Meningococcal disease in Australia; looking at the past, thinking of the future

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Abstract

In 1987 an unexpected change in the epidemiology of meningococcal disease began in Australia. The change was accompanied by an outbreak of serogroup A meningococcal disease among Aboriginal central Australians, and was followed by a progressive rise in notifications of disease caused by both serogroup B and C nationwide. Over the last 4 years, the notification rate has plateaued at 2.1-2.3 per 100,000 population. Virulent clonal groups of serogroup A and C meningococci that have caused outbreaks appear to be identical to strains that have caused large outbreaks in other countries. We cannot predict where and when the next outbreak will occur. However, we can plan to respond swiftly when it does. This report presents an overview of the observed trends, the association between the microbiology and epidemiology of meningococcal disease, and the relevance of this association to outbreaks, with recommendations for management. *Comm Dis Intell* 1997;21:233-236.

Introduction

Neisseria meningitidis is one of the few endemic pathogens in industrialised countries that healthy children and young adults are particularly susceptible to. It can be fatal within a few hours of onset. The threat of meningococcal disease in child-care centres and schools is alarming, and demands swift action by public health authorities. Although outbreaks of the disease attract media and public attention, most cases are sporadic and cannot be linked to another case. However the public health response to sporadic cases is still demanding, with an average of 22 close contacts per case receiving chemoprophylaxis[1]. If the case attended a child-care centre, the number of contacts requiring such attention may be as high as 72[2]. Over the last 4 years, between 350 and 400 cases of meningococcal disease have been notified annually in Australia[3], suggesting that several thousand contacts may have needed follow-up. A cluster of cases, by contrast, is a rare event and historically, very few regions in Australia have experienced this in any one year.

The rising incidence of disease in Australia over the last decade[4-7], as in other industrialised countries[1,8-11] should serve as a warning of possible recurrences. Canada[11,12], the United Kingdom[13], New Zealand[1,14] and the United States of America[8] have had to conduct extensive vaccination programs in response to outbreaks. In Australia, by contrast, vaccination programs have been of a smaller magnitude[7,15-17]. The need may arise for larger

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vaccination programs to control outbreaks in Australia.

The incidence of meningococcal disease in Australia overall rises in June and peaks by October each year. However, it differs from the other types of bacterial meningitis such as *Haemophilus influenzae* type b disease and pneumococcal disease, in its characteristically unpredictable rise and fall in incidence from region to region**.** A close examination of national and global trends suggests that it may be possible to anticipate future outbreaks, enabling us to prepare a response.

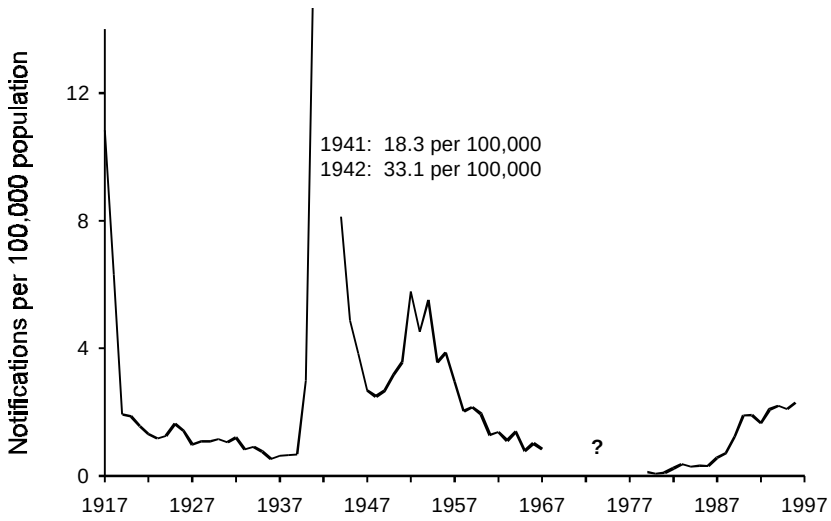
Microbial characteristics and epidemiology

The epidemiology of meningococcal disease is inextricably linked to the microbial characteristics of *N. meningitidis.* The microbe has been subdivided into 13 serogroups. In Australia, over 90% of invasive isolates are serogroups B and C. Further characterisation of invasive isolates is invaluable for guiding public health action, and for following the global spread of invasive strains analogous to that accompanying the antigenic shifts and drifts of the influenza virus.

