Diphtheria in Australia, recent trends and future prevention strategies

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Introduction

Diphtheria has become rare in Australia. There has not been a reported case or death due to this disease since 1992, in stark contrast to the first half of the 20th Century (Figure 1). At the height of the 1921 epidemic, there were 23,199 notifications (annual notification rate 426 per 100,000 population)[1] and, in the decade between 1926 and 1935, there were 4,043 deaths from diphtheria.[2]

Although diphtheria is no longer evident in Australia, a recent case in neighbouring New Zealand[3] and an extensive outbreak in the Newly Independent States (NIS) of the former Soviet Union[4] highlight the potential for diphtheria to re-emerge. This article focuses on the recent epidemiology of diphtheria and ways of preventing its recurrence in Australia.

Diphtheria in Australia (1991-1998)

Australia's National Notifiable Diseases Surveillance System (NNDSS) was established in 1991 and uses the following case definition for notification of diphtheria: isolation of toxigenic *Corynebacterium diphtheriae* and either (a) pharyngitis and/or laryngitis (with or without membrane), or (b) toxic (cardiac or neurological) symptoms.[5] Since the establishment of the NNDSS, there have been 23 notified cases of diphtheria, including one fatality. These cases occurred in 1991 (eight cases) and 1992 (15 cases); 12 were male (male:female ratio 1.1:1). Of the 23 patients, 16 (14 Aborigines) resided in the Northern Territory. Most (64%) of these recent cases were aged at least 15 years (range 1-78 years), in contrast with the pre-vaccine era when less than 30% of cases were aged 15 years and older.[4,6] Even though the numbers of notifications reported here are small, they probably overestimate the true incidence of diphtheria as defined by the notification criteria since only six toxigenic isolates of *C. diphtheriae* from the Northern Territory were identified in 1991-2 (Dr Jan Lanser, Institute of Medical and Veterinary Science, Adelaide; personal communication), compared with 16 notifications for the same period. The remaining 10 notified cases were probably cutaneous infections and/or infections with non-toxigenic strains.

Comparisons with other countries

Despite the potential limitations of Australia's diphtheria notification data, the recent picture is similar to that reported for many industrialised nations with long standing vaccination programs, in that:

- the incidence of diphtheria has declined – now being rare in many European countries,[7] the United Kingdom,[8,9] and the United States;[10]
- recent outbreaks have been concentrated in poorly immunised disadvantaged groups living in crowded conditions, with high notification rates amongst indigenous peoples;[6,11]
- there has been an increase in the proportion of adult cases.

Why are adults at risk of diphtheria?

Diphtheria is now more commonly seen in adults than in children in industrialised countries for several reasons. Firstly, improved living conditions impacted on the incidence of childhood diphtheria even before vaccines became available.[6] Smaller families and less overcrowding meant that preschool children were not exposed to the same intensity of infection as previously. As a result, many reached adulthood without having been exposed to diphtheria. Secondly, the implementation of mass childhood vaccination programs further reduced both the incidence of diphtheria and the circulation of toxigenic *C. diphtheriae*, so there was less opportunity to acquire natural immunity or to boost waning vaccine-induced immunity.

Are Australian adults at risk?

Low levels of adult immunity have been identified in two Australian studies. In 1972, a serosurvey in Victoria showed that only 40% of adults aged 40-49 years were immune.[12] Since this survey, however, there have been changes to the vaccination schedule. Booster doses of diphtheria toxoid vaccine for children aged 5-6 years and young adults aged 15 years were recommended in 1975 and 1982 respectively, while in 1984 the combined adult diphtheria and tetanus toxoid vaccine (Td, 'ADT') replaced tetanus toxoid vaccine for adult booster vaccinations at 10 year intervals.[13-15] In 1998, a study in Sydney of 548 adults aged between 19 and 70 years identified a higher level of immunity (74%) than that found in the Victorian study.[16] However, the proportion of susceptible adults was still high; one-quarter of the study population had no detectable diphtheria antibodies. The results of an Australia-wide serosurvey conducted by the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) will be available soon, and should provide a national picture of age-specific immunity to diphtheria.

