Executive summary

Health Council of the Netherlands. Criteria for the selection of a vaccine against pertussis. The Hague: Health Council of the Netherlands, 2014; publication no. 2014/11.

The request for advice

In the Netherlands, a combination vaccine is used to vaccinate infants against pertussis. This combination vaccine targets six infectious diseases: diphtheria, pertussis, tetanus, polio, invasive infections caused by *Haemophilus influenzae* type b and hepatitis B (DaKTPHibHepB combination vaccine). In recent years, only a single combination vaccine was available, from a single manufacturer. This was Infanrix hexa©, which is manufactured by GlaxoSmithKline. A second hexavalent combination vaccine has recently received European marketing authorisation, and is now available in the Netherlands. This is Hexyon© from Sanofi Pasteur MSD. With regard to the pertussis vaccine, Hexyon© does not meet the criteria formulated by the Health Council of the Netherlands in 2004, in an advisory report entitled 'Vaccination against pertussis'. As a considerable amount of time has passed since that advisory report was published, the Minister of Health, Welfare and Sport has requested the Health Council's advice (Annex A). In particular, she wants to know whether, in the light of recent scientific developments, the Council feels that its 2004 advisory report is in need of revision.

Previous advisory report on the selection of a vaccine

In its 2004 advisory report on vaccination against pertussis, the Health Council gave a detailed description of the requirements that vaccines against this disease must meet. The Council concluded that the immunology of pertussis is complex and only partially understood. Then, as now, the commonly used vaccines were selected on the basis of their ability to generate antibodies against components of the pertussis bacterium. The Council concluded that cellular immunity, mediated by T-helper cells and the innate immune system, is also an extremely important aspect of protection against pertussis.

Based on the contemporary understanding of the immunology of pertussis, the Health Council suggested that, in addition to pertussis toxin, acellular vaccines should also contain pertactin. The Committee took the view that acellular vaccines containing only pertussis toxin and filamentous haemagglutinin (as is now the case with Hexyon©) were not eligible.

Recent insights into the correlates of protection

Since the 2004 advisory report was published, it has become even more evident that the immunology of pertussis is not sufficiently well understood to provide a reliable platform for rational vaccine development. There is still no consensus among scientists about which immunological parameters indicate effective protection against pertussis. The appreciation of the importance of cellular immunity has not contributed to the development of any new pertussis vaccines.

While again emphasising the importance of cellular immunity, the Committee has reconsidered its previous position that, in addition to pertussis toxin, acellular vaccines should also contain pertactin. In retrospect, too little is known about the bacterial components (antigens) needed to generate a protective immune response to support that position. The Committee takes the view that further immunological research and field studies are needed to establish the correlates of protection.

Data on efficacy, effectiveness and safety

The limited nature of the available data makes it impossible to draw firm conclusions about the relative efficacy of Infanrix hexa© and Hexyon© against pertussis, i.e. under controlled circumstances. Nevertheless, the Committee believes that this limited data indicates that the efficacy of Infanrix hexa© is greater than that of Hexyon©. However, when used in a rigorous programme,

such as the Dutch National Immunisation Programme, good effectiveness in the control of pertussis appears possible with both combination vaccines.

Both combination vaccines perform well in terms of safety, which means that they can be included in the National Immunisation Programme. Information concerning the more recent vaccine (Hexyon©) is still limited, so additional monitoring is required in this case.

Over the years, considerable experience has been gained in the use of Infanrix hexa© in children born prematurely and in children with disorders of the immune system. As yet, there is only a limited amount of information of this kind about Hexyon©. While this lack of data does not preclude the use of Hexyon© in public programmes such as the National Immunisation Programme, it does impose certain limitations. It also means that the use of Hexyon© will have to be subject to additional monitoring.

Conclusion and recommendation

As yet, too little is known about the bacterial components (antigens) needed to generate a protective immune response to pertussis to be able to identify specific criteria for the selection of a vaccine against pertussis. The Committee feels that further immunological research and field studies are vital to the development of future pertussis vaccines, offering longer periods of protection.

Based on the immunological research into parameters indicating effective protection against pertussis, together with the available data on efficacy, and available data on use in specific groups, the Committee has a preference for Infanrix hexa©. However, in a rigorous programme, such as the Dutch National Immunisation Programme, good effectiveness in the control of pertussis appears possible with both combination vaccines. A switch to Hexyon© would necessitate extra monitoring.

Scope of the advisory report

In the context of the National Immunisation Programme, vaccination against pertussis is intended to prevent the severe forms of this disease that primarily affect infants below the age of six months.

The question at the heart of this advisory report is what requirements must a DaKTPHibHepB combination vaccine meet if it is to give vaccinated infants effective protection against pertussis. The current vaccination schedule provides for the administration of a combination vaccine of this kind at the ages of 2, 3, 4 and 11 months.

As yet, the vaccination of infants (with a booster vaccination at the age of 4 years) has not been sufficiently effective to substantially reduce the levels of bacteria circulating in the population, nor has it been able to protect infants in the period before they have acquired vaccination immunity. Consideration should be given to modifying the vaccination strategy, with a view to protecting young infants during that period as well. The Health Council will advise on that matter separately.