DYNAMICS OF BACTERIAL CARRIAGE AND DISEASE: LESSONS FROM THE MENINGOCOCCUS. pdf

1: Neisseria meningitidis invasive disease | Ministry of Health NZ

Rates of carriage of the meningococcus vary with host age, with very low carriage rates reported in children under the age of 4, rising to much higher rates, between 20% and 40%, in older teenagers and young adults (Gold et al., ; Cartwright et al.,).

Highlight and copy the desired format. Cassio de Moraes, J. Emerging Infectious Diseases, 20 5 , A cross-sectional study was conducted to assess the prevalence of meningococci carriage among workers at both refineries and to investigate the effect of vaccination on and the risk factors for pharyngeal carriage of meningococci. Among the vaccinated and nonvaccinated workers, rates of overall meningococci carriage However, a MenC strain belonging to the sequence type complex predominated and was responsible for the increased incidence of meningococcal disease in Brazil. A low education level was associated with higher risk of meningococci carriage. Polysaccharide vaccination did not affect carriage or interrupt transmission of the epidemic strain. These findings will help inform future vaccination strategies. In Brazil, meningococcal disease is endemic; 1. Since , a substantial increase has been observed in the proportion of cases attributed to meningococcus serogroup C MenC that is associated with the sequence type ST complex, and MenC is currently responsible for most cases of meningococcal disease in Brazil 1 â€" 3. Several outbreaks of MenC disease have been reported in Brazil in recent years 2 , 4 â€" 6. To control these outbreaks, chemoprophylaxis is administered to contacts of infected persons, and vaccination is often recommended for persons in age groups at higher risk for infection. Published data describing meningococci carriage in Brazil are limited. Few studies have been conducted that assess 1 the role of carriage prevalence in the dynamics of carriage and disease or 2 the potential effect of control programs, such as vaccination, on the transmission of meningococci. A total of 18 cases and 3 deaths case-fatality rate Six of the cases and 2 deaths involved Refinery A workers, and 12 of the cases and 1 death involved contacts family members of the refinery workers. On March 29, health authorities were notified of the first 3 case-patients 2 adult workers at Refinery A and an 8-month-old child whose father worked at Refinery A. An investigation was initiated, and chemoprophylaxis with rifampin was recommended for all close contacts of the 3 index case-patients. During the following 2 weeks, 5 new cases of MenC disease were identified 3 in Refinery A workers and 2 in children who were relatives of Refinery A workers. With these new cases, the incidence of meningococcal disease reached However, despite the vaccination program, 10 new cases of MenC disease occurred: Vaccination began on June 30, and In the months following the vaccination campaign, no more MenC cases were reported, and the outbreak was considered controlled. On July 10, , a worker at Refinery B was reported to have MenC disease, and on July 18, a second worker was reported to be infected. Of the 12 identified case-patients, 6 died. In Refinery B, the incidence of meningococcal disease reached On August 8, 1 new case of meningococcal disease was reported in a family contact of a Refinery B worker; no further cases were reported in Beginning in December , we conducted a cross-sectional study of workers 18â€"39 years of age from Refinery A, where mass vaccination had been recommended, and Refinery B, where mass vaccination had not been advised. All study participants gave informed consent. Specimen Collection During the first 2 weeks of December, , we obtained oropharyngeal swab samples from refinery workers vaccinated workers from Refinery A and nonvaccinated workers from Refinery B. Samples with meningococcus-like colonies were subcultured on blood agar medium for species identification. Isolates identified as Neisseria meningitidis were serogrouped by using an agglutination test. Primers and fluorescent probes were used for the detection of N. Samples positive for N. Multilocus sequence typing was performed according to the methods of Maiden et al. Primers, determination of sequence alleles, and designation of sequence types are described on the Neisseria Multi Locus Sequence Typing website http: Demographic data for all participants and typing results of N. Assessment of risk factors was performed using Fisher exact test. Results Of the oropharyngeal samples tested, Carriage rates were similar among workers from both refineries Of the positive samples, 95 were detected by culture and