The three major serogroups of meningococci cause differing patterns of disease in the community. Serogroup A meningococci are associated with explosive epidemics of meningitis, and very high attack rates of disease, up to 500 per 100,000[18]. Serogroup B meningococci are the major cause of sporadic disease in industrialised countries, and may cause outbreaks with lower attack rates than with serogroup A; some invasive strains have persisted in localities at hyperendemic levels for over a decade. Serogroup C meningococci are usually associated with sporadic disease, and have been implicated in both small clusters and large outbreaks, with attack rates between those seen for serogroups A and B.

Endemic disease in industrialised countries is caused by genetically diverse strains, mainly of serogroups B and C[18]. By contrast, outbreaks are usually caused by genetically homogeneous strains of these serogroups, consistent with the expansion of a virulent subtype.

Figure. Notification rate of meningococcal disease in Australia, by year



Data up to 1990[19] were modified with supplementary data, and updated to 1996 from published annual reports of the National Notifiable Diseases Surveillance Scheme.

These strains usually cause sporadic disease, but when and why they cause an outbreak is not clear. Possible risk factors include preceding infections in the population, such as those caused by the influenza virus or *Mycoplasma pneumoniae* [18]. Poor socio-economic conditions also increase the risk, where conditions such as overcrowding facilitate efficient transmission of virulent strains. This was probably an important factor contributing to the large outbreaks among indigenous populations in Canada [18], United States of America[18], New Zealand[14,18] and Australia[7].

While the rising incidence over the last decade has been attributed to genetically heterogeneous strains in many industrialised countries, the emergence of one or two virulent strains also accounted for a large proportion of that increase[1,8,9,11,18]. Research into bacterial population genetics suggests that the temporal variation in incidence is usually associated with clonal replacement of strains, much like influenza epidemics are driven by antigenic variation.

Meningococcal disease in Australia

The notification rate of meningococcal disease has fluctuated this century (Figure). Notifiable diseases data underestimate the true incidence of meningococcal disease[6,20]. For example, the level of under-reporting of meningococcal meningitis and septicaemia in New South Wales was estimated to be 55% in 1989-1990 and 21% in 1991-1992[6]. As the true incidence of meningococcal disease in Australia is not known, the notification rates have been taken to reflect trends in the incidence of meningococcal disease since 1917.

The epidemics of meningococcal disease caused by serogroup A in Australia at the time of the two world wars were part of a pandemic. After another peak of activity in the early 1950's, there was a continuing decline in the notification rate. In 1987, after over a decade of very low level activity nationally (notification rate under 1 per 100,000), a large outbreak of serogroup A meningococcal disease was reported amongst Aboriginal central Australians[7]. Notifications of disease caused by both serogroups B and C started to rise throughout Australia. The overall rate has plateaued at 2.1-2.3 per 100,000 over the last 4 years. The rise in incidence in sporadic cases has been accompanied by an increased frequency of outbreaks of disease caused mainly by serogroup C meningococci [15,16,21-23]. Although we have limited published information on the phenotypic distribution of invasive strains in Australia, it does provide some insights into outbreaks in the global context.

Predictably, the outbreak strains in Australia, although not always fully

characterised, have been closely related to those in other countries. If a virulent subtype of *N. meningitidis* causes a particular pattern of disease overseas, we should be well prepared to respond if the strain subsequently appears in Australia.

Serogroup A meningococci

The number of outbreaks caused by serogroup A have been low in industrialised countries since the Second World War, and concentrated in the poorest socio-economic groups [7,14,18,19] . Large epidemics continue to affect developing countries, and in 1996, more than 150,000 cases and 16,000 deaths were reported, mainly in west Africa.

Pandemic waves of disease caused by serogroup A meningococci since the beginning of this century have been associated with genetically distinct bacterial clones[18]. Of these, subgroup I-1 caused the 1987-1991 outbreak among Aboriginal central Australians[7,18], and has been associated with many outbreaks overseas. These included an outbreak in the Native Americans in Canada, which spread to skid row residents of the Pacific North West of the United States of America[18], and one in New Zealand in 1985[14,18]. Disease caused by this strain has not recurred in central Australia since 1992.

