SAMJ
Editorial

Opinion

What is the best hepatitis B vaccination strategy for South Africa?

Since the early 1970s, when serological tests for hepatitis B became available, knowledge of the hepatitis B virus (HBV) has grown rapidly. This virus was among the first to have its genome fully sequenced, and HBV vaccine was among the first to be genetically engineered. Universal HBV vaccination of all newborns recently became the international standard.[1] South Africa adopted this practice, but is it the best HBV vaccination strategy for South Africa?

Options for HBV vaccination

The goal of HBV vaccination is to interrupt the spread of HBV and ultimately to eliminate it from the population. The exact levels required for herd immunity are not known, but coverage levels well below the 95% estimate for measles are likely to be adequate. A model developed for the Gambia suggested that coverage levels of about 70% may be adequate.[2]

The major obstacles to achieving this goal are cost of the vaccine and the health service infrastructure required to achieve adequate coverage levels with three doses of vaccine. There are four options for a new HBV vaccination programme, ranged here from least desirable to most desirable.

Option 1 — vaccination of selected high-risk groups only. This was the South African policy until 1995 — during this time only health care personnel received free vaccine from the State. In some countries the selected groups have included renal dialysis patients and haemophiliacs. This strategy was also adopted in the USA until recently.[3] Its fundamental weakness is that large cohorts with immunity are not built up. Coverage through this option has tended to be patchy, and vaccine may not reach those most in need. However, this strategy could be the most efficient one in a country with low prevalence of HBV and where risk groups are well defined.

Option 2 — vaccination of a narrowly selected age cohort, e.g. universal vaccination of all newborns only. This has been South Africa's policy since 1995. This option is cost-effective in infants, since it utilises the existing Expanded Programme on Immunisation (EPI) infrastructure and clinic visits. In South Africa, high vaccination coverage is achieved through routine services, e.g. 80.6% for the third diphtheria, tetanus and pertussis (DTP) vaccination.[4] Some countries have selected adolescents as the target age cohort for vaccination, with the aim of interrupting sexual transmission in areas where this is an important route. Importantly, this option leads to an incrementally growing cohort with HBV immunity. After a few years, vaccinated cohorts entering the age groups at highest risk should have high enough levels of protection to interrupt HBV transmission, thereby altering the epidemiology of HBV. The essence of this approach is the progressively increasing immune cohort, but its shortcoming is the number of years required before significant interruption of the virus transmission occurs.

Option 3 — vaccination of two selected narrow age cohorts, e.g. all newborns and all school entrants. This strategy aims to halve the time required to achieve a sizeable immune cohort without having to undertake mass vaccination of large populations. This option is therefore option 2 together with vaccination in an older cohort for catch-up purposes. In some instances the second older cohort comprises adolescents — in Italy, for example, HBV vaccination is provided to newborns and 12-year-old children.[5] School entrants are a convenient older cohort, since complete vaccination is a requirement of school entry (though this is not uniformly implemented, to avoid discrimination and depriving certain children of schooling because of vaccination status). School health services in South Africa have been giving BCG to children at school entry for many years, though this was stopped recently. In addition, our routine clinic system provides diphtheria and tetanus (DT) vaccine to 5-year-old children before school entry. Introducing routine HBV vaccination at birth and 5 years could lead to the cohort of children from birth to 10 years being protected within 5 years. The choice of age 5 years for the second vaccination cohort is appropriate, since HBV prevalence is well below its peak at this age and vaccination wastage (vaccination of a person who already has at least one HBV marker) is minimised.

