Throat Cultures: Are they Obsolete? Does One Method Fit All

Robert L. Sautter, PhD
Carolinas Pathology Group
Clinical Diagnosis of Streptococcal Pharyngitis

- Based on signs and symptoms
- Not very accurate
- 50% of patients with pharyngitis will be treated but will not be infected with Group A Streptococci
- 30% of patients with pharyngitis will not be treated but will be infected with Group A Streptococci
Signs of Streptococcal Tonsillopharyngitis

- Characteristic signs
  - Tonsillopharyngeal erythema
  - Tonsillopharyngeal exudate
  - Soft-palate petechiae (“doughnut” lesions)
  - Beefy red, swollen uvula
  - Anterior cervical lymphadenitis
  - Scarlatiniform rash

- Uncharacteristic signs
  - Conjunctivitis
  - Anterior stomatitis
  - Discrete ulcerative lesions
Symptoms of Streptococcal Tonsillopharyngitis

- Characteristic symptoms
  - Sudden onset of sore throat
  - Headache
  - Pain on swallowing
  - Abdominal pain
  - Fever
  - Nausea and vomiting

- Uncharacteristic symptoms
  - Coryza
  - Cough
  - Hoarseness
  - Diarrhea

(Bisno, NEJM)
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Estimated Percentage of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td></td>
</tr>
<tr>
<td>Rhinovirus (100 types and 1 subtype)</td>
<td>20</td>
</tr>
<tr>
<td>Coronavirus (3 or more types)</td>
<td>≥5</td>
</tr>
<tr>
<td>Adenovirus (types 3, 4, 7, 14, and 21)</td>
<td>5</td>
</tr>
<tr>
<td>Herpes simplex virus (types 1 and 2)</td>
<td>4</td>
</tr>
<tr>
<td>Parainfluenza virus (types 1-4)</td>
<td>2</td>
</tr>
<tr>
<td>Influenzavirus (types A and B)</td>
<td>2</td>
</tr>
<tr>
<td>Coxsackievirus A (types 2, 4-6, 8, and 10)</td>
<td>&lt;1</td>
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<tr>
<td>Epstein-Barr virus</td>
<td>&lt;1</td>
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<tr>
<td>Cytomegalovirus</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Human immunodeficiency virus type 1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Which Streptococci Cause Sore Throat?

- Group A streptococcus (S. pyogenes)
- Group C streptococcus (S. dysgalactiae subsp. equisimilis)
- Group G streptococcus (S. dysgalactiae subsp. equisimilis)
### Microbial Causes of Acute Pharyngitis (Bisno, NEJM)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Estimated Percentage of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial</strong></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>15-30</td>
</tr>
<tr>
<td>Group C (\beta)-hemolytic streptococci</td>
<td>5</td>
</tr>
<tr>
<td><em>Neisseria gonnorrhoeae</em></td>
<td>&lt;1</td>
</tr>
<tr>
<td><em>Corynebacterium diphtheriae</em></td>
<td>&lt;1</td>
</tr>
<tr>
<td><em>Arcanobacterium haemolyticum</em></td>
<td>≤1</td>
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<tr>
<td><strong>Chlamydial</strong></td>
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<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>Unknown</td>
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<tr>
<td><strong>Mycoplasmal</strong></td>
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<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>&lt;1</td>
</tr>
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</table>
Why Diagnose Streptococcal Pharyngitis?

- Treatment Prevents Sequelae
  - Rheumatic Fever
  - Scarlet Fever
  - Glomerulonephritis
  - Invasive Streptococcal Disease
  - ("Flesh-eating Strep")
Nonsuppurative Sequelae

- Acute Rheumatic Fever
  - 1 to 5 weeks following acute pharyngitis
  - 6 to 15 years of age
  - Attack rate 0.4% (civilian) to 3% (military)
  - M types 1,3,5,6,12,18,19,24
  - Inflammation of the heart (heart valves), joints, blood vessels, and subcutaneous tissues
  - Probably immunological (autoimmune?)
  - Recurrences are common
Nonsuppurative Sequelae

- **Acute Glomerulonephritis**
  - Approx. 10 days following acute pharyngitis; (3 weeks following pyoderma)
  - Winter/Spring (Summer/Fall-pyoderma)
  - 6 to 15 years of age (preschool-pyoderma)
  - Attack rate 10-15% with known neph. strain
  - Limited M types involved
  - Probably immunological (immune complex)
  - Recurrences are rare
Laboratory Diagnosis

