

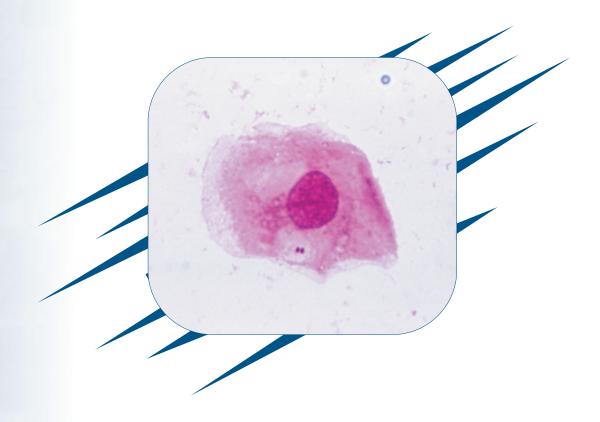
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# **Supplement**

# Guidelines for the Prevention and Control of Meningococcal Disease



# Guidelines for the Prevention and Control of Meningococcal Disease

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#### 1.0 Introduction

Guidelines for the control of meningococcal disease were last published in 1994, following a 1993 Canadian Consensus Conference on Meningococcal Disease<sup>(1)</sup>. Since that time, meningococcal C conjugate vaccines have been licensed. These revised guidelines provide updated case definitions and public health control measures, taking into account new advances in diagnostic and vaccine technology.

#### 2.0 Objectives

These guidelines have been prepared to assist in the public health investigation and management of sporadic cases, outbreaks and persistently elevated rates of invasive meningococcal disease (IMD) in Canada. The guidelines address the following:

- surveillance and reporting;
- public health response to sporadic cases, including those aboard airplanes;
- . chemoprophylaxis and immunoprophylaxis of close contacts;
- outbreak control;
- . communication strategies.

#### 3.0 Epidemiology of Invasive Meningococcal Disease in Canada

Updates on the epidemiology of IMD are published periodically in the Canada Communicable Disease Report (CCDR) and in the National Advisory Committee on Immunization (NACI) meningococcal vaccine statements. The most recent report was published in February 2004<sup>(2)</sup>. Readers are referred to these reports for more detailed information.

Meningococcal disease is endemic in Canada, periods of increased activity occurring roughly every 10 to 15 years with no consistent pattern. The incidence rate of meningococcal disease has varied considerably with different serogroups, age groups, geographic locations and time. The last major epidemic, due to serogroup A, occurred in 1940-1943, when the peak incidence rate was close to 13 per 100,000 population per year. Since then the overall incidence of disease has remained at or below 2 per 100,000 per year (range 0.5 to 2.1) (2-5). There were sporadic localized outbreaks and periods of elevated incidence of serogroup C disease during 1989-1993 and 1999-2001 (2.3). Immunization campaigns using serogroup C polysaccharide and conjugate vaccines were implemented in some regions during that period.

Case-by-case data for IMD in Canada are available from 1985 to 2001. During this period, an average of 305 cases of meningococcal disease were reported annually. Overall, the incidence rate has been highest among children  $\pounds$  1 year of age, and then it declines as age increases except for a smaller peak in the 15-to 19-year age group. Disease occurs year round, but there is seasonal variation with the majority of cases occurring in the winter months.

Of the small numbers of isolates characterized from 1971 to 1974, *Neisseria meningitidis* serogroups A and C were most frequently identified<sup>(6)</sup>. From 1975 to 1989, serogroup B predominated. The majority were serotype 2b, 4 and 15, and the most common subtype was  $P1.2^{(7)}$ . In 1986, a new clone of serogroup

C, serotype 2a characterized by multilocus enzyme electrophoresis (MLEE) as electrophoretic type 15 (ET-15), was identified in Canada for the first time <sup>(7)</sup>. Since then serogroups B and C have been responsible for most of the cases of endemic disease in Canada. Serogroup C isolates have almost exclusively been responsible for outbreaks in schools and communities. In addition, IMD caused by serogroup C has had a higher case fatality ratio and a greater incidence among adolescents than disease caused by serogroup B.

#### 4.0 Definitions

#### 4.1 National Case Definition

Table 1

Confirmed Case	Invasive disease <sup>1</sup> with laboratory confirmation of infection:	
	! isolation of <i>N. meningitidis</i> from a normally sterile site (blood, cerebrospinal fluid [CSF], joint, pleural or pericardial fluid); OR	
	! demonstration of <i>N. meningitidis</i> DNA by appropriately validated nucleic acid test (NAT) <sup>2</sup> from a normally sterile site.	
Probable Case	Invasive disease <sup>1</sup> with purpura fulminans or petechiae and no other apparent cause:  ! with demonstration of <i>N. meningitidis</i> antigen in the CSF; OR  ! in the absence of isolation of <i>N. meningitidis</i> or demonstration of DNA by approately validated NAT <sup>2</sup> from a normally sterile site.	

Invasive meningococcal disease usually manifests itself as meningitis and/or septicemia, although other manifestations may be observed (e.g. orbital cellulitis, septic arthritis). Invasive disease may progress rapidly to purpura fulminans, shock and death.

