Autopsy Biosafety: Recommendations for Prevention of Meningococcal Disease

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ABSTRACT

Introduction: As invasive meningococcal disease progresses rapidly, often affects youth, and has a fairly high mortality rate, such cases are likely to fall under medical examiner/coroner (ME/C) jurisdiction. Morgue personnel may be at risk of contracting secondary meningococcal disease. We review the current scientific literature regarding *Neisseria meningitidis* infection and provide recommendations for the prevention of meningococcal disease at autopsy.

Methods: A PubMed search utilizing applicable medical subject heading terms was performed retrieving articles for review from the preceding two decades. Pertinent current guidelines from multiple national organizations were also retrieved.

Results: Invasive meningococcal disease is transmitted by direct contact with large respiratory droplets or oral secretions. While a surgical mask would normally provide adequate protection from large droplet spread, it does not prevent inhalation of smaller aerosolized particles such as those generated at autopsy. Prosectors are advised to routinely wear N-95 respirator masks or powered respirator hoods. All published cases of secondary meningococcal disease transmission to healthcare workers invariably arose in scenarios in which face masks/respirators were not employed; none of these cases involved meningococcal disease transmission to ME/C or other morgue staff.

Discussion: In the event that no mask—or inadequate coverage such as a surgical mask—is employed during autopsy of a decedent suspected/confirmed to have invasive meningococcal disease, antibiotic prophylaxis is advisable. Assuming appropriate personal protective equipment is utilized, chemoprophylaxis is unnecessary. Routine meningococcal vaccination is not recommended, except for ME/C with specified immunocompromising conditions or traveling to hyperendemic/endemic meningococcal regions. *Acad Forensic Pathol.* 2018 8(2): 328-339

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INTRODUCTION

Invasive meningococcal disease can result in meningitis, disseminated intravascular coagulation, septic shock, and death (1-3). As meningococcal disease can have a fulminant course with a fairly high mortality rate and often affects youth, such cases are likely to fall under medical examiner/coroner (ME/C) jurisdiction. Medical examiners/coroners and other morgue personnel may be at risk of contracting secondary disease. The following review by the National Association of Medical Examiners (NAME) Ad Hoc Bioterrorism and Infectious Disease Committee is intended to educate ME/C and other morgue personnel regarding *Neisseria meningitidis* infection, as well as to provide evidence-based recommendations for the prevention of meningococcal disease at autopsy.

METHODS

A PubMed search utilizing terms “meningococcal” OR “meningococcus” AND “health-care worker” was performed. Common medical subject heading (MeSH) terms were also included in the search e.g., “*Neisseria meningitidis*” and “health personnel.” Limitations included English language-only and publication within the preceding two decades (i.e., 1/1/1998-1/1/2018). A total of 152 articles were retrieved; of these, 25 directly addressed the topic of meningococcal disease/disease prevention in healthcare employees and were reviewed. Also included in the review were pertinent national guidelines such as the Centers for Disease Control and Prevention (CDC) recommendations regarding immunization of healthcare personnel and meningococcal disease prevention, Occupational Safety and Health Administration (OSHA) respiratory protection recommendations, College of American Pathologists (CAP) general autopsy safety recommendations, and NAME biosafety recommendations. Additional references were sought, reviewed, and incorporated as necessary.

RESULTS

Incidence and Transmission

Neisseria meningitidis is an aerobic Gram-negative diplococcus that commonly colonizes the mucosal surfaces of the nasopharynx; the organism is transmitted via direct contact with respiratory tract droplets (1-3). In a recent systematic review and meta-analysis, age was found to be the key determinant of meningococcal carriage; prevalence was 4.5% in infants with a peak of 23.7% in 19-year-olds and subsequent decrease to 7.8% in 50-year-olds (4). Given these relatively high colonization rates, invasive meningococcal disease remains uncommon with historically low annual incidence. From 2005-2011, there were approximately 800-1200 cases of invasive meningococcal disease annually in the United States (3, 5). In 2015 and 2016, this declined to 359 and 372 reported cases, respectively (6, 7). Despite the low incidence, however, the disease continues to have a 10-15% overall mortality with significant survivor morbidity including neurologic damage and complications of disseminated intravascular coagulation, such as digit or limb loss (1-3, 5-7).