- Culture
  - Specimen Collection (10% FN)
  - “Gold Standard” ??
  - Selective vs. non-selective medium
  - Aerobic, 5-10% CO₂, anaerobic atmosphere
  - 1 or 2 day incubation
  - Broth enhancement
Cockerill. 2002. Mayo Clinic Data. AACC Internet Presentation
Rapid Antigen Tests

- Extract (acid) cell wall antigen from organism on throat swab
- Detect presence of extracted antigen by
  - Latex agglutination (LA)
  - Enzyme immunoassay (EIA)
  - Optical immunoassay (OIA)
FDA Approved Kits

- 40 CLIA High Complexity (1993-1999)
  - Abbott TestPack Plus Strep A
  - BD Directogen 1-2-3 Group A Strep
  - J & J CDI SureCell
  - Gen-Probe Group A Strep Direct
  - Effective Date
    - 01-11-1999
    - 10-27-1995
    - 10-06-1995
    - 06-10-1994

- Almost all are used to type organisms from culture
- Gen-Probe most frequently used direct specimen test in this group
FDA Approved Kits

  - Abbott Signify Strep A
  - Quidel Quickvue Strep A Test
  - Abbott TestPack Plus Strep A w/OBC II
  - Binax Strep A Test
  - J & J CDI SureCell
  - Abbott TestPack Plus Strep A
  - Baxter MicroScan Cards O.S.
  - BD Directogen 1-2-3 Grp A Strep
  - Binax Equate Strep A
  - BioStar Strep A OIA
  - Hybritech ICON Strep A
  - Meridian Diagnostics ImmunoCard
  - Quidel Group A Strep
  - Wampole Bactigen Group A Strep

<table>
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<th>Kit Name</th>
<th>Effective Date</th>
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<tbody>
<tr>
<td>Abbott Signify Strep A</td>
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<tr>
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<tr>
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<tr>
<td>J &amp; J CDI SureCell</td>
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<tr>
<td>Abbott TestPack Plus Strep A</td>
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<tr>
<td>Baxter MicroScan Cards O.S.</td>
<td>07-26-1993</td>
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<tr>
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<td>07-26-1993</td>
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<tr>
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<td>07-26-1993</td>
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<tr>
<td>BioStar Strep A OIA</td>
<td>07-26-1993</td>
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<tr>
<td>Hybritech ICON Strep A</td>
<td>07-26-1993</td>
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<tr>
<td>Meridian Diagnostics ImmunoCard</td>
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<td>Quidel Group A Strep</td>
<td>07-26-1993</td>
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<td>Wampole Bactigen Group A Strep</td>
<td>07-26-1993</td>
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FDA Approved Kits


<table>
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<th>Test Name</th>
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<tbody>
<tr>
<td>Genzyme OSOM Ultra Strep A Test</td>
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<tr>
<td>Quidel Quickvue In-Line Strep A</td>
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<tr>
<td>Acon Strep A Rapid Test Strip</td>
<td>12-18-2001</td>
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<tr>
<td>Beckman Coulter ICON DS Strep A</td>
<td>12-18-2001</td>
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<tr>
<td>Quidel Quickvue Dipstick Strep A</td>
<td>07-26-2001</td>
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<tr>
<td>ICON DS Strep A</td>
<td>07-17-2001</td>
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<tr>
<td>Beckman Coulter ICON FX Strep A</td>
<td>03-16-2001</td>
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<tr>
<td>Wyntek Diagnostics OSOM Ultra Strep A</td>
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<tr>
<td>Fisher Sure -Vue Strep A</td>
<td>09-22-1999</td>
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<tr>
<td>Meridian ImmunoCard STAT Strep A</td>
<td>05-19-1998</td>
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<tr>
<td>Abbott Signify Strep A Test</td>
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<td>Biostar Acceava Strep A Test</td>
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<td>Binax NOW Strep A Test</td>
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# Comparison of a CLIA Waived & Moderately Complex Test