Both confirmed and probable cases of IMD are notifiable at the national level. The national case definition underwent revision in 2005. The new case definition will become effective 1 January, 2006 and now includes demonstration of *N. meningitidis* DNA by appropriately validated nucleic acid test (NAT) from a normally sterile site. Meningococcal DNA can be found in the CSF up to 96 hours after antibiotics have been started<sup>(8)</sup>.

#### 4.2 Definitions for Public Health Management

For the public health management of sporadic cases, outbreaks and persistently elevated rates of disease, the following definitions have been developed.

#### 4.2.1 Cases and Contacts

Tables 2 and 3 provide definitions of cases and close contacts.

**Table 2: Description of Cases** 

Sporadic Case	A single case occurring in a community where there is no evidence of an epidemiologic link (by person, place or time) to another case.	
Index Case The first case occurring in a community.		

<sup>&</sup>lt;sup>2</sup>Each jurisdiction will have a validation process for the NAT that they have in place.

	A case with onset of illness subsequent to another case with whom an epidemiologic link can be established. This category includes <b>co-primary cases</b> (a person who develops illness within 24 hours of onset of illness in the index case), as well as <b>secondary cases</b> (a person developing illness > 24 hours after onset of illness in the index case).
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An epidemiologic link can be established when a person has one or both of the following in common with a confirmed case:

- contact with a common, specific individual (including confirmed or probable cases),
- presence in the same location (e.g. work, school, a bar or party) at or around the same time.

#### **Table 3: Definition of Close Contacts**

- ! Household contacts of a case
- ! Persons who share sleeping arrangements with the case
- ! Persons who have direct contamination of their nose or mouth with the oral/nasal secretions of a case (e.g. kissing on the mouth, shared cigarettes, shared drinking bottles)
- ! Health care workers (HCWs) who have had intensive unprotected contact (without wearing a mask) with infected patients (e.g. intubating, resuscitating or closely examining the oropharynx)
- ! Children and staff in child care and nursery school facilities
- ! Airline passengers sitting immediately on either side of the case (but not across the aisle) when the total time spent aboard the aircraft was at least 8 hours (see section 7.1.4)

For public health management, cases that occur after the index case with which an epidemiologic link can be established may have acquired the disease directly from the index case or from another common source. Subsequent cases can be early, intermediate or late. Subsequent cases that occur early (within 24 hours), termed co-primary cases, most likely acquired the disease from a common source. Conversely, subsequent cases that occur after 24 hours, or secondary cases, may have acquired the disease in either fashion.

The likelihood of person-to-person transmission of meningococcal disease is related to both the nature and duration of the contact with a confirmed case. Studies carried out before the routine use of chemoprophylaxis have revealed that people who lived in the same household as an IMD case were at 500 to 1200 fold greater risk of IMD than the general population<sup>(9,10)</sup>. The risk is highest in the first week after onset of illness in a case and decreases thereafter<sup>(9,11)</sup>. Studies of transmission of IMD in child care facilities and nursery schools have been conflicting but suggest that there is an increased risk of secondary cases, although the risk is lower than in the household setting<sup>(9,12)</sup>. Increased risk of IMD has not been shown in casual contacts of sporadic cases<sup>(13-16)</sup>. Therefore school/classroom, transportation, workplace or social contacts are not considered as close contacts unless their specific relationship with the case identifies them as such (see Table 3).

Nosocomial transmission of IMD is very uncommon, especially when routine practices and (large) droplet and contact precautions are followed to prevent the transmission of IMD. In rare instances, direct contact with respiratory secretions of infected persons (e.g. during mouth-to-mouth resuscitation) has resulted in transmission to HCWs. A pediatrician in France developed IMD a week after intubating a comatose child with meningococcal disease (17,18). Therefore, HCWs are considered as close contacts if they have had intensive, unprotected contact (without wearing a mask) with infected patients (e.g. intubating, resuscitating or closely examining the oropharynx) (19).

In certain countries, such as Canada, where chemoprophylaxis of close contacts is routinely administered for sporadic cases, 0.3% to 3% of cases of meningococcal disease occur in contacts of the index case<sup>(10,11,20,21)</sup>, with a median interval between the index and the secondary case of 7 weeks in one study<sup>(11)</sup>. Some of these secondary cases can be attributed to failure of chemoprophylaxis (e.g. failure of administration, poor compliance, presence of antibiotic resistance)<sup>(20,22,24)</sup>. "Late" secondary cases in close contacts may occur several months after the onset of symptoms in the index case<sup>(11,12)</sup>.

#### 4.2.2 Outbreaks

An outbreak is defined as increased transmission of *N. meningitidis* in a population, manifested by an increase in cases of the same serogroup.

Outbreaks can be subdivided into organization-based or community-based outbreaks using the criteria shown in Table 4.

**Table 4: Types of Outbreak** 

Organization- based	Increased transmission of <i>N. meningitidis</i> in an organization or institution with two or more cases of the same serogroup occurring within a 4-week interval. This includes restricted populations, such as schools, day care, sports groups or social groups, as well as nursing homes or long-term care facilities.	
Community-based	Increased transmission of <i>N. meningitidis</i> in a community, with three or more confirmed cases of the same serogroup occurring within a 3-month interval AND an age-specific incidence OR specific community population incidence of approximately 10/100,000, where there is an absence of an epidemiologic link between cases. This is not an absolute threshold and should be considered in the context of other factors (see section 7.2).	

