Executive summary

Health Council of the Netherlands. Vaccination of children against hepatitis B. The Hague: Health Council of the Netherlands, 2003; publication no. 2003/14.

Request for advice

On 1 March 2003, the National Vaccination Programme (NVP) was extended to include vaccination for the children of families in which one or both parents come from a country where hepatitis B is common. Such children are at increased risk of coming into contact with carriers, whether within the family, within their social circle in the Netherlands or when visiting their parent's (or parents') country of origin. This vaccination was prompted by an advisory report which the Health Council produced in 2001. These children are vaccinated with half a dose of vaccine ('child dose') on three separate occasions, at the ages of two months, four months and eleven months.

Another group consists of children whose mothers are carriers of the hepatitis B virus (hereafter referred to as 'children of HBsAg-positive mothers'). Members of this group have been routinely vaccinated since 1989. The vaccination schedule used in the case of these children (who become contaminated with the virus at birth) differs from that used for the new group. Hepatitis B antibodies are administered immediately after birth, followed by vaccination with a whole dose of vaccine ('adult dose') on four separate occasions, at the ages of two months, three months, four months and eleven months. The antibodies provide immediate protection but this is passive in nature. It is intended as a stop-gap measure, until active protection has been built up through vaccination. The vaccination schedule was originally supported by targeted research. Although it was formally included in the NVP only recently, vaccination for this group

has used the latter's organisational structure and vaccination sessions from the very beginning.

The State Secretary for Health, Welfare and Sport has decided that, with effect from 1 March 2003, the vaccination schedule for the group of children of HBsAg-positive mothers will be adapted to conform with the new group. This means that there will be three separate vaccinations (at the ages of two months, four months and eleven months) instead of four and the child dose will be used rather than the adult dose. The administration of hepatitis B antibodies immediately following birth is to be continued. The State Secretary has asked the Health Council whether it is possible to provide scientific support for the amendment to the vaccination schedule that affects children whose mothers are carriers. In addition to assessing the efficacy of the vaccination schedule, the Committee evaluated the workings of the programme's broader aspects.

Risks

Mothers who are carriers of the virus will contaminate their children when giving birth to them. Not all children who are contaminated with the virus at birth go on to develop an actual infection. In the case of mothers who have tested positive for the surface antigen (HBsAg positive) but not for the e antigen (HBeAg negative), the risk of infection is about 15 percent. However, for the new-born children of mothers who are both HBsAg positive and HBeAg positive (an indication that they are more infectious) this risk is about 90 percent. Infection can also be transferred after birth, via breast-milk for example, or via cuts in the nipples or skin. The risk that newly infected individuals will become carriers is highly dependent on their age. Young children have a very high risk of becoming carriers. In the case of new-born children, the risk that an infection will become chronic and that they will go on to become carriers is about 90 percent.

If the children of carriers are not treated, many of them will also go on to become carriers. The dangers posed by this situation include further spread of the disease, chronic liver inflammation, liver cirrhosis and primary liver cancer. Transmission from mother to child is one of the mechanisms that maintains the spread of hepatitis B in a population. Given the chronic complications involved, this is enormously costly for the infected individuals and for society in general.

Vaccination

In the vast majority of cases, vaccination soon after birth can prevent new-born children from becoming carriers. Accordingly, in addition to the vaccination of infants or pre-adolescents, the World Health Organization (WHO) attaches great importance to

screening pregnant women and to vaccinating the children of carriers. A programme to tackle this particular issue was introduced in the Netherlands in November 1989.

On an annual basis, that screening and vaccination programme prevents about 200 infections and the creation of 180 new carriers. Each year, at least 1000 children are born to HBsAg-positive mothers. About 200 of these mothers are also positive for the e antigen. In the absence of a vaccination programme, this would lead to about 300 infections and about 270 new carriers as a result of transmission during birth.

