Challenge M242-1

August 2024

Throat - *Arcanobacterium haemolyticum*

HISTORY

A simulated throat sample collected from a 14 year old female with rash and sore throat was sent to category A laboratories.

Participants were expected to isolate and report *Arcanobacterium haemolyticum.*

CMPT QA/QC/STATISTICS

All simulated throat samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of *Arcanobacterium haemolyticum*

The samples are assessed for homogeneity and stability using in-house quality control methods and random selection of samples before and during production, and post sample delivery. The number of random samples selected is 15% of the total production batch.

The challenge sample lot was confirmed to be homogeneous and stable for 14 days.

Organism identification was confirmed by a reference laboratory.

All challenge components have in-house assigned values based on the most clinically appropriate result; the most clinically appropriate result is determined by expert committee evaluation. No further statistical analysis is performed on the results beyond that described under "Suitability for grading."

MAIN EDUCATIONAL POINTS from M242-1

1. Arcanobacterium haemolyticum is associated with pharyngitis and should not be ignored in throat cultures, particularly in situations of recurrent pharyngitis, with or without accompanying rash, in treatment failure, and when the patient is adolescent or a young adult (10-30 years).
2. For laboratories where a throat culture is not routinely performed and presence of group A Streptococcus is tested by an alternate method, culture for other organisms should be available and performed when clinically indicated.

SURVEY RESULTS

Reference laboratories: 11/13 (85%) labs reported *Arcanobacterium haemolyticum*, 2 labs reported no group A ± C or G Streptococcus

Participants: 44/51 (86%) participants reported *Arcanobacterium haemolyticum* or *Arcanobacterium* species, refer; 5 reported no group A +/- C or G streptococcus (Table 1).

Suitability for Grading

A challenge is considered suitable for grading if agreement is reached by 80 percent of selected reference group and at least 50 percent of the participants.

Organism identification was correctly performed by at least 80 percent of reference laboratories and greater than 50 percent of all laboratories and was thus, determined to be suitable for grading.

Grading

Maximum grade: 4

Reporting *Arcanobacterium haemolyticum* or Arcanobacterium species, refe was graded 4.

Table 1. Identification results

Reported	Total	Grade
Arcanobacterium haemolyticum ± presumptive/suspecté ± no group A Streptococcus isolated	43	4
Arcanobacterium species, refer	1	4
Gram positive bacilli, refer for identification	1	1
Culture: Oropharyngeal Flora. 4+ Culture: Negative for Beta-Hemolytic Streptococcus (Groups A, C, and/or G).	1	0
No Group A, ± C or G Beta Hemolytic Streptococci isolated	4	0
Culture is negative	1	0
Total	**51**	

COMMENTS ON RESULTS

Participants were expected to culture and report the presence of *Arcanobacterium haemolyticum*. 86% (445/51) of participant laboratories that reported a result for this challenge reported correctly.

ISOLATION AND IDENTIFICATION

The *Arcanobacterium* genus presently contains nine species, of which *A. haemolyticum, A. bernardiae*, and *A. pyogenes* have been recovered from human clinical specimens. [1] All clinically relevant arcanobacteria are catalase-negative, non-motile, and ferment glucose. [1, 2]

A. haemolyticum are 0.5 mm in diameter after 48 hours of incubation at 37°C. *A. haemolyticum* easily passes unrecognized in bacteriological cultures as a result of its coryneform appearance in the Gram stain and weak haemolytic activity on conventional media. [2]

A. haemolyticum may be missed on routine throat cultures because of the use of rapid group A streptococcal antigen assays. Additionally, cultures for pharyngitis are usually evaluated at 24 hours, when *A. haemolyticum* colonies are very small and demonstrate minimal hemolysis, resulting in the culture being discarded before the colonies are evident. [2]