When threshold incidence rates are being calculated in order to establish whether continued transmission of *N. meningitidis* is occurring in a community, the calculation should be specific to the situation. If the cases are occurring among persons of a specific age range, the calculation should be an age-specific incidence. However, if the population is defined geographically, the calculation should use the total community population defined by that region. For the calculations, subsequent cases among close contacts should be excluded from the numerator. Age-specific incidence should be calculated for 5-year age groups (e.g. 0 to 4 year olds, 5 to 9 year olds, 10 to 14 year olds). For example, in a community with 10 cases, of which 2 live in the same household, only 9 cases are included when calculating age-specific incidence rates for the purpose of determining whether an outbreak or ongoing transmission is occurring.

#### 4.2.3. Persistently Elevated Rates

Persistently elevated rates of disease are observed when there is ongoing occurrence of cases of meningococcal disease of the same serogroup at rates above the expected level of disease in a given population. These cases can be sporadic or outbreak-related and continue to occur despite local public health control measures.

#### 5.0 Diagnosis and Bacterial Typing

Laboratory confirmation of a clinical diagnosis of IMD is important for the identification and management of cases and outbreaks, as well as for regional and national surveillance and detection of

epidemiologic trends over time. Meningococcal isolates from all IMD cases should routinely be sent to the provincial/territorial laboratory to ensure appropriate and timely monitoring of serogroups and for antibiotic susceptibility testing. Isolates are forwarded to the Public Health Agency of Canada's National Microbiology Laboratory (NML) for further phenotypic typing and genetic analysis.

Culture of blood, cerebrospinal fluid (in the absence of contraindications to lumbar puncture) and other normally sterile sites is required for isolating bacteria for identification. Polymerase chain reaction (PCR) testing is available in several centres across Canada for rapid molecular diagnosis of meningococcal infection and serogroup identification on whole blood and cerebrospinal fluid. PCR has greater sensitivity than culture, particularly if there has been prior administration of antibiotics (8.25-27). Latex agglutination antigen testing may be a useful adjunct.

Several laboratory methods are used to track the epidemiology of *N. meningitidis* in Canada. The serogroup, serotype and serosubtype of the organism can be determined using antibody or by DNA sequencing of the responsible genes. Antigenic variation in proteins located in the outer membrane of the organism can be detected. For example, an isolate of *N. meningitidis* C:2a:P1.2 is of serogroup C, serotype 2a and serosubtype P1.2.

In addition, genotyping procedures can be done, such as multilocus enzyme electrophoresis (MLEE), multilocus sequence typing (MLST) and pulsed field gel electrophoresis (PFGE). MLEE and MLST are most suitable for studying global molecular epidemiology. PFGE can be useful in discriminating strains of *N. meningitidis* within a population, particularly during a period of increased incidence of disease. Knowledge of PFGE patterns can be most useful for smaller populations in which the incidence of disease may be very high but there are only a few cases, and more discriminatory tests are required to determine whether these are unrelated cases caused by different strains or whether there is increased transmission of a particular strain.

#### 6.0 Surveillance of Invasive Meningococcal Disease in Canada

IMD is reportable in all provinces and territories and is nationally notifiable. Each province or territory has procedures in place for the rapid notification of cases to medical officers of health and timely reporting to the appropriate provincial or territorial public health official.

Both confirmed and probable cases of IMD are notifiable at the national level. Provinces and territories report case-by-case data with basic core variables on a weekly basis to the Notifiable Diseases Reporting System. In addition, the Immunization and Respiratory Infections Division (IRID), Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, conducts enhanced surveillance for IMD. Provinces and territories report more detailed epidemiologic and laboratory data for each case to the IRID. Detailed surveillance reports are published periodically in the *CCDR*; the most recent report was published in February 2004<sup>(2)</sup>.

Most jurisdictions rely on passive surveillance for identification of cases. When an increase in the incidence of IMD is suspected in a particular region, there should be heightened surveillance for cases and the collection of more detailed epidemiologic and microbiologic information.

The following steps should be taken:

- The provincial or territorial epidemiologist or medical health officer should be consulted immediately to decide whether the increased incidence constitutes an outbreak.
- Active surveillance should be initiated. Epidemiologic information should be obtained on each case, with the objective of identifying high-risk groups and determining associations that will permit targeted control interventions. The data collected should include age; sex; place of residence; vaccination status, including the type of meningococcal vaccine, the number of doses and age at vaccine administration; recent travel; attendance or employment at a day care centre or school; and participation in recent athletic or recreational events and gatherings. Other information relevant to the outbreak should also be collected (e.g. social or cultural setting).
- . Basic epidemiologic analysis should include age-group-specific attack rates (calculated for 5-year age groups), serogroup-specific rates and case fatality ratios. Techniques such as historical modeling can be used to determine whether the current incidence is greater than in previous years; this is particularly important in light of the seasonality of the disease.
- The province or territory should notify the IRID of the increase in IMD incidence, and the IRID will relay the information to the other provinces and territories.
- When an outbreak is suspected, serogroup determination becomes critical for appropriate decisions regarding control measures. Provincial and territorial public health laboratories, in collaboration with the NML, may conduct typing, subtyping and other genotyping tests (e.g. PFGE) that have proven helpful in characterizing outbreaks and determining disease trends.
- During outbreaks or whenever there is failure to isolate or determine the serogroup of an organism, clinical specimens should immediately be forwarded by the provincial laboratory to the NML, Public Health Agency of Canada, for molecular diagnostic testing and further strain identification.