The majority of young adults in the United States have detectable antibodies to pathogenic *N. meningitidis* serogroups (2). Invasive disease most commonly arises in seronegative individuals who are exposed to the organism. Scenarios in which transmission often occurs are those involving entry of a seronegative individual into a crowded new environment such as daycare center, college campus, military training camp, or nursing home (2, 5). In addition to crowding, other factors that may increase the likelihood of colonization include tobacco smoke inhalation (active or passive), recent upper respiratory tract infection, and chronic underlying illness (2, 3, 5). The highest rates of invasive meningococcal disease occur in children less than one year of age, followed by a second smaller peak in adolescents/young adults 16-23 years of age, and finally a third small peak in older adults > 65 years of age (5, 8). Of the five pathogenic *N. meningitidis* serogroups (A, B, C, Y, W-135), three (B, C, and Y) account for the majority of meningococcal disease

in the United States. While overall, serogroups B, C, and Y each cause approximately one-third of disease cases in the United States, serogroup B accounts for proportionately more of the childhood cases (2, 3, 5, 8).

At Risk Populations

Certain populations have been designated as being at increased risk of acquiring meningococcal disease by the CDC. For instance, individuals with persistent complement pathway deficiencies (i.e., C3, C5-C9, properdin, Factor D, or Factor H) have up to 10 000 times greater risk of acquiring meningococcal disease and are also at risk for recurrent disease (5, 9). The complement deficiency may be genetic or acquired. Eculizumab (Soliris, Alexion Pharmaceuticals), a terminal complement inhibitor approved for treatment of paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, and generalized myelasthenia gravis may predispose to meningococcal infection (9, 10). Likewise, individuals with anatomic or functional asplenia are at increased risk for infection by encapsulated bacteria including *N. meningitidis*, and have an increased mortality rate (40-70%) if infected (5, 9). More recently, studies have confirmed an increased risk for meningococcal disease among HIV-infected individuals, who were found to be 5- to 24-fold more likely to become infected as compared to non-HIV infected individuals (11).

In addition to these populations with immune system compromise, individuals traveling to or residing in geographic regions in which meningitis is hyperendemic/epidemic (e.g., Saudi Arabia or sub-Saharan Africa) and microbiologists who are routinely exposed to *N. meningitidis* isolates are also considered at increased risk (2, 3, 5, 9, 12, 13). In one study, 16 cases of probable laboratory-acquired meningococcal disease were identified nationwide between the years 1985-2001; the vast majority of cases (15/16; 94%) arose in clinical microbiologists manipulating isolates without respiratory protection (14). The increased rates of laboratory-acquired meningococcal disease—as well as other infectious diseases—have been reported by multiple other authors as well (15-

19). Within the US it is estimated that the incidence of meningococcal disease among microbiologists is 50-fold higher than in the general population, i.e., 13 per 100 000 persons versus a general incidence rate of 0.2 per 100 000 (14, 15, 20). Due to their increased risk of meningococcal infection, augmented vaccination/boosters are recommended for these special populations.

Other than clinical microbiologists, healthcare personnel are not generally deemed a “high risk” population. Healthcare personnel are broadly defined as individuals providing health care services who:

...have the potential for exposure to patients and/or infectious materials, including body substances, contaminated medical supplies and equipment, contaminated environmental surfaces or contaminated air (20).

Autopsy pathologists and morgue staff would thus be included in this group. It is suspected that the relative rarity of occupationally-acquired meningococcal disease outside of the laboratory setting may be attributable to the widespread utilization of personal protective equipment by healthcare personnel (21). The few cases of secondary transmission of meningococcal disease to healthcare personnel that have been reported invariably entail unprotected exposure (i.e., lack of surgical mask or respirator) during respiratory procedures such as endotracheal intubation, airway suctioning, mouth-to-mouth resuscitation, or oxygen administration to infected patients (21-26). No reports of secondary transmission of meningococcal disease to autopsy pathologists or other morgue staff were found within the reviewed literature nor on additional PubMed searches.

Disease Manifestations

Invasive meningococcal disease typically manifests as meningitis and/or meningococcemia (2, 3, 5). The interval between acquisition of organism and invasive disease is relatively short, with an average incubation period of three to four days (range: two to ten days) (3). In many patients in whom *N. meningitidis* has