real-time PCR, 1 was detected by culture only, and 8 were detected by real-time PCR only. The serogroup and genogoup could be determined for 56 of the meningococci-positive samples: The serogroup could not be determined for 48 The difference in MenC carriage rates among workers at the 2 refineries was not significant: Serotyping and Multilocus Sequence Typing A total of 38 different serotypeâ€"serosubtype antigen combinations were identified among the 96 N. Among MenC isolates, phenotype C: Eleven different STs were found among 27 isolates characterized by multilocus sequence typing. The 11 STs were grouped into 6 different clonal complexes: We did not find an increased risk of meningococci carriage associated with any of the potential risk factors studied, except low level of education. A low education level i. These findings likely indicate that the workers received direct protection against MenC from vaccine. However, after the vaccination campaign, 9 new cases of MenC infection occurred in children who were household contacts of vaccinated workers, without any known contact among them. More striking, carriage rates among vaccinated and nonvaccinated workers were similar. Most of the studies conducted among nonmilitary populations demonstrated that these vaccines cannot significantly reduce meningococcal carriage 17 â€" The short-term persistence of circulating antibodies and the quality of the immune response induced after vaccination with a polysaccharide vaccine may partly explain why these vaccines have no effect on carriage 20 â€" In contrast to polysaccharide vaccines, conjugate vaccines lead to the production of very high antibody concentrations, even in infants, and induce immunologic memory with higher antibody avidity and increased serum bactericidal activity, thus providing more robust long-term protection. In addition, conjugate vaccines also prevent the acquisition of carriage among vaccinees and, by interrupting transmission, provide indirect protection to unvaccinated, susceptible persons; this herd immunity proved key to the success of MCC vaccination programs in various countries 25 â€" The characterization of the N. The characterization showed that all MenC isolates were genetically related and displayed the same phenotype, C: These strains displayed 2 STs: In Brazil, the increase in MenC disease during the last decade has been associated with the emergence of this virulent clone belonging to the ST complex 2 , The ability of MCC vaccines to effect carriage of strains from the ST complex has yet to be shown. The recent introduction of MCC vaccine in the routine immunization program in Brazil will provide this opportunity, highlighting the importance of carefully designed studies to measure the effect of the vaccine on carriage and transmission. Meningococcal carriage was not associated with any of the risk factors evaluated in our study, except the level of education, which was inversely related to the prevalence of carriage. The higher percentage of MenC carriers among study participants with a lower level of education presumably reflects associated socioeconomic conditions and social behaviors. Less-educated workers in oil refinery settings are also more likely to perform activities that require the use of ear devices as protection from the loud environment. The wearing of such devices forces workers to stay very close to each other to facilitate conversation among them, and such close working situations also facilitate transmission of meningococci. Although the relationship between meningococci carriage prevalence and disease incidence is not fully understood, the evidence gathered during this study showed a dominance of the C: Also, in accordance with previous findings from other studies, we observed that polysaccharide vaccination had no effect on carriage and did not interrupt transmission to susceptible contacts 4 , His primary research interests include epidemiology and prevention of childhood infectious diseases. An unrestricted education grant from Sanofi Pasteur vaccines was provided for this study. References Brazilian Ministry of Health. Health surveillance [cited Aug 20]. The epidemiology of meningococcal disease in Latin America â€" Respiratory transmitted diseases [in Portuguese] [cited Aug 30]. Enferm Infecc Microbiol Clin. Laboratory methods for the diagnosis of meningitis caused by Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenza. Production and immunochemical characterization of Neisseria meningitidis group B antiserum for the diagnosis of purulent meningitis. Braz J Med Biol Res. Use of real-time PCR to resolve slide agglutination discrepancies in serogroup identification of Neisseria meningitidis. Lack of immunity in university students before an outbreak of serogroup C meningococcal infection. Meningococcal carriage in relation to an outbreak of invasive disease due to Neisseria meningitidis serogroup C in the Netherlands.

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Surveys on the rates of healthy carriers of Neisseria meningitidis and characterization of circulating strains. Rev Esp Salud Publica. Prevention of meningococcal disease: Pediatr Infect Dis J. Reconsideration of the use of meningococcal polysaccharide vaccine. Epidemiology and prevention of meningococcal disease: Meningococcal vaccines and herd immunity:

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2: Dynamics of bacterial carriage and disease: lessons from the meningococcus. â€” Oxford Neuroscience

The dynamics of meningococcal colonisation and disease are incompletely understood, and hence we embarked on a long-term study to determine how levels of colonisation with different bacterial.