At this time conjunctivitis and pneumonia cases due to N. meningitidis are not nationally notifiable and reported to the Public Health Agency of Canada. However the following definitions and suggested treatments have been made. A conjunctivitis case requires isolation of N. meningitidis from the eye or the conjunctival sac in association with purulent conjunctivitis. A pneumonia case is one with a Gram strain (if done) showing Gram-negative diplococci and a polymorphonuclear cell response from sputum or respiratory aspirate, isolation with heavy growth of N. meningitidis and clinical or radiological evidence of pneumonia. Patients with N. meningitidis conjunctivitis or pneumonia should be treated with appropriate systemic antibiotics<sup>(28)</sup>.

#### 7.0 Management of Invasive Meningococcal Disease

The management of cases of IMD is divided into two sections, the management of sporadic cases and the management of outbreaks.

#### 7.1 Management of Sporadic Cases

The public health response to a sporadic case of IMD includes management of the sporadic case, contact identification and tracing, and maintenance of surveillance for further cases.

#### 7.1.1 Case Management

When there is a strong clinical suspicion of IMD and laboratory confirmation of the diagnosis may be delayed, a specimen from a normally sterile site should be obtained for culture (or other laboratory identification of *N. meningitidis*) if possible and empiric therapy started quickly. The case or a proxy for the case should be interviewed to determine who are the close contacts (see Table 3). In addition to therapeutic antibiotics, the case should receive chemoprophylaxis before hospital discharge unless the infection was treated with an antibiotic that is effective in nasopharyngeal eradication of *N. meningitidis* (25). Nasopharyngeal cultures, used to demonstrate carriage of *N. meningitidis*, have no role in the identification or management of cases and contacts.

#### 7.1.2 Contact Management

The cornerstone of prevention of secondary cases of IMD is aggressive contact tracing to identify people at increased risk of disease (i.e. close contacts). The management of close contacts of cases with conjunctivitis or pneumonia is the same as for close contacts of invasive disease. Chemoprophylaxis should be provided to close contacts in order to eliminate meningococci from any carrier within the network of close contacts, thereby reducing the risk to other susceptible individuals in the social network (see Section 10.0 Recommendations for Chemoprophylaxis) (30). Nasopharyngeal carriage of meningococci is common: at any given time about 10% of the population carry meningococci. The rationale for providing chemoprophylaxis for HCWs who are close contacts (see Table 3) is different from that for other close contacts. The time of exposure can be clearly identified. Antibiotics that eliminate carriage given soon after that exposure would be expected to eliminate carriage and prevent potential development of disease in treated individuals. Currently, no studies have assessed the effectiveness of chemoprophylaxis in this situation (31).

Close contacts of an IMD case are at increased risk of secondary disease <sup>(9-11)</sup>. They should be alerted to signs and symptoms of meningococcal disease and be advised to seek medical attention immediately should they develop febrile illness or any other clinical manifestations of IMD. Chemoprophylaxis should be offered to all persons having close contact with an IMD case during the infectious period (the 7 days before onset of symptoms in the case to 24 hours after onset of effective treatment), regardless of their immunization status (see section 10.0 Recommendations for Chemoprophylaxis). Chemoprophylaxis of close contacts should be administered as soon as possible and preferably within 24 hours of case identification but is still recommended for up to 10 days (the incubation period) after the last contact with an infectious case. Chemoprophylaxis should be considered for close contacts of a case that is strongly suspected to be IMD, even if laboratory confirmation cannot be obtained within 24 hours.

The vaccination status of close contacts, including the type of meningococcal vaccine, the number of doses and age at vaccine administration, should be determined. Vaccination of susceptible close contacts, in addition to chemoprophylaxis, should be considered when the serogroup is vaccine preventable, as it may further reduce the risk of subsequent meningococcal disease; vaccination should be carried out as soon as possible (see section 11: Indications For and Use of Meningococcal Vaccines). The increased risk of disease for household contacts persists for up to 1 year after disease in the index case and beyond any protection from antibiotic chemoprophylaxis (10,11,20,21).

In the United Kingdom (UK) it is recommended that close contacts of cases with vaccine-preventable strains of *N. meningitidis* who received chemoprophylaxis should be offered an appropriate vaccine (32). However, in the UK a different definition of "close contacts" is used than in Canada. The National

Advisory Committee on Immunization (NACI) recommends that vaccination of unimmunized household and intimate social contacts may further reduce the risk of secondary cases beyond the benefit of chemoprophylaxis $^{(33)}$ .

#### 7.1.3 Cadavers and Infectious Risk

While cadavers with meningococcal disease have traditionally been considered a possible source of infection risk, if the deceased person had been treated with an effective antibiotic for at least 24 hours before death, any risk is likely to be very low. If the deceased had not been treated with an effective antibiotic before death, then it is prudent for those who have occupational contact with a cadaver to follow routine infection control practices with additional droplet and contact precautions (30,34,35).