penetrated mucosal cells to enter the bloodstream, the organism will subsequently traverse the blood-brain barrier causing bacterial meningitis, which is the most common presentation of invasive meningococcal disease (3). Clinical history suggestive of meningococcal meningitis would include the classic triad of fever, neck stiffness, and headache. Additional disease manifestations such as altered mental status, photophobia, and nausea/vomiting may also be reported. Meningococcal sepsis without meningitis reportedly occurs in a minority (5-20%) of invasive meningococcal disease cases (3). Clinical history suggestive of meningococcal sepsis would include fever, myalgia, hypotension, shock, adrenal hemorrhage, and petechial rash. There is frequently overlap between meningococcal meningitis and meningococcemia: for instance, in a prospective cohort study of 258 adults with meningococcal meningitis, a rash was reported in 64% (27). Other presentations of meningococcal disease are far less common, e.g., pneumonia (5-15% of cases), arthritis (2%), otitis media (1%), and epiglottitis (< 1%) (3). While the overall mortality rate of invasive meningococcal disease is 10-15%, case fatality ratios are notably higher in cases of meningococcemia (up to 40%) and in patients > 65 years of age (23.8%) (3, 5).

Autopsy Biosafety

Because infectivity status is frequently unknown at the time of autopsy, all autopsies should be performed in a facility with adequate air handling systems and by personnel wearing appropriate personal protective equipment (PPE). Minimal PPE includes a surgical cap, impervious surgical gown with full sleeve coverage, shoe covers, mask/respirator, eye protection, and double gloves (**Image 1**) (28-32). *N. meningitidis* is transmitted primarily by means of direct contact with large respiratory droplets from a carrier. Surgical masks are intended to protect the wearer from transmission of infectious droplets to the mucous membranes of the wearer's nose or mouth, and thus are considered adequate droplet protection for healthcare personnel by the CDC and OSHA in cases of meningococcal disease (33). However, surgical masks do not protect against inhalation of aerosolized particles smaller than droplets, and certain medical procedures

are known to generate higher concentrations of smaller infectious airborne particles than would typically arise via coughed/sneezed droplets.

Autopsy is an aerosol-generating procedure by nature: oscillating saws, fluid aspirator hoses, and compression/dissection of lungs may all contribute to generate aerosols (30-34). Given that other aerosol-generating procedures (e.g., endotracheal intubation, airway suctioning) have been associated with meningococcal disease transmission, the CDC and OSHA suggest that utilizing respirators rather than surgical masks may be prudent in known or suspected cases of invasive meningococcal disease (33). Unlike surgical masks, N-95 particulate filter respirator masks are fitted, and contain a filter that is designed to filter 95% of particles that are one micron in diameter (**Image 2**) (30-33). Autopsy personnel who cannot be fitted for a respiratory mask due to facial hair or other fit issues should instead don a powered air-purifying respirator (PAPR) (**Image 3**) (30-33). It has also been established that utilization of a face shield rather than safety glasses can be helpful in further reducing the contamination of respirators by particles (35).

In addition to PPE, air-handling systems for autopsy suites can be key factors in minimizing personnel infectious exposures. It is recommended that autopsy suites have a minimum of 12 air exchanges per hour and be negatively pressurized relative to surrounding office spaces (30-32). Air should be exhausted outside of the facility and away from areas of high pedestrian traffic. Ideally, morgue laminar air flow would travel from clean to progressively less clean areas with downdraft table ventilation to decrease personnel exposure to aerosolized pathogens (30-32).

Vaccination

In general, forensic pathologists should not require meningococcal vaccination, as it is not routinely recommended after the age of 18 (2, 3, 5, 36). Exceptions to this would include pathologists at high risk of contracting meningococcal disease, e.g., functionally/anatomically asplenic, complement component deficient, or who are HIV positive (5, 9, 11, 36). Foren-

Image 1: Recommended personal protective equipment (PPE) includes a surgical cap, impervious surgical gown with full sleeve coverage, shoe covers, respirator mask, full face shield, and double gloves.

sic pathologists or autopsy assistants meeting any of these criteria are advised to receive a booster dose of quadrivalent conjugate meningococcal vaccine (Men-ACWY) every five years (3, 5, 11, 36). The Men-ACWY vaccine provides protection against meningococcal serogroups A, C, W-135 and Y. As it does not provide protection against serogroup B, vaccination with a MenB conjugate vaccine is also advised; the two vaccines may be administered concurrently (9). Also, any pathologist intending to travel to a geographic area in which meningococcal disease is hyperendemic/epidemic is advised to receive a booster dose of Men-ACWY if they have not already done so within the past five years; MenB vaccination is not recommended; however, as meningococcal disease is not typically caused by serogroup B in these regions (5, 9). Current CDC travel health recommendations, including meningococcal epidemic advisories, can be

accessed electronically at: <https://wwwnc.cdc.gov/travel>.