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<th>Mod. Complex ADT</th>
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<tr>
<td></td>
<td>Sens. (%)</td>
<td>Spec. (%)</td>
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<tr>
<td>Waived ADT</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>Gold Standard</td>
<td>Sens. (%)</td>
<td>Spec. (%)</td>
</tr>
<tr>
<td>Waived ADT</td>
<td>80</td>
<td>95</td>
</tr>
<tr>
<td>Gold Standard</td>
<td>Sens. (%)</td>
<td>Spec. (%)</td>
</tr>
<tr>
<td>Mod. Com ADT</td>
<td>82</td>
<td>100</td>
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### Sensitivity and Specificity of the OIA

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<tr>
<th>Study</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tbody>
<tr>
<td>Harbeck 1993</td>
<td>97.4</td>
<td>95.6</td>
</tr>
<tr>
<td>Harbeck 1993</td>
<td>98.9</td>
<td>98.4</td>
</tr>
<tr>
<td>Dale 1994</td>
<td>81</td>
<td>97.5</td>
</tr>
<tr>
<td>Roe 1995</td>
<td>83</td>
<td>89</td>
</tr>
<tr>
<td>Heiter 1995</td>
<td>92.3</td>
<td>95.4</td>
</tr>
<tr>
<td>Fries 1995</td>
<td>94</td>
<td>98</td>
</tr>
<tr>
<td>Harris 1995</td>
<td>96</td>
<td>94</td>
</tr>
<tr>
<td>Baker 1995</td>
<td>78</td>
<td>90</td>
</tr>
<tr>
<td>Gerber 1997</td>
<td>84</td>
<td>93</td>
</tr>
<tr>
<td>Hart 1997</td>
<td>77</td>
<td>62</td>
</tr>
<tr>
<td>Pitetti 1998</td>
<td>79.5</td>
<td>96.5</td>
</tr>
<tr>
<td>Kuhn 1999</td>
<td>89</td>
<td>96.5</td>
</tr>
<tr>
<td>Chapin 2002</td>
<td>86.1</td>
<td>97.1</td>
</tr>
</tbody>
</table>
Conclusions: Rapid Antigen Kit Analytical Sensitivity Comparison

- Detection of different isolates by different tests showed no differences

- Analytical Sensitivities were best for the OIA ($3.3 \times 10^4$ CFU) and worst for Directigen ($5 \times 10^5$ CFU)

Cockerill. 2002. Mayo Clinic Data. AACC Internet Presentation
Molecular Tests for Detection of Group A Streptococcus from Throat Swabs - Not Point-of-Care

- Group A Streptococcus Direct Test (Gen-Probe)
- PCR – Conventional or Real Time
Gen-Probe Group A Streptococcus Direct Test

- Test detects rRNA sequences using a chemiluminescent single-stranded DNA probe

- Enhanced sensitivity vs. Antigen detection methods
### Performance of the *illumi*gene group A assay compared to that of the extracted culture (Modified)

Multicenter Clinical Evaluation of the *illumi*gene Group A Streptococcus DNA Amplification Assay for Detection of Group A Streptococcus from Pharyngeal Swabs

0.1128/JCM.00176-13 J. Clin. Microbiol. May 2013 vol. 51 no. 5 1474-1477

<table>
<thead>
<tr>
<th>Clinical test site no.</th>
<th>No.</th>
<th>Sensitivity (%) [95% CI]</th>
<th>Specificity (%) [95% CI]</th>
<th>PPV (% [95% CI])</th>
<th>NPV (% [95% CI])</th>
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<tbody>
<tr>
<td>1</td>
<td>338</td>
<td>100 (92–100)</td>
<td>98.6 (96–99)</td>
<td>92.2 (81–97)</td>
<td>100 (98–100)</td>
</tr>
<tr>
<td>2</td>
<td>241</td>
<td>93.3 (77–99)</td>
<td>96.2 (92–98)</td>
<td>77.8 (60–89)</td>
<td>99 (96–99)</td>
</tr>
<tr>
<td>3</td>
<td>217</td>
<td>100 (86–100)</td>
<td>97.9 (94–99)</td>
<td>86.2 (68–96)</td>
<td>100 (98–100)</td>
</tr>
<tr>
<td>Total</td>
<td>796</td>
<td>98.0 (93–99)</td>
<td>97.7 (96–98)</td>
<td>86.2 (78–91)</td>
<td>99.7 (98–99)</td>
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</tbody>
</table>
Detection of *Streptococcus pyogenes* Using * illumigene®* Group A *Streptococcus* Assay

Amanda M. Henson et.al. Published ahead of print 18 September 2013, doi: 10.1128/JCM.01892-13

- Sensitivity (100%) compared to culture or PCR, and high specificity (99.2%) compared to PCR. Resistance to erythromycin and clindamycin was 8.8% and 6.9% respectively.
Back up Molecular Tests?