In general, when caring for the deceased, attention to routine infection prevention and control practices is sufficient, specifically, adherence to the routine infection control practices for hand washing/hand hygiene, mask/eye protection/face shields, glove and gown use. In addition, individuals who die in a home setting should be wrapped in a sheet (ideally using a plastic bag to protect the mattress and contain body fluids) and preferably kept in a cool, dry location until collected by funeral services<sup>(35)</sup>.

#### 7.1.4 Invasive Meningococcal Disease in Travellers

When an IMD case has been identified in a traveller who was within the infectious period during the journey, a decision on the need for contact tracing and chemoprophylaxis should be based on the mode of transportation, the length of time fellow travellers could have been exposed to the case and the type of exposure. Any decision should be made in collaboration with the provincial or territorial epidemiologist or medical health officer.

To date, there have been no published cases of IMD resulting from transmission aboard aircraft. However, there have been reports of transmission of tuberculosis during air travel<sup>(36,37)</sup>. Current surveillance systems may not detect secondary cases resulting specifically from air travel. Therefore the theoretical risk of transmission during air travel should be considered. Contact tracing of specified passengers is advised by the Centers for Disease Control and Prevention in the United States and by the Communicable Diseases Network Australia<sup>(30,36)</sup>. However, prophylaxis of persons travelling in the next seat on the same plane is not advised in the United Kingdom, unless the individual is already identified as a close contact<sup>(32)</sup>.

On the basis of expert opinion and the extrapolation of data on secondary transmission of tuberculosis cases aboard aircrafts, it is recommended that contact tracing be initiated if

- the case travelled during the infectious period (7 days before onset of symptoms to 24 hours after the onset of effective treatment)
- the flight occurred within the previous 10 days (i.e. still eligible for prophylaxis)

#### **AND**

the total time spent aboard the aircraft was at least 8 hours, including ground time on the tarmac.

It is important to note that aircraft passenger manifests are rarely kept after 48 hours, and contact tracing may be more difficult after that time.

An attempt should be made to trace, contact and offer antimicrobial chemoprophylaxis and vaccination, if appropriate, to the following:

- persons travelling with the index case who have had prolonged close contact (e.g. room-mates);
- passengers who were sitting immediately on either side of the index case (but not across the aisle);
- passengers or flight staff who have had direct contact with the respiratory secretions of the index case.

These individuals may be at increased risk, as bacteria transmitted through respiratory droplets can be propelled short distances (< 1 m) during coughing and sneezing<sup>(35)</sup>.

#### 7.2 Detection and Management of Outbreaks

Outbreaks can be broadly classified as organization-based or community-based (see Table 4). Regardless of the type of outbreak, contract tracing, identification of close contacts and provision of chemoprophylaxis to close contacts need to be conducted as described for sporadic cases (see section 7.1). There is no evidence to support the provision of widespread chemoprophylaxis for persons who are not close contacts. Widespread use may result in eradication of benign strains of *Neisseria* that provide protective antibodies, the generation of drug-resistant strains and an increase in the prevalence of drug-related adverse events<sup>(38)</sup>.

Outbreak detection and management require complex decision-making that takes into account a variety of factors. When evidence suggests that an outbreak is occurring with increased transmission of *N. meningitidis* involving a vaccine-preventable serogroup in a delineated population, vaccination of persons at high risk should be considered. The type of association between cases helps to define the group at risk. Decisions regarding the use of vaccine in communities with a higher than expected rate of disease should be made in consultation with the provincial or territorial epidemiologist or medical health officer.

The following considerations can be useful in determining whether there is increased transmission of *N. meningitidis* within a defined population:

- . An increased rate of disease, as outlined in Table 4.
- In smaller populations, the clustering of disease in an age group. In large populations, one may see a shift in age distribution during an outbreak.
- . The same serogroup occurring in the cases. For IMD caused by serogroup B and C, the likelihood that two strains are related increases as one goes from common serogroup, to common serotype to common electrophoretic type. A discussion with a medical microbiologist or laboratory expert is required to ascertain the degree of relatedness.

The criteria for vaccination should be sufficiently broad to control the outbreak. Ongoing surveillance to assess the effectiveness of outbreak control is essential and may result in changes to the target group for which vaccination is recommended.

The presence of a particular vaccine-preventable serogroup is the most important laboratory characterization in evaluating the need for immunoprophylaxis (i.e. serogroup C, W135, Y or A). The following additional factors should be taken into account when considering a vaccination campaign:

- The population at risk of the disease must be clearly defined. Identification of target groups and boundaries for vaccination programs (e.g. age, place of residence or activity) may be determined on the basis of the characteristics of the community and the epidemiologic features of the cases.
- The risk of disease must be sufficiently high to justify implementing a vaccination campaign (statistical modeling techniques may be helpful).
- The most appropriate available vaccine should be used for the population at risk (refer to section 11.0).
- . Mechanisms for sufficient vaccine acquisition and delivery must be in place.
- . For optimal outbreak control, vaccine program planning should aim to achieve high coverage rates in target groups (39).
- Environmental factors that might increase a population's susceptibility (e.g. influenza epidemic) should be considered.

#### 7.3 Management of a Persistently Elevated Rate of Meningococcal Disease

Effective local management of cases and identified outbreaks remains the cornerstone of prevention and control of IMD. Consideration of a systematic regional or provincial/territorial vaccination strategy may be needed if there are unacceptably high projected rates of disease and mortality despite ongoing regional outbreak interventions.