As adults often suffer a severe form of illness, existence of a pool of susceptible adults in Australia would be of concern.

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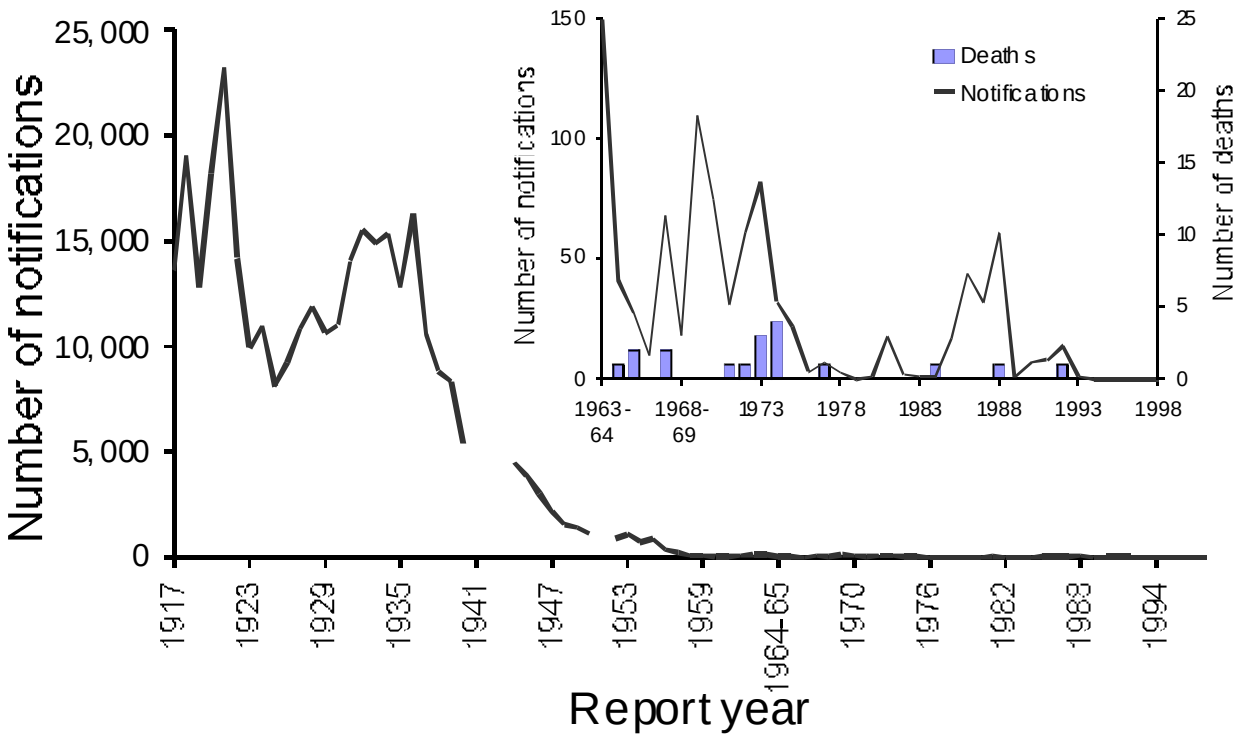
Figure 1. Diphtheria notifications (1917-1999) and deaths (1963-1998) for Australia[1]



1. Data sources:
Historical notification data: Hall R. Notifiable disease surveillance, 1917 to 1991. *Commun Dis Intell* 1993;17:226-36.
Notification data 1992-1999: the National Notifiable Diseases Surveillance System
Death data: the Australian Bureau of Statistics Causes of Death Collection.