- This remains to be seen
CONTROVERSY
Back-up Throat Culture for Adults with a Negative Rapid Strep Test

- A. What is not recommended by the IDSA?
- B. What is not recommended by ESCMID?
- C. What is mandated by the College of American Pathologists (CAP)?
- D. What is recommended by the FDA?
- E. What are all of the above (correct answer)
Diagnosis of GAS Pharyngitis

- **IDSA:** "Routine use of back-up throat cultures for those with a negative rapid antigen detection test is not necessary for adults in usual circumstances."
  - Back up cultures for children is required by IDSA
- **ESCMID:** "Throat culture is not necessary after a negative rapid antigen test."
- **CAP:** "If group A *Streptococcus* direct antigen testing is performed, additional confirmatory testing is performed on negative samples."
- **FDA:** "No rapid test has been cleared, approved, or waived through the regulatory process as a stand alone test. ... lack of a backup method for a rapid GAS test result constitutes off label use."
Back up of throat cultures

- An additional suggestion came in our system to discontinue “culture back up” on strep throat screens.
Throat Screens

1. FDA states that back-up cultures should be performed, see link. If not performed, the practice would be classified as an off label use.
   - [http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109407.htm](http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109407.htm)

2. CAP has a standard requiring back up.

3. Also, without back up cultures additional strep would not be isolated. Group C, G and Arcanobacterium sp.
   - Group C in several studies accounts for 5-11% of exudative pharyngitis cases.
New 07/11/2011
MIC.22140 Group A Streptococcus Direct Antigen Detection Phase 1

If group A Streptococcus direct antigen testing is performed, additional confirmatory testing is performed on negative samples.

Note 1: Guidelines should be established for use of culture or other additional tests on specimens that test negative, as appropriate. These guidelines should take into account the sensitivity of the assay in use, the age and clinical presentation of the patient, and other factors.

Note 2: Direct antigen tests should be performed and reported in a timely fashion, since their principle advantage (compared to more sensitive methods as culture) is a rapid turn-around-time.
Query to ClinMicroNet

- All 7 responses were that back up cultures MUST be performed.
- In addition, a review of our ED streps primarily from the summer months showed an 11% false negative rate for our rapid strep.
- Additionally “look back” from January revealed that we would have missed 185 patients without a strep back up culture for the rapid tests performed.
Throat recommendation

- Continue performing back up cultures for rapid strep screens at all hospitals that send work to our hospital
ASM Poster 2013 supports our stance

- 369 patients, aged 13 years or older, with a negative RADT and positive GAS culture
- 77% had ≥ 2+ GAS recovered on culture
- Serious complications: 5.7% had peritonsillar abscess requiring surgical drainage, 0.5% had acute rheumatic fever

Dingle et al., presented at ASM General Meeting, Denver, CO, May 2013.
Study Numbers - Adult and Adolescent Patients

- 40845 total RADT performed
  - 35629 Negative
  - 5216 Positive
  - 22683 reflexed to culture
    - 975 Positive for GAS
    - 21708 Negative for GAS
Study results of patients with negative RADTs and positive GAS cultures. RADTs can miss patients with serious complications of infection (peritonsillar abscess and rheumatic fever). Clinicians used culture results to direct treatment in more than one-third of cases.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number of Patients (%) n=369</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>192 (52.0)</td>
</tr>
<tr>
<td>Female</td>
<td>177 (48.0)</td>
</tr>
<tr>
<td>Age</td>
<td>Average 31 (Range 13-76)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td>358 (97.0)</td>
</tr>
<tr>
<td>Absence of cough</td>
<td>245 (66.4)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>186 (50.4)</td>
</tr>
<tr>
<td>Trismus</td>
<td>14 (3.8)</td>
</tr>
<tr>
<td>Odynophagia</td>
<td>127 (34.4)</td>
</tr>
<tr>
<td>Signs</td>
<td>Tonsillar swelling/exudate</td>
</tr>
<tr>
<td></td>
<td>162 (43.9)</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
</tr>
<tr>
<td>Peritonsillar abscess</td>
<td>21 (5.69)</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Labs</td>
<td></td>
</tr>
<tr>
<td>Leukocytosis (&gt;10000/uL)</td>
<td>57 (15.4)</td>
</tr>
<tr>
<td>Fever (&gt;38°C, &gt;100.4°F)</td>
<td>52 (14.1)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Patient treated</td>
<td>238 (62.6)</td>
</tr>
<tr>
<td>Patient treated based on culture results</td>
<td>86 (36.1)</td>
</tr>
<tr>
<td>Surgical Drainage</td>
<td>20 (5.4)</td>
</tr>
</tbody>
</table>
Case- History