Outbreak management is usually carried out as an emergency measure and results in disruption of routines, a higher cost of vaccine delivery, overuse of chemoprophylaxis and the sudden demand for large quantities of vaccine. If a large proportion of the population is vaccinated because of the occurrence of multiple localized outbreaks and disease is still occurring, the decision to extend vaccination to the remainder of the population at risk may be considered.

Although general recommendations for systematic regional and provincial/territorial vaccination cannot be made, consideration may be given to this strategy in the circumstances outlined above. All levels of public health jurisdictions should ensure that they have specific contingency plans for mass vaccination. A decision of this nature must take into account public concern and political realities but cannot be based solely on these factors.

The effectiveness of outbreak control measures should be evaluated in order to ascertain whether continued occurrence of cases after a mass vaccination campaign is due to vaccine failure, poor immunization coverage, inadequate definition of the target population or other reasons.

#### 8.0 Communication Strategies

#### 8.1 Communication Pertaining to Sporadic Cases

There is usually no need to inform the general public of a sporadic case, even if it involves a fatality. However, it is important that a communication strategy be prepared in advance in order to address any questions that may arise among those concerned with the control measures. Details of the communication strategy need to be tailored to the context of the sporadic case (e.g. liaison with school authorities is important when a case is a student).

#### 8.2 Communication Pertaining to Outbreaks

It is essential that a communication strategy be in place to provide timely information to the public when an outbreak occurs. A communication strategy aimed at the health care community should also be developed. This should include the criteria and the process for reporting to public health, timely surveillance reports and updates, guidelines on early diagnosis (including signs and symptoms), and recommended treatment and prophylactic measures. It is important to involve the health care community as early as possible after the recognition of an outbreak. An outbreak advisory committee comprising public health representatives, clinicians and medical laboratory personnel should be established. It is particularly important that the adjacent local, provincial and/or territorial jurisdictions be informed about the outbreak and related control strategies. The IRID of the Public Health Agency of Canada should be informed of all outbreaks and is responsible for informing other Canadian and international public health authorities.

#### 8.3 Communication Pertaining to Persistently Elevated Rates

It is essential that a communication strategy be prepared before a decision is made to undertake a program of systematic vaccination. This should be designed and managed with input from a communications expert. In addition to the principles previously described, essential elements of a communication strategy include the following:

- Wide consultation with public health representatives, clinicians and laboratory personnel before any decision is made.
- . Clearly designated responsibilities. Public health authorities should be responsible for the announcement of the decision and the management of communications with respect to the operation of a control program.
- Within each organization, one spokesperson should be responsible for communicating with the media.

#### 9.0 Recommendations for Travellers

#### 9.1 Travellers to Destinations Within Canada

Under most circumstances, Canadians travelling within Canada do not need to take special precautions to protect themselves from meningococcal disease. The risk of acquiring IMD as a traveller in North America is low, even in areas with higher than usual rates of disease. Therefore, preventive measures, including the use of vaccine, are not warranted.

Special circumstances under which a Canadian travelling within Canada should consider vaccination include the following:

- the individual is travelling to an area where there is an outbreak for which an immunization program is in progress AND
- . the individual travelling is of an age that falls within the population targeted for immunization by the local health authorities AND
- the individual's duration of stay in the outbreak area is for an extended period of time (e.g. attendance for a school term).

These persons are more likely to interact with the population at increased risk of transmission (the population targeted for immunization). The decision to recommend vaccination for travellers within Canada who meet these criteria should be based on individual risk assessment. The nature of the travel and the type of contact with the population at risk are important factors to consider (e.g. a child staying in a hotel has a different risk from a teenager attending parties). The traveller should be appropriately counselled on the risk-benefit in order to make an informed decision. In most circumstances, immunization upon arrival at the outbreak or hyperendemic area is sufficient, but consideration could be given to immunization before arrival.

#### 9.2 Students Attending Colleges in the United States

The Advisory Committee on Immunization Practices in the United States (US) has recommended that all US college students should be informed of the risk of meningococcal disease and the availability of a vaccine, so that they are able to make informed individual decisions regarding vaccination against serogroup C meningococcal disease (40). These recommendations were made in light of outbreaks that have occurred in US colleges. No such outbreaks have occurred in Canada. Canadian students who will be attending college in the US should inform themselves of the policies of the institution that they will be attending, as they may be required to provide proof of serogroup C immunization before starting their studies. NACI recommends that all Canadian adolescents and young adults be immunized with meningococcal C conjugate vaccine (33). As students attending colleges and universities are included in this recommendation by virtue of their age, there is no need to make special recommendations for this group of people.