Beta-hemolysis is enhanced by incubation in 5-8% CO_2 and prolonging incubation to 48 hours, or by the use of trypticase soy agar with 5% sheep blood, [1] although some authors observed better hemolysis on trypticase soy agar with 5% horse [2] or human blood. [3]

Gram staining of arcanobacteria shows irregular gram-positive bacilli, slightly curved. *A. haemolyticum* is ("reverse") CAMP inhibition test positive – this is due to phospholipase D production which gives *A. haemolyticum* the ability to inhibit the haemolytic effect of beta-haemolysin produced by *Staphylococcus aureus* (Figure 1). [1, 2]

A. haemolyticum can be also routinely identified by API Coryne V2.0 system and by MALDI-TOF.[9]

Figure 1. CAMP inhibition test,

ANTIMICROBIAL SUSCEPTIBILITY

A. haemolyticum is usually susceptible to antimicrobial agents used to treat streptococcal tonsillitis however, tolerance to penicillin has been described which has been associated with clinical failure. [4, 5]

Improved bacteriological eradication in pharyngitis has been associated with the use of macrolides.

CLINICAL RELEVANCE

A. haemolyticum infections are a relatively uncommon cause of pharyngitis and/or tonsillitis and skin rash in adolescents and young adults. Common clinical symptoms and signs at presentation include throat exudate, skin rash, and lymphadenopathy, which are clinically similar to features of infection caused by group A Streptococcus. [2]

An incidence of 0.5-3% of cases of pharyngitis has been reported. [6] The diagnosis is often made only after recurrent infections initially misdiagnosed as beta hemolytic streptococcal or viral infection.

Less frequent infections caused by *A. haemolyticum* include osteomyelitis, cellulitis, sinusitis, endocarditis, wound infections, pneumonia, meningitis, and septicemia. [7]

In the elderly population, especially those with diabetes mellitus or are immunocompromised, *A. haemolyticum* is more likely to cause soft-tissue infections. [7, 8]

REFERENCES

1. Bernard KA. *Coryneform gram-positive rods*. In: Carroll, Pfaller, Landry, McAdam, Patel, Richter, and Warnock, ed. *Manual of Clinical Microbiology*. Vol 1. 12th ed. ed. Washington, DC.: ASM; 2019:488-524.

2. Garcia-de-la-Fuente C, Ruiz De Alegria C, Cano ME, et al. Phenotypic and molecular characterization of *Arcanobacterium haemolyticum* isolated from clinical samples. *Diagn Microbiol Infect Dis*. 2012;72(1):1-7.

3. Unusual throat isolates. (Reverse CAMP Test). MicrobLog: Microbiology Training Log November, 2008 – 14:04

4. Carlson P, Kontianinen S, Renkonen OV, Sivonen A, Visakorpi R. *Arcanobacterium haemolyticum* and streptococcal pharyngitis in army conscripts. *Scand J Infect Dis*. 1995;27(1):17-18.

5. Mehta CL. *Arcanobacterium haemolyticum*. *J Am Acad Dermatol*. 2003;48(2):298-299.

6. Chen Y, Colodner R, Chazan B, Raz R. Pharyngotonsillitis due to *Arcanobacterium haemolyticum* in northern Israel. *Isr Med Assoc J*. 2005;7(4):241-242.

7. Tan TY, Ng SY, Thomas H, Chan BK. *Arcanobacterium haemolyticum* bacteraemia and soft-tissue infections: Case report and review of the literature. *J Infect*. 2006;53(2):e69-e74.

8. Vu MLD, Rajnik M. *Arcanobacterium haemolyticum*. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2021. http://www.ncbi.nlm.nih.gov/books/NBK560927/. Accessed Jun 8, 2021.

9. Vila J, Juiz P, Salas C, et al. Identification of Clinically Relevant Corynebacterium spp., Arcanobacterium haemolyticum, and Rhodococcus equi by Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry. *Journal of Clinical Microbiology*. 2020;50(5):1745-1747. doi:10.1128/jcm.05821-11