- The patient was an 19 yo female college student, sudden onset of chills and night sweats and body aches.
- She had a sore throat, it hurt when swallowing, but no cough.
- Initial diagnosis was streptococcal sore throat.
- Subsequently she was seen in the ED as her condition worsened.
History cont.

- During sedation for the CT, she desaturated and when the anesthesiologist went to look at her airway he saw an exudates in the posterior pharynx and a “necrotic” epiglottis.
- ENT was called emergently and noted a membrane at her epiglottis. The specimen was sent to the lab for culture. The patient was intubated and transferred to the PICU.
The isolate
The bacterium now named *Arcanobacterium haemolyticum* described in 1946 causing pharyngitis and cutaneous infections.

As a result of its close resemblance to *Corynebacterium pyogenes*, a possible mutant of this species and appended a subspecies name, *C pyogenes* subsp *hominis*. 
● *A haemolyticum* is a pleomorphic, facultatively anaerobic, nonmotile, nonsporulating, non–acid-fast, hemolytic gram-positive rod.

● Gram staining can show variable results if examined after 24 hours of growth.

● The 70 strains are divided into smooth and rough biotypes.

● The smooth form is found in wound infections, and the rough predominates in respiratory tract infections.
- *A haemolyticum* causes pharyngitis but has been implicated in a wide spectrum of diseases.
- Several investigators reported *A haemolyticum* as the main pathogen in patients presenting with pharyngitis.
Pharyngitis caused by *A. haemolyticum* must be differentiated from the more prevalent pharyngitis caused by streptococcal organisms.

*A. haemolyticum* may be missed on routine throat cultures because of the use of rapid group A streptococcal antigen assays and the use of special culture media for optimal isolation of group A streptococcal species.

Most cultures for pharyngitis are evaluated at 24 hours, at which point *A. haemolyticum* colonies are very small and demonstrate minimal hemolysis, and the cultures may be discarded.
Therapy

- Most isolates are susceptible to penicillin, however macrolides are now considered the drugs of choice due to tolerance to penicillin in some strains.
The patient was an 11 month old who presented with 2-3 days of fever, approximately 3 weeks after returning from a month long trip to India.

During the course of hospitalization (day 4 of hospitalization), she developed drooling and stridor and was noted to have an exudative pharyngitis (not present at admission). A lateral neck film was performed but inconclusive for epiglottitis, so a CT was done the next day.
During sedation for the CT, she desaturated and when the anesthesiologist went to look at her airway he saw an exudates in the posterior pharynx and a “necrotic” epiglottis. ENT was called emergently and noted a membrane at her epiglottis. The specimen was sent to the lab for culture. The patient was intubated and transferred to the PICU.
Following Therapy
Diphtheria is an acute infectious disease of humans affecting the upper respiratory tract and occasionally the skin, caused by the action of diphtheria toxin produced by toxigenic *Corynebacterium diphtheriae* or by *C. ulcerans*. 
The most characteristic feature of diphtheria affecting the upper respiratory tract is a membranous pharyngitis.

The pseudo-membrane may cause respiratory obstruction.