However, ongoing transmission has not occurred in most countries with documented evidence of low adult immunity; for diphtheria to spread extensively, a pool of susceptible children, acting as the reservoir for infection, is also required.[4] Thus large scale outbreaks are unlikely at present, since Australian children are estimated to have high coverage with the primary course of diphtheria vaccinations.[17]

The epidemic of diphtheria in the Newly Independent States (NIS)

During the 1990s in the NIS, there were both low levels of adult immunity and poor childhood vaccination coverage. These circumstances contributed to the largest outbreak of diphtheria in an industrialised country since the epidemic of over one million cases during World War II. Between 1990 and 1997 there were 140,000 cases of diphtheria and over 4,000 deaths in the NIS.[4] An important feature of this outbreak was the high proportion of adult cases. In the early and late phase of the epidemic about 70% of cases were aged at least 15 years.[6]

The following factors contributed to the outbreak in the NIS.

- An increase in adult susceptibility as a result of vaccination programs implemented prior to the break-up of the Soviet Union – those born around the time when the diphtheria vaccine was introduced (1940s and 1950s)[4] were most at risk, as they may not have been reached by newly implemented programs, and, as circulation of toxigenic *C. diphtheriae* had already declined, had not had their immunity boosted by natural reinfection.
- A reduction in childhood vaccination coverage to 70% during the 1980s[4] - this occurred mainly because of political and economic problems associated with the break-up of the Soviet Union, but also because of an increase in the number of accepted contraindications to vaccination.[4]
- Changes to childhood vaccination practices, which resulted in a reduction in immunity - during the 1980s, childhood vaccines with a lower antigenic content (the adult formulation) were used, and from 1986 children did not receive a booster dose at school entry.[4]
- Mass population movements, and a reduction in living standards associated with the break-up of the Soviet Union, made conditions favourable for the transmission of diphtheria to susceptible populations.
- Changes to the predominant circulating strain of *C. diphtheriae*.

Although microbial factors distinguishing epidemic and non-epidemic strains have not been identified, the emergence of a clone of *C. diphtheriae* during the NIS epidemic supports a role for the agent in the development of this epidemic, although the source of the strains responsible is unknown. However, high carriage rates were identified in

the military, and diphtheria had never been eradicated from central Asian countries.[4] Another possibility is that, as reservoirs of infection have also been identified in the United States,[8] South East Asia[18] and central Australia,[19] a highly transmissible strain of *C. diphtheriae* had been imported.

Implications for Australia

A case of respiratory diphtheria in New Zealand in 1998 (the first to be reported in 19 years) indicates that, as reservoirs of toxigenic *C. diphtheriae* still exist, diphtheria could re-emerge in Australia if immunity were not to be maintained, This patient, an unimmunised 32 month old child, was probably infected by his father who had returned from Bali with an infected skin abrasion.[3] Most recent cases in the United Kingdom,[20] the USA,[8] and countries bordering the NIS,[7] have also been associated with imported infections. To reduce the risk of imported cases of diphtheria in Australia, travellers need to be up-to-date with their vaccinations.

To prevent sporadic cases and transmission in Australia, such as occurred in the NIS, high levels of immunity are required in all age groups. To improve immunity in adults, the NHMRC has revised its recommendations for diphtheria vaccination. Adults who have been fully vaccinated in the past should receive a booster dose of adult tetanus-diphtheria vaccine (Td, 'ADT') at the age of 50 years unless either a booster has been documented in the previous ten years or five doses have been completed as an adolescent or adult. For adults who have no history of vaccination, primary vaccination with three doses of Td or monovalent adult diphtheria vaccine (d) - each two months apart - is required, followed by two boosters at ten year intervals.[21] To increase coverage with five doses of a diphtheria-containing vaccine, Td can be administered for the prophylaxis of tetanus-prone wounds.

Although there has not been a case of diphtheria notified in Australia since 1992, the potential for sporadic cases and outbreaks exists. Clinicians, laboratory workers and the public need to be aware of this. To reduce the risk of diphtheria re-emerging, vaccination coverage should be high in all age groups.

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The NCIRS was established by the National Centre for Disease Control, Commonwealth Department of Health and Aged Care. The Centre analyses, interprets, and evaluates national surveillance data on immunisation coverage and vaccine preventable diseases. NCIRS also identifies research priorities, and initiates and coordinates research on immunisation issues and the epidemiology of vaccine preventable diseases in Australia.