The Committee considers vaccination of the children of HBsAg-positive mothers to be both a form of prevention and a medical treatment (post-exposure prophylaxis). This is, after all, not simply about the prevention of hepatitis B at the population level, it is also a matter of providing health care for the individual. The situation is fundamentally different from that of the children of families in which one or both parents were born in a country where hepatitis B is endemic, but where the mother is not HBsAg positive.

Effectiveness of the vaccination

The indication of a vaccination for a specific group should be based upon targeted research into its efficacy (here: the percentage of children shown to have been prevented from becoming carriers) of a specific vaccine administered in accordance with a defined vaccination schedule. After taking stock of scientific insights into the effectiveness of vaccinating the children of HBsAg-positive mothers, the Committee has concluded that there is no scientific basis for the vaccination schedule that was introduced on 1 March 2003. The Committee has identified various vaccination schedules that are worthy of recommendation.

Regarding the use of half doses of vaccine (‘child dose’) and a vaccination schedule consisting of three doses, the Committee has concluded that both have some degree of scientific support, provided that the initial dose of vaccine is given immediately after birth, together with the hepatitis B antibodies.

Effectiveness of the programme

The Committee then evaluated the workings of the programme's broader aspects. In addition to the effectiveness of the vaccination schedule, the coverage of the programma is implicated, i.e. the percentage of children of HBsAg-positive mothers who have completed the full programme.

The programme was first linked to the NVP for purely pragmatic reasons. Modifying the programme to conform to the NVP has, in the Committee’s view, led to several adverse compromises, including postponement of vaccination and relatively low coverage. The individuals and institutions associated with the programme’s

implementation should be well aware of the programme's medical nature and purpose. The Committee has the distinct impression that this is not the case.

Another important conclusion is that the national programme has by no means achieved the worthy goal of full coverage. The average coverage of approximately 90% that has been achieved by 'hitching a ride' with the NVP is quite inadequate.

That a higher coverage is possible, is demonstrated by the programme as implemented in Amsterdam. There they opted for a different approach right from the start, one that did not involve the NVP. The active approach adopted there is in accordance with WHO recommendations. It involves starting vaccination as soon as possible after birth, which complies more fully with the programme's objective. It has been shown that approaches of this kind can achieve almost total coverage.

Recommendations

The Committee recommends that the feasibility of using the Amsterdam model in other parts of the country be investigated. Given the enormous cost of hepatitis B in new-born children, to the infected individuals and to society in general, and the expected gains from an active approach and strict supervision of the programme, the Committee feels that the extra effort involved would definitely be worthwhile.

In the new approach the Committee recommends that, in accordance with WHO recommendations, 150 IU of hepatitis B antibodies be administered immediately after birth, that an initial dose of vaccine (child dose) be administered as soon as possible after birth (but no later than the infant's first week of life), the second dose should be given at the age of one month and the third dose at six months.

The Committee takes the view that administration of the initial dose of hepatitis B vaccine by the midwife or by the physician attending the birth would certainly be in keeping with the Netherlands' excellent tradition of perinatal care. Midwives are qualified to carry out procedures of this kind.

At the age of 12 months, serological tests should be carried out to determine whether the vaccination has resulted in the production of antibodies (anti-HBs) or whether the child has become a carrier (HBsAg). In the latter case, treatment should be intensified.

A switch to the proposed approach should be implemented with great care, and under the strict supervision of a programme committee. It would be a good idea to test this concept in a few selected regions first.

While they may vary from place to place in terms of procedural detail, active supervision and regular evaluation are essential elements of the programme. The Committee's vision involves supervision and evaluation at local level by the Municipal

or Regional Public Health Services, and at national level by the Health Care Insurance Board's Coordinating Committee for Prenatal and Postnatal Screening.

If, contrary to the Committee's preference, there is a desire to retain the link to the NVP, the Committee recommends that a schedule be introduced that involves vaccination immediately following birth and at the ages of two months, four months and eleven months. The dose to be used in conjunction with this schedule should be the child dose.