Molecular typing of C. diphtheriae

A variety of methods for the epidemiological typing of C. diphtheriae isolates have been described. These include ribotyping and pulsed field gel electrophoresis (PFGE)\(^1\),\(^2\),\(^3\),\(^4\),\(^5\). They have been used to demonstrate predominant ribotypes among toxigenic isolates of both C. diphtheriae var gravis and var mitis from Russia and surrounding countries. They have also been used to trace the origin of imported cases in western Europe\(^6\).

Multiple clones of nontoxigenic C. diphtheriae var gravis, with one predominating (six of seven isolates from cases in New South Wales), were shown to have caused invasive infections in Australia\(^1\). PFGE was used to demonstrate similarity between the New South Wales isolates and those from three patients with endocarditis and five of their contacts in Victoria\(^7\). Dr Aruni DeZoysa (CPHL, London) reported that, among 118 nontoxigenic C. diphtheriae var gravis isolates referred to the CPHL in 1995, there were 23 different ribotypes. However, 75% belonged to a single ribotype which, on the basis of preliminary results, appears to be very similar to a ribotype found among isolates from Eastern Europe.

Unfortunately, because different endonucleases, probes and ribotype nomenclature are used, the results of one study cannot be compared with those of another. It was therefore proposed by Professor Patrick Grimont of the Institut Pasteur, Paris that a standard ribotyping method and common nomenclature be adopted. This would enable the establishment of a database of ribotypes, validated using appropriate computer software. It would also assist in the international surveillance of outbreaks of diphtheria and nontoxigenic C. diphtheriae infections, contribute to a better understanding of the epidemiology of this disease and improve disease control worldwide.

Ribotyping and PFGE of C. diphtheriae are being performed at the ICPMR, Westmead. Ribotyping will be standardised with the international method once this has been established. However, in a recent comparison of the two methods using 100 toxigenic and nontoxigenic isolates of C. diphtheriae, we found that PFGE was significantly more discriminatory than ribotyping (K Cheung and L Gilbert, unpublished data).

References


Editorial: Diphtheria - the Australian perspective

Henry Kilham and Richard Benn

Diphtheria has been a major cause of morbidity and mortality in Australian history. A decline in the incidence of this disease began with the implementation of public health measures before the infective nature of the disease was understood. The death rate was greatly reduced when antiserum became available a century ago. Active immunisation began in the 1920s. This was in widespread use by the 1940s and led to the almost complete elimination of the disease by the 1960s. However sporadic cases have continued to occur in unimmunised individuals. In 1984 the National Health and Medical Research Council recommended the use of ADT (adult diphtheria-tetanus toxoid) in place of tetanus toxoid for adult booster immunisation.

1 The New Children’s Hospital, PO Box 3515 Parramatta New South Wales 2124.
2 The Royal Prince Alfred Hospital, Camperdown New South Wales.

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Death from diphtheria in Australia is now rare. However notifications of bacteriologically proven diphtheria-related conditions continue to occur. The National Notifiable Diseases Surveillance System recorded eight cases in 1991, 14 in 1992 and one in 1993. Toxigenic as well as non-toxigenic strains of Corynebacterium diphtheriae remain endemic in parts of Australia.

The most important lesson to be learnt from recent outbreaks in the former Soviet Union, is that diphtheria recurs when community susceptibility increases and toxigenic organisms recirculate. In Australia many adults will now be susceptible, even if previously immunised, because of lack of natural boosting. This is a direct result of previous success in eradicating the organism from the community. We now have a large population of individuals whose only protection came from childhood immunisation. They have had no subsequent boosting either from further vaccine or from occasional contact with the organism. In the former Soviet Union there was social disruption and a considerable reduction in childhood immunisation. This provided conditions which enabled imported diphtheria to spread more easily resulting in a high incidence of disease, particularly in adults whose immunity had lapsed.

There have been no diphtheria serosurveillance studies carried out in Australia recently. However, using the international standard of susceptibility (antitoxin <0.01 IU/mL), 35% of United Kingdom-born blood donors aged 40 to 49 years are susceptible, and 53% of those aged 50 to 59. It can be assumed that similar rates would apply in Australia, the United States of America and the former Soviet Union up until 1990. Spread of toxigenic C. diphtheriae into a susceptible Australian population could be expected to produce outbreaks and deaths. It should not be forgotten that there is no effective treatment for diphtheritic myocardiopathy, which is commonly fatal.

Some countries close to the former Soviet Union such as Finland and Poland have commenced adult immunisation against diphtheria. In Australia there appears to be no cause for alarm at present. However the possibility of a resurgence of diphtheria must be acknowledged. The following measures are pertinent:

- improving the uptake of childhood immunisation, to reduce the number of susceptible children and hence spread of any imported organism in the community;
- maintaining adequate surveillance, which must include maintaining skills in bacteriological diagnosis, even if only at selected laboratories.

The need for booster injections in adult life is unclear. However, as protective antibody levels wane with age, it is considered prudent for adults to have booster injections, which may be given as Td (ADT) vaccine, at 10 years intervals. Diphtheria can be a significant risk for travellers to some countries, so all international travellers should ensure that their Td (ADT) vaccination is current.

National Health and Medical Research Council recommendations on diphtheria vaccination

The National Health and Medical Research Council recommends diphtheria vaccination as part of the standard childhood vaccination schedule. Primary vaccination is achieved with three doses of a diphtheria toxoid-containing vaccine at one to two monthly intervals, with boosters at 18 months and four to five years.

Prior to the eighth birthday DTP (diphtheria, tetanus, pertussis vaccine) should be given. If there is a genuine contraindication to pertussis vaccine DT (adsorbed diphtheria, tetanus vaccine, CDT paediatric formulation) should be used. After the eighth birthday, the adult formulation (Td, ADT) should be given. The change to Td (ADT) (low dose diphtheria toxoid) after the eighth birthday is related to the reduced tolerance of older children and adults to diphtheria toxoid.

Older children who have not received diphtheria vaccination are also likely to have missed tetanus vaccination. Those who have not reached their eighth birthday should receive three injections of DTP (or DT, CDT) at intervals of one to two months, and those individuals who have passed their eighth birthday should receive three doses of Td (ADT) at intervals of two months.

The European experience detailed by Dr Gilbert, in this issue, should assist in choosing the best approaches:

- achieving better adult immunisation, especially in migrants arriving without evidence of adequate childhood immunisation. Also for Australians intending to travel to areas where diphtheria is endemic;
- being prepared to embark upon localised mass immunisation of susceptible populations, for both adults and children, should an outbreak occur, the use of other public health interventions such as active case-finding and isolation for such outbreaks.

References