Advanced Search Abstract BackgroundNeisseria meningitidis is a diverse commensal bacterium that occasionally causes severe invasive disease. The relationship between meningococcal genotype and capsular polysaccharide, the principal virulence factor and vaccine component, was investigated in carried meningococci isolated from children and young adults in Bavaria, Germany MethodsOf the meningococci isolated carriage rate, Statistical and population genetic analyses were applied to these data ResultsThe rapid increase in carriage rates with age of carrier, the low prevalence of hyperinvasive meningococci, and the relative prevalence of the 4 disease-associated serogroups were consistent with earlier observations. There was no genetic structuring of the meningococcal population by age of carrier or sampling location; however, there was significant geographic structuring of the meningococci isolated in civil, but not military, institutions. The rate of capsule gene expression did not vary with age of carrier or meningococcal genotype, except for serogroup C, for which increased expression was associated with ST formerly ET complex meningococci ConclusionsSerogroup C capsule expression during carriage may contribute to the invasive character of ST complex meningococci and to the high efficacy of meningococcal serogroup C conjugate polysaccharide vaccine Neisseria meningitidis although responsible for bacterial meningitis and septicemia worldwide, causes disease infrequently relative to the prevalence of its asymptomatic carriage [1 , 2]. Phenotypic and genotypic investigations have shown that carried meningococci are more diverse [3 , 4] than disease-associated meningococci [5 , 6]. For example, carried meningococci may be either encapsulatedâ€”such that they express 1 of 13 capsular polysaccharides, each of which corresponds to a particular serogroup [7]â€”or acapsulate, because of genetic down-regulation of capsule expression [8 , 9], inactivation of genes in the capsule gene cluster cps or the absence of cps in capsule null cnl meningococci [10 , 11]. In contrast, the majority of disease-associated isolates express polysaccharide of 1 of 5 serogroups: A, B, C, W, and Y [12]. The polysaccharide acid capsules corresponding to serogroups B, C, W, and Y predominate in Europe, Australia, and the Americas, whereas the polysialic acid capsules corresponding to serogroup A are predominant in Africa and Asia [12 , 13]. The nature of meningococcal transmission suggests that disease outbreaks follow the spread of carried hyperinvasive meningococci [1 , 18]. In many countries, disease mainly occurs in infants and young children, whose carriage rates are low, although increased disease incidence also occurs in young adults, whose carriage rates are much higher [19 , 20] The most widely used meningococcal vaccines are composed of purified polysaccharide [21] and have the ability to contain disease outbreaks; however, they are ineffective in infants and do not confer memory responses in adults [22]. Polysaccharide-protein conjugates address these problems for serogroup C and probably for serogroups A, W, and Y, but poor immunogenicity and similarity to host antigens have hampered the development of serogroup B vaccines [23 , 24]. A number of protein-based outer membrane vesicle vaccines have been developed [25â€”27], but they are poorly cross-protective [28]. The few disease isolates available from Bavaria at the time of this study were consistent with the national data. Disease clusters caused by serogroup C meningococci of the ET variant of the ST complex had occurred in Bavaria before the study was initiated [32]. Combining genotypic and phenotypic typing data for the carriage isolates elucidated relationships among capsular operons, capsule expression, and clonal complexes and determined the relative prevalence of genotypes among regions, institutions, and age groups Participants, Materials, and Methods Isolation of carried meningococciSampling was conducted from November to March At each sampling location, several educational institutions covering different age groups were chosen by the local health authorities, in consultation with school directors. In many cases, an informational event was organized for parents and guardians of students at the school, and the parents and guardians were provided with written information,