Chemoprophylaxis

Nosocomial transmission of meningococcal disease is uncommon (23, 26, 37). Since 1972, roughly 12 cases of secondary transmission to healthcare workers have been cited in the literature; no face mask/respirator utilization was reported in any of the cases (26). Currently in the US, post-exposure antibiotic prophylaxis is only recommended for healthcare personnel who have:

...intensive, unprotected contact (i.e., without wearing a mask) with infected patients (e.g., intubating, resuscitating, or closely examining the oropharynx of patients) (36).

Image 2: An N-95 respirator mask provides protection against aerosolized infectious particles as well as larger droplets (A). Surgical masks provide infectious droplet protection only (B).

Image 3: A powered-air-purifying respirator (PAPR) is recommended for prosecutors with facial hair prohibiting tight respiratory mask fit.

Similar guidelines have been instituted in the United Kingdom and Australia (38, 39). Thus, in cases of suspected or confirmed invasive meningococcal disease in which autopsy is performed in a facility with adequate air handling systems and by personnel wearing appropriate personal protective equipment, antimicrobial prophylaxis would not be indicated.

Chemoprophylaxis can result in adverse reactions such as anaphylaxis and may cause antibiotic resistance (23, 38, 40-44). In a study of the risk of secondary meningococcal disease in healthcare workers in the United Kingdom, a total of three cases were identified in a 15-year span; all involved personnel who were not wearing surgical masks at the time of exposure. Overall, the relative risk of healthcare personnel has been established to be far lower than that of household contacts; whereas the attack rate among exposed healthcare personnel is 25 times higher than that of the general population, the rate among exposed household contacts is 500-800 times higher (3, 5, 23). It is estimated that if all healthcare workers in contact with patients having meningococcal disease received chemoprophylaxis, approximately 144 000 personnel would need to be treated to prevent a single case (23). The potential antibiotic resistance resulting from such an approach would far outweigh the benefits. Unfortunately, it appears unnecessary chemoprophylaxis may be all too common: in one survey, it was found that while antibiotic prescribing practices of hospital physicians in cases of meningococcal disease were largely in alignment with clinical guidelines, community general practitioners prescribed 118% more chemoprophylaxis than recommended (40). In addition to generating antibiotic resistance, antibiotics may eradicate commensal *Neisseria* species that help protect against colonization by pathogenic meningococci; normally, the incidence of invasive meningococcal disease is reciprocally related to antibody titers and antibodies are induced through the carriage of *Neisseria lactamica* as well as other similar commensal species (1, 38, 42).

In the event that appropriate personal protective equipment (i.e., N-95 respirator mask) is not worn at the time of autopsy of a decedent with invasive meningococcal disease, there may be exposure to infectious

droplet secretions and antibiotic prophylaxis would be advisable. Currently, recommended first-line antibiotic regimens for adults would include either rifampin (600 mg every 12 hours for two days), ciprofloxacin (500 mg single dose), or ceftriaxone (250 mg single intramuscular dose) (2, 3, 5, 36, 45). Both rifampin and ciprofloxacin are contraindicated in pregnancy (2, 5, 46). Ideally, the chemoprophylaxis would be administered within 24 hours of the exposure. If later than 14 days after exposure, antibiotics are unlikely to confer any added benefit (2, 3, 5, 20, 36).

DISCUSSION

Although incidence of invasive meningococcal disease in the US and other industrialized nations is low, epidemic outbreaks continue to occur (1, 3). As the disease progresses rapidly, often affects youth, and has a fairly high mortality rate, such cases are likely to fall under ME/C jurisdiction. Invasive meningococcal disease is transmitted by direct contact with oral secretions (e.g., kissing, mouth-to-mouth resuscitation) or direct exposure to infectious droplets (1-3). *Neisseria meningitidis* bacteria require a human host and cannot remain viable long in droplet form; the radius limit for large droplet spread is approximately 1 meter (3 feet) (1, 3, 38). While a surgical mask would normally be considered sufficient protection from large droplet spread, it does not prevent inhalation of smaller aerosolized particles such as those generated at autopsy (30-34). Prosectors are thus advised to wear N-95 respirator masks or PAPRs at autopsy in cases in which invasive meningococcal disease is suspected/confirmed (33). Given that it may not be known prior to autopsy whether there is a potentially aerosolized infectious disease or not, prosectors are encouraged to consider utilizing fitted N-95 respirator masks rather than surgical masks as a general practice (30, 31). The cost of disposable N-95 respirator masks vs. surgical masks is negligible while the aerosol-transmitted diseases against which surgical masks are deemed inadequate protection are myriad including *Mycobacterium tuberculosis*, measles, varicella (chickenpox), disseminated herpes zoster, severe acute respiratory syndrome (SARS), monkeypox, smallpox, and aerosolizable spore-containing powders (e.g., anthrax)

(33). Additionally, when engaged in an aerosolizing procedure such as autopsy, diseases that would normally require standard droplet precautions (i.e., a surgical mask) now instead require aerosol precautions (i.e., a respirator mask) (33).

