Challenge M243-2

November 2024

Eye: *Neisseria meningitidis*

HISTORY

A simulated eye swab sample collected from a 6 month old child with purulent discharge from the eye was sent to category A laboratories.

Participants were expected to isolate and report *Neisseria meningitidis.*

CMPT QA/QC/STATISTICS

All simulated eye swab samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of *Neisseria meningitidis.*

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 7 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."

SURVEY RESULTS

Reference laboratories

Identification: 12/12 (100%) labs reported *Neisseria meningitidis*, 1 lab indicated it does not normally process this type of sample

Notification to PH: 8 labs indicated they would notify PH authorities; 2 indicated they were not required, 2 indicated they would not notify.

Participants

Identification: 41/48 (85%) labs reported Neisseria meningitidis; details of reports and grading are posted in Table 1.

MAIN EDUCATIONAL POINTS from M243-2

1. Bacterial conjunctivitis can be highly infectious and is spread by direct contact with the secretions or contaminated shared objects.
2. Correctly identifying *N. meningitidis* from conjunctival samples is important because the treatment is different than that of most other bacterial entities.
3. *Neisseria* species, including N. meningitidis, can cause a hyperacute bacterial conjunctivitis that is severe and sight threatening.

Notification to PH: 24/48 labs indicated they would notify PH authorities; 15 did not or indicated they were not required, 10 indicated they would refer (Table 2).

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. Notification to Public Health authorities did not reach consensus among reference laboratories therefore, this component is not suitable for grading.

Grading

Maximum grade: 4

Reporting *Neisseria meningitidis* was graded 4.

Table 1. Colony count results

Reported	Total	Grade
Neisseria meningitidis ± group W (1 lab)	41	4
Neisseria sp ou *Moraxella* sp. Possibilité de *Neisseria Méningitidis*, refer	1	4
Neisseria species, refer	1	4
Gram negative diplococci, refer	1	3
Diplocoque Gram négatif, extra cellulaire ayant morphologie de Neisseria gonorrhoeae (extracellular having the morphology of *N.gonorrhoeae*), refer	1	3
Scant gram negative coccus, refer	1	3
Moraxella group, refer	1	0
Neisseria gonorrhoeae	1	0
no report	1	0
sample not normally processed	2	ungraded
Total	**51**	

COMMENTS ON RESULTS

41/51 laboratories reported *Neisseria meningitidis*. 2/51 laboratories incorrectly identified the organism as *Moraxella* group or *Neisseria gonorrhoeae.* Several labs provided a Gram stain result with or without referral to another laboratory.

Public Health notification of results was not consistent with 24/51 laboratories reporting isolate to public health. 10/51 laboratories stated that the specimen would have been referred to another laboratory therefore, public health reporting not performed. There may be provincial differences in public health reporting for non-invasive specimens.

Table 2. Notification to Public Health - Ungraded

Public/Medical Health notification	Total
Yes	24
No	12
Our province does not require notification in this case, ± required if Neisseria meningitidis isolated on sterile body site.	3
no report/Int'l lab	1
n/a, no report for Identification	1
refer, sample not normally processed	10
Total	**51**

ISOLATION AND IDENTIFICATION

Ideally, both eyes should be sampled as the uninfected eye can serve as a control with which to compare the organisms isolated from the infected eye.[1]

Gram stains of conjunctival scrapings are useful because they can provide etiologic information. Smears from bacterial infections reveal numerous neutrophils. Lymphocytes and monocytes are predominant in viral infections, while eosinophilia can be observed in allergic disease. [2–4]

ANTIMICROBIAL SUSCEPTIBILITY

According to Clinical and Laboratory Standard Institute (CLSI), antimicrobial susceptibility testing of *Neisseria meningitidis* should be performed using one of the following media: 1) disk diffusion with Mueller Hinton agar with 5% sheep blood; 2) broth microdilution with cation-adjusted Mueller-Hinton broth (CAMHB) supplemented with lysed horse blood (LHB); or 3) agar dilution with Muller Hinton agar supplemented with sheep blood (5% v/v). The media should be incubated at 35°C ± 2°, with 5% carbon dioxide and 20- to 24-hour period. However, individual laboratories may opt for their own developed methods, if verification studies synthesize acceptable results as per CLSI.[5]