including a consent form. At military camps, the commander chose the company to be sampled; military recruits were sampled within 2 weeks of arrival. Most of the individuals who were approached agreed to participate. Retropharyngeal swab sampling was performed at each institution, and a single meningococcus was isolated from each culture-positive sample by direct plating onto Martin-Lewis agar plates gift from Becton Dickinson. The data were assembled by use of the Staden suite of computer programs [33]. Alleles, sequence types, and clonal complexes were assigned on the basis of the Neisseria MLST database available at: The positive control isolates were as follows: The negative controls were gonococcal strain FA gift from M. Age and 2-term fractional polynomial forms of age were used to test for monotonic or polytonic continuous associations [37]. Age was grouped as follows: The association between age and capsule expression was evaluated by use of a logistic regression model, with 2-term fractional polynomial forms of age as explanatory variables. A logistic regression model was used to assess the degree to which carrier age group might have confounded the results. The association between clonal complex and capsule expression was estimated by likelihood ratio tests across all 4 serogroups. This program computed an F statistic [40 , 41] by applying a permutation test to assess statistical significance. AMOVAs were performed on the data as grouped by institution, institution excluding military camps, military camps versus all other institutions, age of carrier, carrier age group, and geographic location of the institutions. Two further analyses were performed on geographic subsets of the data, one excluding military camps and one including military camps only. For the analysis by carrier age group, the age groups described above were used. The locations of the institutions sampled were used for all geographic analyses in this study. Although the locations of origin mainly Bavaria were known for most of the military recruits, this was not amenable to analysis, because they were distributed throughout Bavaria The following genetic characteristics were analyzed: For the small genetic differences detected, analysis of the nucleotide sequences of individual loci lacked statistical power, but power was recovered when the concatenated nucleotide sequences, concatenated allele designations, and sequence types were used. Where appropriate, the Bonferroni correction was applied, to account for multiple comparisons Mantel testCorrelation between genetic distance and geographic distance was assessed by use of the Mantel test [42]. Square n-by-n matrices were generated, where n was the number of isolates and, with the exception of the diagonal elements, each element of the matrix corresponded to an isolate pair. The correlation coefficient was calculated for the distance matrices, and its significance was assessed by permutation [35]. The geographic distance for a pair of isolates was taken to be the geographic distance between the towns at which the isolates were collected. For a pair of isolates, the genetic distance was defined variously, as follows: All definitions of genetic distance were used to investigate the effect on the analysis; where appropriate, the Bonferroni correction was applied, to account for multiple comparisons Results Meningococcal carriage ratesFrom the children and young adults sampled, The remaining meningococci were isolated from military recruits 18â€”26 years old at 6 camps Roth, isolates; Volkach, 96 isolates; Bayreuth, 95 isolates; Kempten, 50 isolates; Sonthofen, 21 isolates; and Ebern, 10 isolates Figure 1.

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3: Hot Topics in Infection and Immunity in Children - Google Books

Maiden M.C.J. () Dynamics of Bacterial Carriage and Disease: Lessons from the Meningococcus. In: Pollard A.J., McCracken G.H., Finn A. (eds) Hot Topics in Infection and Immunity in Children. Advances in Experimental Medicine and Biology, vol

Open in a separate window aThis ratio is calculated on from data deposited the PubMLST database, which contains only those isolates submitted to it by members of the Neisseria research community. Although it represents a comprehensive overview of the diversity observed to date, this database is not a coherent population sample. More precise calculations of the ratio of disease to carrier ratios for particular populations are available in Refs. The propensity to cause disease is polygenic, depending on combinations of genes or allelic variants of genes also present in less invasive meningococci [50]. As a virulence determinant, however, even the role of capsule is ambiguous as only 5 or 6 of the 12 capsule variants are ever associated with a significant number of disease cases. While capsule expression is usually considered necessary although rare cases caused by non-encapsulated meningococci have been reported in immunocompetent patients [54â€”56] , it is not sufficient for a meningococcus to cause disease. In addition to nucleotide sequence variation at shared loci meningococci exhibit extensive variation in gene content. This has been explored by the comparison of whole or partially sequenced genomes [61â€”65]. Meningococcal genome structure is also diverse in various other ways, including the presence and absence of ISs and large repertoires of repeat elements of various sizes, tracts of repeated nucleotides, and short nucleotide repeats [63,66]. Many of these are involved in mechanisms of gene regulation and at least 65 genes show potential for highly variable gene expression [67]. Which genes are expressed and when has a major influence on the development of disease. For example, many meningococci express capsules during transmission, but downregulate this expression during carriage [69]. Invasion of the mucosal epithelium requires the meningococcus to be acapsulate, but once in the bloodstream meningococci must be capsulate to grow to cause bacteraemia. Tropism to the meninges also requires the expression of different genes. The role of differential gene expression during invasion and spread remains to be fully defined. The existence of defined genetic types with different phenotypes provides the prospect of identifying the genetic traits that are responsible for those phenotypes by genome wide association studies [70] performed with well-defined isolate collections [71]. To date studies of differences in gene content have failed to detect consistent gene content differences among the Neisseria species, with the majority of genes shared among the meningococcus, gonococcus and N. Genomic studies have, by and large, also failed to identify major differences among meningococci that have not been previously identified by more conventional molecular microbiology [74,75]. Several genome wide association studies have been undertaken within the meningococcus but, as yet, the only new element to be associated with meningococcal disease is a putative phage, identified by whole genome comparisons of disease and carriage isolates [76]. Intriguingly, although this element is associated with particular clonal complexes, it has a measurable effect on the likelihood of a meningococcus causing disease, independent of this association. Further this effect is predominantly seen in meningococci isolated from teenagersâ€”the element is underrepresented in isolates from younger children and over-represented in adolescents [77]. Meningococcal evolution The meningococcus, in common with other members of the genus Neisseria, is naturally competent for transformation by exogenous DNA and studies of horizontal genetic exchange among these bacteria [78â€”82] played an important role in the development of models of bacterial speciation and population structure at the sub-species level. These studies are also important in understanding meningococcal epidemiology and virulence. High observed recombination rates in meningococcal populations, together with the fact that as the N. These paradoxes have to be addressed by models of meningococcal evolution and, given that invasion of the host is an evolutionary dead-end, such models need to be tested with data obtained from carried populations of meningococci. Although recombination has attracted interest as a mechanism for generating diversity [83] , much â€” indeed most â€”

