Each patient was subjected to two Rayon throat (posterior oropharynx) swabs as a part of their routine strep throat workup in the clinic. BD Veritor™ testing was performed in the clinic where patients were initially seen.
Study Design

Clinic:
- Swab 1
- Result

Lab:
- Swab 2
- RT-PCR (for discordants)
- aliquot
- Result
- Result
Distribution of positive results

- Culture: 0
- ID NOW™: 9
- BD Veritor™: 5

Berry et al., J. Clin. Microbiol., 2018
Distribution of positive results

*Assay adjudication was done for each of the single-assay positive results 0/5 (0%) of BD Veritor™ and 8/9 (89%) of the ID NOW™, were confirmed by RT-PCR

Berry et. al, J. Clin. Microbiol., 2018
Table 1: Sensitivity, Specificity, Accuracy, and Kappa Index analysis of each assay

<table>
<thead>
<tr>
<th>Assay</th>
<th>POSITIVE</th>
<th>NEGATIVE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ID NOW™</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>42</td>
<td>15</td>
<td>57</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>158</td>
<td>158</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>173</td>
<td>215</td>
</tr>
<tr>
<td>Sensitivity (95% CI) (%)</td>
<td>100.0 (91.6, 100.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity (95% CI) (%)</td>
<td>91.3 (86.1, 95.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy (95% CI) (%)</td>
<td>93.0 (88.8, 96.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kappa Index</td>
<td>0.805 (0.711, 0.898)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kappa Index P-value</td>
<td>&lt;.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Veritor™</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>32</td>
<td>11</td>
<td>43</td>
</tr>
<tr>
<td>Negative</td>
<td>10</td>
<td>162</td>
<td>172</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>173</td>
<td>215</td>
</tr>
<tr>
<td>Sensitivity (95% CI) (%)</td>
<td>76.2 (60.5, 87.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity (95% CI) (%)</td>
<td>93.6 (88.9, 96.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy (95% CI) (%)</td>
<td>90.2 (85.5, 93.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kappa Index</td>
<td>0.692 (0.569, 0.815)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kappa Index P-value</td>
<td>&lt;.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Berry et. al, J. Clin. Microbiol., 2018
### Table 2: Sensitivity, Specificity and Accuracy of RT-PCR Adjudicated Results

<table>
<thead>
<tr>
<th>Assay</th>
<th>Culture + RT-PCR Positive</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>POSITIVE</td>
<td>NEGATIVE</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td><strong>ID NOW™</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>56</td>
<td>1</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>158</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>159</td>
<td>215</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100.0 (%)</td>
<td>(93.6, 100.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>99.4 (%)</td>
<td>(96.6, 99.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>99.5 (%)</td>
<td>(97.4, 99.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Veritor™</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>37</td>
<td>6</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>10</td>
<td>162</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>168</td>
<td>215</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>78.7 (%)</td>
<td>(64.3, 89.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>96.4 (%)</td>
<td>(92.4, 98.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>92.6 (%)</td>
<td>(88.2, 95.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ID NOW™: 14/15 confirmed by RT-PCR  
Veritor™: 5/11 confirmed by RT-PCR

Berry et al., J. Clin. Microbiol., 2018
Antibiotics chart review

- 73/215 (34%) patients given antibiotics at the time of clinic visit
- 26/73 (36%) treatment inappropriate - confirmed GAS negative result
  - In 20/26 (77%) cases, ALL tests were negative
  - All 5 false positive BD Veritor™ results were treated with antibiotics
  - 19% (5/26) of inappropriately treated cases
  - 13/215 (6%) cases where the BD Veritor™ result was negative and antibiotics were not started at the time of the clinic visit, but that were subsequently detected by RT-PCR
    - ID NOW™ result was positive in 13/13 (100%) of these same cases
    - In 6/13 (46%) cases, the antibiotics were started 2-6 days after the clinic visit, after receiving culture results

Berry et. al, J. Clin. Microbiol., 2018
Summary - GAS study

• The ID NOW™ had higher sensitivity and specificity when compared to BD Veritor™

• RT-PCR showed that none of the 5 positives (0%) detected only by the BD Veritor™ confirmed, while 8/9 (89%) of positives detected by the ID NOW™ confirmed

• 36% (n=26) of patients who were given abx had no GAS identified. Of this group 19% (n=5) had false-positive BD Veritor™ results

Berry et. al, J. Clin. Microbiol., 2018
Summary – GAS study (continued)

• 6% (n=13) of positive cases were missed by the BD Veritor™, while the ID NOW™ detected all 13 (100%) cases.

• Antibiotics were started 2-6 days after the visit in 6 (46%) cases, with one patient lost to documented follow-up.

• The remaining 6 (46%) patients were culture negative and were therefore not treated, but were RT-PCR confirmed as positive. Use of the ID NOW™ assay could have potentially led to these 6 (100%) missed patients being treated and the cobas® Liat® would have led to 4/6 (67%) of these patients being treated.

Berry et. al, J. Clin. Microbiol., 2018
Conclusions of GAS study

• The ID NOW™ had superior performance over the BD Veritor™

• More accurate results could assist in better utilization of antibiotics in real time

• Molecular platforms should be considered as viable alternative POCT devices for diagnosis of GAS pharyngitis

Berry et. al, J. Clin. Microbiol., 2018
Overall conclusions

• There are many different testing options for Flu/RSV and GAS.

• Molecular testing options help accommodate skill sets and testing environments

• Molecular testing methodologies have the ability to drastically improve diagnostic turnaround times, increase overall testing accuracy, and drive more appropriate therapy choices for better patient outcomes
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Thank You!

Questions?

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