In cases of invasive meningococcal disease at autopsy, PPE including N-95 respirator masks provides adequate protection for prosectors and no subsequent chemoprophylaxis is necessary. As chemoprophylaxis can result in adverse drug reactions, increased antibiotic resistance, and eradication of nonpathogenic *Neisseria* species that provide cross-reactive immunity, it should be utilized only when necessary (23, 38, 40-44). In cases in which no mask—or inadequate coverage such as a surgical mask—was employed at autopsy, chemoprophylaxis is advised due to the potential for large droplet or aerosol particle inhalation and subsequent infection. Rifampin, ciprofloxacin, or ceftriaxone are currently considered first-line therapies for meningococcal prophylaxis (2, 3, 5, 36, 45). Ideally, antibiotic prophylaxis should be initiated within 24 hours of exposure to be most efficacious (2, 3, 5, 20, 36). In the event that a patient has been given intravenous antibiotics 24 hours prior to death, infectivity is likely to be minimal thereafter (38). In general, morgue personnel are not considered to be a population at high-risk of acquiring secondary meningococcal disease. In the preceding 20 years, there have been no published cases of invasive meningococcal disease transmission to ME/C or other morgue staff. Accordingly, meningococcal vaccination is not recommended for forensic pathologists unless they are HIV positive, functionally/anatomically asplenic, deficient in complement components, or are planning travel to a hyperendemic/endemic meningococcal disease region (5, 9, 11, 36). Meningococcal disease is a nationally notifiable condition: medical examiners/coroners should immediately report suspected cases to the local health authority (21).

CONCLUSION

At autopsy, prosectors may be exposed to a wide array of infectious agents including *Neisseria meningitidis*. The risks of secondary transmission of disease can

be minimized, however, by adoption of appropriate pre- and post-exposure preventative measures. These would include vaccination of those with immunocompromising conditions placing them at high risk for invasive meningococcal disease, appropriate autopsy facility design with adequate air exchange/flow, regular utilization of personal protective equipment including an N-95 respirator mask, and chemoprophylaxis in the event appropriate PPE is not worn or malfunctions at autopsy (**Table 1**).

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Table 1: Recommendations for Prevention of Meningococcal Disease at Autopsy

Chemoprophylaxis	1.	If full PPE (including an N-95 respirator mask or PAPR) is employed at autopsy in cases of suspected/confirmed invasive meningococcal disease, no chemoprophylaxis is indicated.
	2.	If no mask (or inadequate protection such as a surgical mask) is employed at autopsy in cases of suspected/confirmed invasive meningococcal disease, prompt chemoprophylaxis is recommended.
	3.	Current first-line chemoprophylaxis regimens are rifampin (600 mg every 12 hrs for two days), ciprofloxacin (500 mg single dose), or ceftriaxone (250 mg single intramuscular dose).
Vaccination	1.	Routine meningococcal vaccination is not recommended unless immunocompromised (i.e., HIV positive, functionally/anatomically asplenic, complement component deficient) or traveling to an area in which meningococcal disease is endemic.
	2.	Pathologists who are immunocompromised as defined above should receive booster doses of Men-ACWY quadrivalent conjugate vaccine every five years + MenB conjugate vaccine.
	3.	If travelling to a geographic area in which meningococcal disease is endemic, a booster dose of Men-ACWY quadrivalent conjugate vaccine is recommended if it has been greater than five years since last vaccination.
Facility Design	1.	It is recommended that autopsy suites have a minimum of 12 air exchanges per hour and be negatively pressure relative to surrounding office space.
	2.	Air should be exhausted outside of the facility and away from areas of high pedestrian traffic.
	3.	Downdraft table ventilation is recommended to decrease exposure to aerosolized pathogens.

PPE - Personal protective equipment

PAPR - Powered air purifying respirator

HIV - Human immunodeficiency virus

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