genetic exchange is almost certainly among very closely related meningococci i. The distribution of DUS is therefore consistent with recombination being primarily a mechanism for genome repair that can occasionally result in generation of diversity, which, even more occasionally, is adaptive. It may be that this repair function is especially important in the Neisseria, which lack several DNA repair genes [66] ; this is also consistent with the distribution of restriction modification systems among meningococci, with particular systems associated with given clonal complexes [86]. The restriction modification systems may therefore act to promote genetic exchange among very close relatives while reducing but not absolutely preventing genetic exchange among meningococci belonging to different clonal complexes and related species. Clonal complex structure, which is such a feature of meningococcal populations, can be explained by models of clonal descent with periodic selection [87] , but such models are not consistent with the lack of a clonal phylogeny of meningococci [42] , and high observed rates of recombination [44]. These models envisage structure in meningococcal populations reflecting short-term dominance of particular clones and can explain the patterns of variation seen in cross-sectional surveys quite well [89]. These models cannot, however, explain the persistence of clonal complex structures or the association of some lineages with the hyperinvasive phenotype [90]. Alternative dynamic models explore the organisation of populations into strains in the context of selective forces [91]. Structuring of antigen variants encoded at multiple loci can be explained in meningococci, and other recombining pathogens such as Plasmodium falciparum, by immune selection acting on them. Depending on the intensity of positive selection, i. Importantly, the antigenic repertoires of strains generated by this mechanism will be characteristically non-overlapping, in that the different strains circulating in the population will not share variants at each of the loci under selection. Such non-overlapping repertoires have been observed in the meningococcal surface genes, especially the porins and Opa proteins [90,92,93]. The consequent limitations of the repertoires of such antigens available to circulating meningococci therefore have major implications for rational vaccine design [35,36]. These immunological models can also explain clonal complex structure if the combinations of housekeeping genes were hitch-hiking with genes encoding the antigenic variants repertoire; however, the antigenic structuring although mirroring clonal complex, is not always congruent with it, with some members of the same clonal complex exhibiting different antigenic repertoires and occasional examples of the same antigen occurring in different clonal complexes. Combined with high rates of recombination, this makes hitch-hiking an unlikely explanation for clonal complex structure. A major limitation of all of the models discussed so far is that they provide no explanation for the association of certain clonal complexes with an increased propensity to cause disease. If, however, the clonal complexes are regarded as units of selection, with particular STs being associated with fitness for transmission, both clonal complex structure and the hyperinvasive phenotype can be explained within the context of competition for hosts among different meningococcal genotypes [90]. This insight has the important implication that the observed genetic structuring must have a phenotypic consequence. If this is the case, STs are subject to selection and not neutral markers as previously thought; the model further demonstrates that fitness differences among distinct types are very small [90]. These insights are complementary to a stochastic model of meningococcal disease outbreaks, which showed that for large disease outbreaks, very small differences in pathogenic potential are necessary [94]. Diversity, and the forces which structure it, therefore appear to be central to the biology and pathogenicity of meningococci. Implications for vaccine design Meningococcal disease remains incompletely controlled by immunisation, largely as a consequence of the diversity of N. In terms of vaccine candidates, the existence of five, or at most six different polysaccharide capsules is not a challenge, given the successful implementation of conjugate polysaccharide vaccines available against pneumococci that contain multiple components [95]. However, the fact that the meningococcal serogroup B capsular antigen is chemically similar to the host antigen NCAM [96] has raised safety concerns that have precluded the development of comprehensive capsular vaccines against the meningococcus [45]. The immunology of conjugate polysaccharide vaccines that target meningococcal capsules was thought to be well understood at the time of their introduction into national immunisation programs [97,98]. The conjugation of