#### 9.3 Travellers to International Destinations

International travellers should be aware of the risk of IMD at their destination of choice. IMD occurs sporadically worldwide and in focal epidemics. The traditional endemic or hyperendemic areas of the world (the "meningitis belt") include the savannah areas of sub-Saharan Africa extending from Gambia and Senegal in the west to Ethiopia and Western Eritrea in the east. Health care professionals advising Canadian travellers should remain current with global meningococcal activity. Current meningococcal outbreak information can be obtained through the Public Health Agency of Canada, Travel Medicine Program (<www.travelhealth.gc.ca>) and the World Health Organization (WHO) (<a href="http://www.who.int/csr/don/archive/disease/meningococcal\_disease/en/>).">http://www.who.int/csr/don/archive/disease/meningococcal\_disease/en/>).</a>

Quadrivalent meningococcal vaccine is recommended for Canadian international travellers requiring meningococcal vaccine. Meningococcal C conjugate vaccine alone is not appropriate for protection of travellers, as it does not protect against serogroups A or W135, which are endemic in selected regions of the world. The Committee to Advise on Tropical Medicine and Travel (CATMAT) provides guidelines for health care providers counselling Canadian international travellers on meningitis vaccination. For complete information on CATMAT's Statement on Meningococcal Vaccination for Travellers visit <a href="https://www.catmat.gc.ca">www.catmat.gc.ca</a>.

#### 9.4 International Travellers Arriving in Canada

Under the authority of the *Quarantine Act*, international travellers arriving in Canada who are ill and assessed as possibly having IMD will be referred for medical examination at local health facilities. Information about these travellers will be transferred to appropriate public health authorities.

#### 10.0 Recommendations for Chemoprophylaxis

The purpose of chemoprophylaxis is to eradicate nasopharyngeal colonization by *N. meningitidis* and thus prevent disease in contacts and transmission to susceptible persons<sup>(30,31,41)</sup>. In addition, levels of chemotherapeutic agents in nasal secretions may prevent acquisition of the organism for a few days<sup>(31)</sup>. Chemoprophylaxis is not effective in preventing disease once invasion of tissue has taken place. Internationally, there are no uniform recommendations regarding chemoprophylaxis. Most jurisdictions recommend chemoprophylaxis for household contacts, but jurisdictions vary with respect to their recommendations for other types of close contacts and for the index case<sup>(29)</sup>. A recent systematic review of evidence for control policies for IMD determined that the evidence supports the use of chemoprophylaxis for household contacts and for index cases. However, there were insufficient studies to examine evidence for chemoprophylaxis in child care settings<sup>(29)</sup>. Further studies are needed.

On the basis of the available evidence and expert opinion, it is recommended that cases and all close contacts (Table 3) should receive chemoprophylaxis. The index case should receive antibiotics that eradicate nasopharyngeal carriage before discharge from hospital, unless treated with an agent that also effects nasopharyngeal eradication of N. meningitidis (e.g. ceftriaxone), as therapy alone may not eliminate carriage of the organism  $^{(29,42)}$ .

Chemoprophylaxis is not routinely recommended for health care contacts, including emergency personnel. Only those health care workers who have had intensive unprotected contact (i.e. without wearing a mask) with infected patients (e.g. intubating, resuscitating or closely examining the oropharynx) require prophylaxis.

Chemoprophylaxis is unlikely to be of benefit if given > 10 days after the most recent exposure to an infectious case. Chemoprophylactic agents should be administered only to close contacts whose most recent exposure to the case was within the period of communicability (see section 7.1). Provincial and territorial public health authorities should ensure that chemoprophylaxis is available free of charge to all close contacts, as defined in Table 3. Its distribution should be facilitated through local public health authorities or, with their agreement, obtained through hospital pharmacies.

The chemoprophylactic agents recommended for the eradication of nasopharyngeal colonization by *N. meningitidis* are rifampin, ciprofloxacin and ceftriaxone (Table 5)<sup>(41,43)</sup>. It is important to ensure that contacts requiring chemoprophylaxis complete the recommended course. Ciprofloxacin can be given in a single oral dose and is an alternative in adults, but it is contraindicated in pregnancy and is not recommended for prepubertal children. Ceftriaxone is the recommended chemoprophylactic agent for pregnant women. A case-control study among young adults in Cairo, Egypt, showed that a single dose of azithromycin (500 mg, given orally) was effective and was comparable to rifampin (600 mg twice a day for 2 days, given orally) in the short-term eradication of *N. meningitidis* from the nasopharynx of carriers. In addition there has been a report of the successful control of an outbreak of serogroup B meningococcal disease among pre-school children using azithromycin after failure of rifampin chemoprophylaxis<sup>(44,45)</sup>. At this time, there is no specific recommendation to use azithromycin routinely for chemoprophylaxis in Canada, but further studies are warranted.

Table 5: Chemoprophylaxis for Close Contacts of IMD Cases

Drug	Dosage	Comments
Ciprofloxacin	Adults 3 18 years of age: 500 mg x 1 dose PO	Contraindicated during pregnancy and lactation. Only approved for persons > 18 years of age. Not recommended for prepubertal children.
Rifampin	Adults: 600 mg PO q12h x 4 doses Children 3 1 month of age: 10mg/kg (maximum 600 mg) per dose PO q12h x 4 doses Infants < 1 month of age: 5mg/kg per dose PO q12h x 4 doses	Contraindicated in pregnancy. Urine and tears may be stained red. Advise against wear of soft contact lenses as they can also be stained. Can reduce effectiveness of oral contraceptives. Advise use of alternative contraceptive measures.
Ceftriaxone	Adults: 250 mg IM x 1 dose Children <12 years: 125 mg IM x 1 dose	Recommended drug for pregnant women. Alternative for persons who cannot tolerate oral medication. Dilute in 1% lidocaine to reduce pain at injection site.