Serogroup B meningococci

Two complexes of serogroup B meningococci have caused increased disease activity in industrialised countries over the last three decades. The ET-5 complex (mainly phenotype B:15:P1.16), whilst being associated with outbreaks overseas, does not appear to have become established in Australia yet.

A second ET complex known as lineage III (B:4:P1.4), has also been associated with disease overseas,and now accounts for the major proportion of serogroup B isolates in the United Kingdom [9]. The number of isolates began to rise in New Zealand in 1991, with a rise in the incidence of meningococcal disease from 1.5 per 100,000 in 1989-1990, to 14.5 per 100,000 in 1996[24]. Vaccine trials are now being planned for this strain *(personal communication, Michael Baker, New Zealand).* It is of concern that this strain was detected in New South Wales, Queensland and Victoria in 1996[25].

Serogroup C meningococci

Two clonal complexes of serogroup C meningococci have caused increased activity in many countries, including Australia. The ET-37 complex, characterised mainly by C:2a:P1.5,2 has a global distribution, and has been the most common of the serogroup C strains causing endemic disease and localised outbreaks in industrialised countries[18]. This phenotype caused two localised clusters of cases in north Queensland between 1993 and 1994[15]. It was also responsible for the cluster of cases that affected mainly young adults in Penrith, New South Wales in 1996[23].

A second phenotype, C:2b:P1.2, has been associated with the ET complex known as the A4 cluster. This phenotype caused localised outbreaks in New Zealand[1] and the United Kingdom[9,13] that were controlled by community-wide vaccination programs. It was also associated with the high incidence of disease and a cluster of cases in south western Sydney in 1991, and was genetically identical to the outbreak strain identified in 1990-1991 in an Aboriginal community [17,22]. This phenotype also caused clusters in two other north Queensland communities over the same time period[15].

Future Management

The National Health and Medical Research Council (NH&MRC) has developed guidelines[26] for detecting, treating and documenting cases of meningococcal disease, and for planning and implementing control measures for sporadic cases and clusters. It also provides information for parents of children who may be at risk of the disease, and informative letters to general practitioners, child-care centres, schools, and the media.

It is not possible to predict exactly where and when the next outbreak may occur, how extensive it may be, or which particular subtype may be responsible. We can however, plan to respond swiftly when it does occur. With a sensitive surveillance system, we can detect an outbreak at the earliest opportunity, and control the incidence of secondary cases and of localised outbreaks in child-care centres, schools and other institutions. Each new case requires a response from the local public health unit to minimise transmission of the invasive strain among close contacts. The case must be documented and notified so that related cases can be detected readily at the local and regional levels.

We need accurate data on the incidence of meningococcal disease in Australia, and the associated morbidity. An assessment of the burden of disease is necessary to determine the cost effectiveness of a possible routine childhood vaccination program. Conjugate vaccines against serogroups A and C, and multivalent vaccines against a range of serogroup B strains are expected to become available within the next few years. The United Kingdom[27] and New Zealand (*personal communication, Michael Baker, New Zealand*) have indicated their intention to incorporate appropriate vaccines into the routine childhood vaccination schedule.

Regional and national surveillance data should be linked to microbiological data, and be interpreted in the context of global trends. They should be used to forecast possible future outbreaks, so that strategies to control the disease can be established.

Australia was caught by surprise by the change in the epidemiology of meningococcal disease that began to emerge in 1987. Outbreaks are unpredictable, and we were not well prepared to control the outbreak in central Australia[7]. The rising incidence elsewhere in Australia in the late 1980's was first suspected after noting the rising frequency of admissions to the Royal Children's Hospital in Melbourne[4]. The first publication that confirmed the new national trend appeared in 1992[5], and in 1993 the first meeting of the NH&MRC Working Party to address Australia's response to this change was convened. Although the incidence appears to have plateaued over the last 5 years, outbreaks of the disease are still likely to recur. This prediction is based on the evolving epidemiology of the disease in other industrialised countries, and serves as a warning for us to be prepared.

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