the polysaccharide to a protein elicits a T-cell-dependent immune response and immunological memory, both of which are absent when pure polysaccharide is used as an immunogen. Studies of carriage during vaccine introduction in the United Kingdom, together with continued disease surveillance in countries where the vaccines have been introduced, have demonstrated an additional powerful herd immunity effect. As well as providing strong personal protection, meningococcal conjugate vaccines protect the population, including unvaccinated individuals, by interrupting the transmission of capsulate meningococci [99,]. Intriguingly in the UK this effect was strongly directed at serogroup C meningococci belonging to the ST complex and made a major contribution to the success of this vaccine introduction [48]. The magnitude of this effect could be attributed to the inclusion of teenagers, among whom most meningococcal transmission occurs, in the immunisation campaign [16]. Carriage studies therefore provide an additional way of monitoring the effectiveness of immunisation programmes, as well as indicating the most efficient implementation strategies. Although providing an apparent alternative to conjugate polysaccharides, especially in the case of serogroup B meningococci, the sub-capsular antigens provide challenges of their own [45]. Where sub-capsular vaccines, particularly the outer membrane vesicle vaccines, have been successful this has been a consequence of their effectiveness against particular hyperinvasive lineages, and their design has been based on epidemiological knowledge of the prevalent disease causing lineages [â€”]. These approaches will, however, have a limited impact on disease caused by a variety of hyperinvasive meningococci, such as its typical of endemic disease in Europe and North America [,] , and there is little evidence of effective herd immunity induced by such vaccines. Therefore, if sub-capsular vaccines are to be effective against a broad range of meningococci, they will either have to be based on major surface components that are antigenically invariant and reliably expressed in all or most disease-associated meningococci if such components indeed exist, which remains an open question or they will have to contain cocktails of vaccine antigens carefully formulated on the basis of the molecular epidemiology of the meningococcus []. In either case, knowledge of the molecular epidemiology and evolution of disease and carried meningococci will be central to the design implementation and assessment of such vaccines. In conclusion, studies of the carrier state of the meningococcus remain of central importance in combating this important pathogen. Understanding the spread of invasive meningococci depends on appreciating the natural history of the organism and defining the dynamics of asymptomatic transmission. Resolving the apparent paradox of meningococcal virulence depends on refining models of meningococcal evolution, a process that occurs exclusively during carriage and transmission. Finally, the design and optimal use of meningococcal vaccines depends on acknowledging their effect on carriage. While much had been learned concerning each of these subjects over the last decade, much remains to be elucidated in this intriguing and important area of meningococcal biology. Discolsed conflicts of interest: Natural immunity to Neisseria meningitidis. Evolution of meningococcal disease. The meningococcus and mechanisms of pathogenicity. Epidemiology of Neisseria meningitidis, prevalence and symptoms from the upper respiratory tract in family members to patients with meningococcal disease. Scand J Infect Dis. Transmission of Neisseria meningitidis among asymptomatic military recruits and antibody analysis. Asymptomatic carriage of Neisseria meningitidis in a randomly sampled population. Genetic analysis of meningococci carried by children and young adults. Pathogenesis and pathophysiology of invasive meningococcal disease. Handbook of meningococcal disease. Emergency management of meningococcal disease: Epidemiology, surveillance and population biology: Humana Press; Totowa, NJ: A novel porA-based real-time PCR for detection of meningococcal carriage. Detection of meningococcal carriage by culture and PCR of throat swabs and mouth gargles. Secretor status, smoking and carriage of Neisseria meningitidis. Meningococcal carriage in the African meningitis belt. Social behavior and meningococcal carriage in British teenagers. J Hyg Epidemiol Microbiol Immunol. Pharyngeal carriage of Neisseria meningitidis in year-old individuals in Uganda. Longitudinal study of meningococcal carrier rates in teenagers. Int J Hyg Environ Health. Bull World Health Org. Global epidemiology of meningococcal disease. Meningococcal meningitis in Africa. Genetics and evolution of Neisseria meningitidis: Epidemic meningitis, meningococcaemia, and

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Neisseria meningitidis. Prospective study of a serogroup X Neisseria meningitidis outbreak in northern Ghana. Characterization of Neisseria meningitidis isolates collected from to in Japan by multilocus sequence typing. Identification of a new Neisseria meningitidis serogroup C clone from Anhui province, China. Molecular epidemiology of Neisseria meningitidis isolates from an outbreak of meningococcal disease among men who have sex with men, Chicago, Illinois, Molecular typing of meningococci:

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4: Meningococcal carriage and diseaseâ€”Population biology and evolution

Dynamics of bacterial carriage and disease: lessons from the meningococcus. Dynamics of bacterial carriage and disease: lessons from the meningococcus. Maiden MCJ.