Institutional antibiograms may not include *Neisseria meningitidis* because of insufficient sample size encountered during the analysis period (e.g. minimum of 30 isolates per year).[6] However, cumulative antimicrobial susceptibility test results of *N. meningitidis* are sometimes available in peer-reviewed articles, which could be subject to bias due to patient population, culturing practices, laboratory testing and report policies, and temporal outbreaks.[6] In 2012–2016, the American Centers for Disease Control and Prevention (CDC) conducted a surveillance study of 695 *N. meningitidis* isolates whose susceptibility was assessed by broth microdilution.[7] Penicillin G, ampicillin, ciprofloxacin, or levofloxacin resistance was seen in <1% of isolates; however, penicillin G and ampicillin intermediate susceptibility were observed in 26.3%-31.5% and 26.3%-28.9% of the isolates, respectively. In 2004-2018, none of the 50 *N. meningitidis* isolates detected in Nova Scotia were resistant to penicillin G, azithromycin, ciprofloxacin, minocycline, and rifampin, but a rise in penicillin G minimum inhibitory concentration (MIC) was observed over the study period.8 In 2013-2015, only 2 of the 346 *N. meningitidis* isolates tested in the National Microbiology Laboratory, Winnipeg, was found to be ciprofloxacin resistant. Molecular sequencing determined that these two isolates were likely imported strains.[9]

CLINICAL RELEVANCE

Conjunctivitis is a common condition. Acute conjunctivitis is marked by unilateral hyperemia (red eye), mucopurulent discharge, and in some cases chemosis (conjunctival edema).[10] It is a diagnosis of exclusion and can be made only if the vision is normal and there is no evidence of keratitis, iritis, or angle closure glaucoma.[11]

Bacterial conjunctivitis is spread by direct contact and is highly contagious.

S. aureus, S. pneumoniae, H. influenzae and *M. catarrhalis* are the most common causes of bacterial conjunctivitis.

N. meningitidis conjunctivitis is uncommon, but occurs more frequently in children and young adults and has been reported in up to 2% of cases of conjunctivitis.[12]

Acute conjunctivitis caused by *N. meningitidis* is classified into primary and secondary disease. Primary meningococcal conjunctivitis (PMC) may be acute or hyperacute and is accompanied by a significant purulent discharge.[4,13] The hyperacute form is severe and sight threatening and requires immediate ophthalmologic referral.[11] It can rapidly progress to corneal ulceration and perforation. PMC can present as invasive or noninvasive form. In the invasive form, conjunctivitis is followed by systemic meningococcal disease (10–29.4%). In the noninvasive form, conjunctivitis is an isolated phenomenon.

Secondary meningococcal conjunctivitis follows systemic meningococcal disease and is a rare occurrence.[13,14]

If the clinician suspects *Neisseria* infection, a bacterial Gram stain and culture should be obtained immediately. The diagnosis of meningococcal conjunctivitis should be considered when gram-negative diplococci are observed.[14,15]

Treatment of conjunctivitis should include systemic therapy in view of the potential for invasiveness of *N meningitidis*, with topical antibiotics as an adjunct. The risk of invasive disease in those treated initially with topical therapy alone was estimated to be 19 times greater than for those receiving systemic antibiotic. [14]

Ceftriaxone is the treatment of choice for *N meningitidis* conjunctivitis.[4]

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PUBLIC HEALTH NOTIFICATION

Not all provinces in Canada require cases of suspected primary meningococcal conjunctivitis to be reported to Public Health authorities.

Since 2017 confirmed cases of primary meningococcal conjunctivitis are no longer required to be reported to BCCDC Epidemiology Services. [16)]

In Manitoba and Newfoundland and Labrador the isolation of *N. meningitidis* from the eye or the conjunctival sac, in association with purulent conjunctivitis, is reportable to Public Health authorities. [17]

At this time conjunctivitis and pneumonia cases due to *N. meningitidis* are not nationally notifiable and reported to the Public Health Agency of Canada.

Some guidelines consider meningococcal conjunctivitis to be an indication for chemoprophylaxis of close contacts.[12]

LABORATORY SAFETY

When handling cultures where there is potential for laboratory professional exposure to potential pathogens the CLSI M29-A4 publication (18) Protection of Lab Workers from Occupationally Acquired Infections is a valuable resource. Biosafety training is the cornerstone for protecting employees. This training should educate employees on the infectious agents they may encounter, risk assessment review of processes that are performed and how the chain of infection may result in employee exposure.

Activities performed in the laboratory present opportunities for occupational exposure. These include: primary specimen processing, subculturing, assessment of culture and many others. Therefore, it is important to review these steps and procedures in the laboratory to determine and mitigate risk.

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