The toxin also may cause paralysis and cardiac failure.
See Plates and smears
Over 100 reported cases
Between 50 and 100 reported cases
1-49 reported cases
No cases reported/Information
Not Available
Early stages:
- Sore throat
- Low fever
- Swollen neck glands

Late stages:
- Airway obstruction and breathing difficulty
- Shock (low blood pressure, rapid heartbeat, paleness, cold skin, sweating, and anxious appearance)
Risk Factors

- Outbreak in the community
- Crowded or unsanitary living conditions
- Immunity gaps in adults
- Lack of mass immunization programmes amongst children and adults at high risk
- Lack of vaccines in many areas

Possible complications

- Heart inflammation and heart failure.
- Suffocation, due to blockage from pseudo-membrane.
- Nerve inflammation.
- Misdiagnosis as a less-serious infection, resulting in dangerous delay of treatment.
3 IDENTIFICATION

3.1 MICROSCOPIC APPEARANCE

Gram stain (see BS02TP 30: Staining Procedures)

Gram-positive rods, pleomorphic, slightly curved with tapered or clubbed ends.
Cells may occur singly or in pairs, often in a “V” formation (forming “chinese letters”). Cells
usually stain weakly and unevenly giving a beaded appearance.

3.2 PRIMARY ISOLATION MEDIA

Blood agar - skin swabs incubated in 5 - 10% CO₂ at 35 - 37°C for 40 - 48 h and throat swabs
incubated anaerobically at 35 - 37°C for 16 - 24 h.
Hoyles tellurite agar incubated in air at 35 - 37°C for 16 - 48 h.
β-haemolytic streptococci may also be present, particularly in throat swabs.

3.3 COLONIAL APPEARANCE

Appearance varies among species; for more information refer to Section 3.4 Test procedures.

3.4 TEST PROCEDURES

All potentially toxigenic corynebacteria are catalase positive (see BS02TP 8: Catalase Test)
and pyrazinamidase* negative. For non-toxigenic corynebacterium the catalase test results
are variable. Rapid (4 h) tests should be performed for urease, pyrazinamidase, catalase and
nitrate reduction.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Culture media</th>
<th>Biochemical tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hoyles’s tellurite agar</td>
<td>Blood agar</td>
</tr>
<tr>
<td>C. diphtheriae biotype var. gravis[25,26]</td>
<td>dull grey/black opaque colonies, 1.5-2.0 mm in diameter, matt surface, stable, tending to break into small segments when touched with a straight wire</td>
<td>non-haemolytic</td>
</tr>
<tr>
<td>C. diphtheriae biotype var. mitis[25,26]</td>
<td>grey/black opaque colonies, 1.5 - 2.0 mm in diameter, entire edge and glossy smooth surface; size variation is common</td>
<td>colonies exhibit a small zone of β-haemolysis</td>
</tr>
<tr>
<td>C. diphtheriae biotype var. intermedius</td>
<td>small, grey, black, wavy surface, discrete, translucent colonies, 0.5-1.0 mm in diameter</td>
<td>colonies exhibit a small zone of β-haemolysis</td>
</tr>
<tr>
<td>C. diphtheriae biotype var. bulleri[25]</td>
<td>grey/black, opaque colonies, 1.5-2.0 mm in diameter, entire edge and glossy smooth surface; size variation is common</td>
<td>colonies exhibit a small zone of β-haemolysis</td>
</tr>
<tr>
<td>C. ulcerans[25,26]</td>
<td>grey/black, very dry opaque colonies</td>
<td>colonies exhibit a small zone of β-haemolysis</td>
</tr>
</tbody>
</table>

* The catalase test is not recommended for non-toxigenic corynebacterium.
The Isolate in this case is on the left
Case :PC

Case records of the Levine Children’s Hospital
May, 2013
History

- 9-year-old girl presents with involuntary movement
- Increasing movement, left greater than right, of her extremities
- Tongue rolling and face twitching
- Difficulty sleeping
- Difficulty with simple tasks due to inability to control movement
Fourth grade teacher noted increased difficulty performing tasks

Emotional lability
Past history

- Generally well
- Normal development
- Febrile illness one month ago, did not seek medical attention
Physical exam

- No fever, vitals stable
- Normal growth
- Constant motion which she tries to hide and pretend that it is voluntary (video)
- Unable to do simple manual tasks (video)
- No “milkmaid’s grip”
- Spooning of upper extremities noted
- Normal mental status, reflexes and cranial nerves
Evaluation

- MRI, CT scan, EEG all normal
- ASO: 756 Todd units
- Anti-DNase B. titer 1530
- Throat culture **positive** for group A streptococcus (after hospitalization).
- No record of culture performed in her physician’s office
Diagnosis and management

- **Diagnosis**: *Sydenham’s chorea*
- **Treatment**:
  - Penicillin for group A strep
  - Penicillin (secondary) prophylaxis until age 21
  - Prednisolone
  - Clonazepam