References and further information Epidemiology in New Zealand Despite rates dropping significantly in recent years since the meningococcal B epidemic and vaccination programme, there are still a number of cases of invasive meningococcal disease in New Zealand each year and sometimes community outbreaks. As with the epidemiology in other temperate climates, there tends to be a seasonal pattern, with more cases seen in winter and spring. More detailed epidemiological information is available on the Institute of Environmental Science and Research ESR surveillance website. Case definition Clinical description Meningococcal disease is a serious invasive disease with an acute onset and may start as a mild flu-like illness and rapidly progress to fulminant septicaemia and death. Cases typically experience acute fever, malaise, nausea, myalgia, arthralgia and prostration. A rash occurs in about two-thirds of cases â€” this may be ill defined and macular, petechial or purpuric. More severe infection leads to shock, disseminated intra-vascular coagulation DIC , acrocyanosis and multi-organ failure. Approximately 75 percent of cases with invasive disease have meningitis typically causing headache, photophobia and neck stiffness. Infants present with less-specific features. Other locations of invasive disease with Neisseria meningitidis are possible though rare, such as orbital cellulitis, septic arthritis, and pericarditis. Nasopharyngeal carriage of meningococci is relatively common, in roughly 15 percent of the population, and is generally more prevalent in young adults, people who are living in conditions of severe overcrowding Baker et al , smokers and military recruits. The events that cause meningococcal disease are poorly understood but include a combination of organism, host and environmental factors Stephens Laboratory tests for diagnosis Laboratory confirmation requires at least one of the following: Case classification Under investigation: A case that has been notified, but information is not yet available to classify it as probable or confirmed. A clinically compatible illness. A clinically compatible illness that is laboratory confirmed. A case that has been investigated and subsequently found not to meet the case definition. Although not meeting the definition of a confirmed case, meningococcal infection of the conjunctiva is considered an indication for public health action because of the high immediate risk of invasive disease refer Health Protection Agency Other sites may also require public health follow-up on a case-by-case basis, as determined by the local medical officer of health. Spread of infection 2â€”10 days, commonly 3â€—4 days. Mode of transmission Transmission is from person to person through droplets or secretions from the upper respiratory tract, from a carrier or case. Period of communicability Therapy with rifampicin, ceftriaxone or ciprofloxacin eradicates N. Notification procedure Attending medical practitioners or laboratories must immediately notify the local medical officer of health of suspected cases. Notification should not await confirmation. Management of case Investigation Obtain a history of vaccination and possible contacts. Obtain a history of any antibiotic treatment, to help clarify if there may be partially treated disease. Ensure laboratory confirmation has been attempted, including strain identification group and subtype. Restriction Droplet precautions until 24 hours after the start of ceftriaxone, rifampicin or ciprofloxacin. Close contacts do not require isolation even if they are taking prophylaxis. Pre-hospital treatment Parenteral antibiotics should be administered to all cases as soon as meningococcal disease is suspected before admission to hospital or in hospital if delays and assessment in hospital are likely to be more than 30 minutes. See the latest edition of the Immunisation Handbook Ministry of Health Eradication of carriage It is important that the case receives an antibiotic that will eliminate throat carriage before discharge from hospital, usually rifampicin, ciprofloxacin or ceftriaxone. Unless one of these has been used in the course of treatment, it should be prescribed for the index case before discharge. Counselling Advise the case and their caregivers of the nature of the infection and its mode of transmission. Management of contacts Definition Anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the 7 days before onset of illness to 24