#### 11.0 Indications For and Use of Meningococcal Vaccines

NACI publishes detailed recommendations pertaining to the use of meningococcal vaccines. Readers are referred to these recommendations for more detailed information (33,46). Recommendations are also contained within the most recent edition of the *Canadian Immunization Guide* (47). Recommendations are updated as new information becomes available.

Briefly, there are two different types of meningococcal vaccine currently available in Canada: purified capsular polysaccharide vaccines and protein-polysaccharide conjugate vaccines. Polysaccharide vaccines include bivalent vaccine against serogroups A and C (MenAC-Ps) and quadrivalent vaccine for serogroups A,C, Y and W135 (MenACYW-Ps). Three monovalent meningococcal C conjugate vaccines (MenC-conjugate) are currently available: Menjugate $^{\text{TM}}$  (Chiron Corporation), Neis Vac- $C^{\text{TM}}$  (ID Biomedical Corporation) and Meningitec $^{\text{TM}}$  (Wyeth Pharmaceuticals).

Meningococcal C conjugate vaccines are safe, immunogenic and effective, and can be given to children < 2 years of age. The conjugate vaccine is also expected to confer longer duration of immunity compared with the polysaccharide vaccine. In addition to outbreak control, the Public Health Agency of Canada and NACI recommend routine childhood immunization with meningococcal C conjugate vaccine (33,47).

Polysaccharide vaccines cover three additional serogroups compared with conjugate meningococcal C vaccines (i.e. serogroups A, Y, W135), but they are not immunogenic for children < 2 years of age and have a shorter duration of protection. Polysaccharide vaccines are recommended for outbreak control, for the protection of persons travelling to locations with epidemic disease attributable to vaccine serogroups and for persons who may be at increased risk of meningococcal disease. Polysaccharide vaccines are not recommended for routine childhood immunization (33).

#### 11.1 Close Contacts

Bivalent (A, C) or quadrivalent (A, C, Y, W135) polysaccharide vaccine should be considered for eligible susceptible close contacts of cases with IMD known to be caused by serogroup A; quadrivalent polysaccharide vaccine should be considered for eligible susceptible close contacts of cases of serogroup Y or W135 disease (see section 11.3 for information on revaccination). For susceptible close contacts of known serogroup C disease, meningococcal C conjugate vaccine is preferred because of longer duration of protection and induction of immunologic memory. However, polysaccharide vaccines will provide protection in older children and adults during the 1-year period of increased risk. Polysaccharide vaccines are ineffective against serogroup C disease in children < 2 years of age, and meningococcal C conjugate vaccine should be given to children in that age group. No vaccine is currently available in Canada for contacts of individuals with serogroup B disease.

Vaccination is not generally indicated for contacts of cases of disease in which the serogroup has not been determined. With the increasing use of PCR techniques the sensitivity of diagnosis will improve; serogroup identification should be obtained before immunoprophylaxis where possible. Factors that may assist in decisions regarding whether "empiric" immunization of contacts should be provided include the availability of diagnostic tests, the epidemiologic situation (e.g. there is an outbreak of serogroup Y in the community and the index case is in the at-risk group), and the age and clinical presentation of the case. If a contact has received meningococcal vaccine in the past, decisions regarding revaccination should follow current NACI guidelines (see section 11.3).

#### 11.2 Outbreaks

Outbreaks of serogroup C meningococcal disease in teenagers and adults may be controlled by use of meningococcal C conjugate or polysaccharide vaccines; however, the use of conjugate vaccine may be preferable because of the induction of immunologic memory and prolonged duration of protection (33). In adults and children previously immunized with a polysaccharide vaccine, antibody response has been found to be lower after a second than after the first dose when the time interval between the two doses is less than the recommended 5 years. This response has been termed "immunologic hyporesponsiveness" (48-50) and has not been observed with conjugate vaccine (48). Adults who have been vaccinated with a second dose of polysaccharide vaccine after the recommended interval have demonstrated an adequate response. The clinical significance of immunologic hyporesponsiveness is unknown, but if revaccination is considered in persons who received polysaccharide vaccine in the past, the use of meningococcal C conjugate vaccine is recommended. In younger children (< 10 years of age) meningococcal C conjugate vaccine is preferred for control of outbreaks in view of superior immunogenicity and efficacy in this age group. Children < 2 years of age should not receive the polysaccharide vaccine for prophylaxis but should complete a full course of conjugate vaccine appropriate to their age, according to the NACI recommended schedule (33).

Outbreaks of meningococcal A disease have not occurred in Canada since the 1940s. If this rare event occurs, polysaccharide vaccine is recommended. Readers are referred to the most recent NACI meningococcal vaccine recommendations for further information (33,46,47). For the control of outbreaks associated with serogroup Y or W135 meningococci, one dose of a quadrivalent polysaccharide vaccine is recommended for persons \$ 2 years of age.

#### 11.3 Revaccination

The need for and effectiveness of revaccination with polysaccharide vaccine has not been fully established. For persons fully immunized with meningococcal C conjugate vaccine, revaccination is not thought to be necessary at this time, although there are insufficient data to predict persistence of immunologic memory (and presumed protection) beyond 5 years. This recommendation may be revised in the future; further research is warranted. Readers are referred to the most recent NACI meningococcal vaccine recommendations for further information (33,46,47).

# **APPENDIX 1:**

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