hours after onset of effective treatment. Public health follow-up is most important for household contacts and contacts that have had similarly close exposure. Examples of such contacts are: Unless one of these criteria is met, low-level salivary contact such as kissing on the cheek or mouth or sharing food or drink does not require public health follow-up or treatment given evidence that it does not increase risk of transmission. Post-mortem If the case has been treated with an effective antibiotic for at least 24 hours before death, any contact risk is low. If the case has not been treated, then occupational contacts should follow routine infection control practices with additional droplet and contact precautions. Kissing the body is not considered a risk. Body bags are not necessary, and transport to other countries for burial or cremation does not pose a risk. There is no restriction on embalming. Laboratory workers Laboratory workers who handle high concentrations or large quantities of organisms or are routinely exposed to isolates should be protected with the quadrivalent vaccine. Routine throat or nasopharyngeal culture of contacts is not recommended because asymptomatic carriage is common. Antimicrobials Antibiotic prophylaxis should be given as soon as possible ideally within 24 hours after the diagnosis of the index case. After 24 hours, chemoprophylaxis and vaccine if appropriate should still be considered for close contacts; however, there is little value in offering this more than 14 days after the diagnosis of illness there is a low risk of further cases after this period, see CDC b. The purpose of antibiotic prophylaxis is to eradicate nasopharyngeal colonisation by meningococci and thus prevent transmission to other susceptible people. Prophylaxis will not treat illness that the person may be incubating, so it is essential that the contacts be advised to seek urgent medical attention if they become unwell. Options Rifampicin Children under 1 month old: Children over 1 month old, and adults: Avoid rifampicin if pregnant or breastfeeding. Ceftriaxone mg for children under 12 years of age, and mg for older children and adults, intramuscularly as a single dose. This is the preferred prophylaxis for women who are pregnant or breastfeeding. Do not use in infants under 4 weeks of age. Ciprofloxacin mg or mg orally as a single dose for children over 12 years of age and adults, except pregnant and lactating women. This is the preferred prophylaxis for women on the oral contraceptive pill. Also preferable for prophylaxis of large groups. Consult Medsafe data sheets for appropriate use and dosages of ciporofloxacin in children. Resistance to ciprofloxacin is rare but has been described. A meningococcal C outbreak in in Fiji has shown to be resistant to ciprofloxacin. If such a strain is suspected, ciprofloxacin should not be used for antibiotic prophylaxis. Ideally the strain, or at least the group, should be determined first; therefore timely laboratory results are important. If there are delays in grouping or this is not possible, consider using a quadrivalent vaccine if over 2 years of age. Conjugate vaccine has been shown to reduce nasopharyngeal carriage and is therefore the preferred type of vaccine for contacts of meningococcal disease conjugate vaccines are currently available for group A, C, W and Y in New Zealand. Current meningococcal vaccines have short-term efficacy, estimated to be around 3 to 5 years. Discuss immunisation in the outbreak setting with the Ministry of Health Communicable Diseases and Immunisation teams. If case is group B In a multi-occupancy residential meningococcal B outbreak an emergency supply of meningococcal B vaccine Bexsero is available for use and will be supplied under section 29 of the Medicines Act The process for obtaining the vaccine is as follows. Under this scenario, HCL will be responsible for the supplier requirements of section 29, and the MOsH will be the prescriber under Section 25 of the Medicines Act Revaccination Information on revaccination is limited, but it may be appropriate for individuals with ongoing higher risk. See the Immunisation Handbook Ministry of Health for more details. Counselling All contacts should be encouraged to seek medical advice if symptoms develop, especially fever and petechial rash. Other control measures Management of contacts when there are large groups involved In instances where large groups of people have been exposed to a case, it is likely that contacts will have returned to a variety of health districts. Any follow-up needs to be coordinated by the appropriate medical officer of health to ensure that districts provide consistent advice and treatment. Two or more cases of disease associated in time, place or person. A single case in the absence of a previous known contact with another case. A case that occurs in the absence of previous known close contact with another case. A close contact who develops the disease within 24 hours of onset of illness in the primary case. A close contact who develops the disease

more than 24 hours after onset of illness in the primary case where the microbiological characteristics of the organism are the same. Two or more cases of the same strain group and serotype occurring within a 4-week period at the same early childhood service, school, sports group, social group, nursing home, university, etc. Three or more confirmed cases of the same strain group and serotype within a 3-month period and an age-specific incidence or specific community population incidence of approximately 10 per ,, where there is no other obvious link between the cases this is not an absolute threshold. The numerator is defined by the number of unlinked cases that is, they are not close contacts of each other and do not share a common affiliation. The denominator is defined as the population at risk that makes best sense in terms of population residence and movement, and therefore transmission of meningococcal bacteria. The aim of the intervention in such settings is to eradicate carriage of the strain from a population at high risk. The medical officer of health determines necessary action in discussion with the Ministry of Health. Identification of source Check for other cases in the community. Do not perform screening cultures because asymptomatic carriage is common. Disinfection Clean and disinfect surfaces and materials soiled with respiratory secretions. Health education Key messages include being aware of signs and symptoms, and the importance of early medical advice and treatment. Ensure people are aware of the availability of and recommendations for meningococcal vaccines. General recommendations for meningococcal vaccination are for: It is also recommended, but not funded, for: Reporting Ensure complete case information is entered into EpiSurv. Pediatric Infectious Diseases Journal Prevention and control of meningococcal disease: Department of Health and Ageing, Australia. Control of Communicable Diseases Manual 20th edition.

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