Option 4 — vaccination of a wide age band initially, e.g. all children from birth to 10 years in the start-up year of the programme, followed by option 2 thereafter. This option would require substantial effort during the start-up process of the HBV vaccination programme. However, it could be cost-efficient if it is linked to the mass immunisation days for measles, which target children from 1 to 10 years. Coverage achieved through the 1997 measles mass immunisation campaign was 78.9% (R Eggers — personal communication). Unlike measles, however, two follow-up vaccinations will be required for HBV, but both these doses could also be organised as part of the mass immunisation days. The advantage of this approach is that it creates a large cohort of immune children in a very short space of time and may therefore be worth the extra effort required. The amount of effort and vaccine required can be balanced with the projected benefit by adjusting the width of the age band for the mass immunisation. At the extreme, it is possible to make the age band very wide and say that everyone should be vaccinated during the start-up period. This is likely to be expensive and very difficult to implement. It is therefore better to define a narrower age band — instead of 10 years being the cut-off, 5 years could be used instead. HBV transmission increases substantially after 5 years,[6] so vaccinating a group from birth to 5 years against HBV will have enormous immediate benefit and will also involve minimal wastage (i.e. vaccination of an HBV carrier or a person already immune to HBV). In each 1-year cohort, as the cohort gets older, vaccination wastage becomes more significant. However, HBV incidence (i.e. the number of new cases) is a function of the prevalence of HBV carriers, where incidence increases as the number of HBV carriers rises until a point is reached where the number of susceptible members of the population is too low to sustain a rising incidence rate. At this point the incidence rate

declines until a steady state is reached where HBV transmission is maintained at low endemic levels. On the basis of this model of HBV transmission, vaccination of age cohorts with an increasing prevalence of HBV markers could contribute substantially to interrupting HBV transmission by decreasing the number of susceptibles (members of the population with no HBV markers). Hence, vaccination wastage may not be an important factor mitigating against vaccination of children in the first decade of life.

Which is the best vaccination option for South Africa?

Given the high levels of HBV transmission in childhood, particularly during the preschool and primary school years, it is important to have the cohort of children from birth to 10 years protected as soon as possible. Option 3 is my proposed option. It is unfortunate that this decision was not made in 1994/95 so that the dual vaccination age could have been implemented right at the start of the HBV vaccination programme. Even though HBV vaccination is in its 3rd year, the introduction in 1998 of routine HBV vaccination at both birth and 5 years would substantially speed up HBV protection in childhood. This approach would mean that by the year 2000, the cohort of birth to 7 years will be vaccinated. This catch-up vaccination at 5 years would need to be implemented for 3 years only, from 1998 to 2000. Thereafter, only the routine newborn vaccination need continue.

Why select 5 years for the catch-up vaccination?

HBV transmission is still well below its peak at 5 years. There are high levels of susceptibles at 5 years. The routine EPI of the South African health service includes a vaccination visit at 5 years for DT. Including the first dose of HBV vaccine at this visit will minimise the effort involved in informing mothers to bring their children for HBV vaccination at 5 years. During vaccination with the first dose, appointments for the follow-up doses can be provided together with counselling on the importance of not missing them. A further point is that HBV vaccination coverage in 5-year-old children can be monitored at 6 years when the children enter school.

In conclusion, data on the age-specific prevalence of HBV infection suggest that a dual-age HBV vaccination strategy is a better option than the current strategy of infant vaccination. HBV control is within our grasp in South Africa; using a dual-age strategy will mean that we can realise this goal sooner rather than later.

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Clinical Lesson

Low-molecular-weight heparins allow selected outpatient treatment for venous thrombosis

The conventional treatment for patients with an acute deep-vein thrombosis (DVT) at present consists of an initial continuous intravenous infusion of unfractionated heparin, administered for a minimum of 5 - 7 days.[1] Oral anticoagulation is started at the same time, while the patient is still in hospital, and is continued for at least 3 months. The initial treatment with heparin, which aims to prevent pulmonary embolism and recurrent thrombosis, has been found to be effective,[2] but the anticoagulant response to unfractionated heparin varies markedly. As a consequence the dosage of unfractionated heparin must be monitored carefully by frequent measurement of activated partial thromboplastin times (aPTTs), necessitating hospitalisation of the patient for the period that the unfractionated heparin is being administered.

Low-molecular-weight heparins (LMWHs), prepared from digestion of heparin by chemical or enzymatic depolymerisation (to produce molecules that are usually less than 18 saccharide units in length), have several advantages over the parent compound.

1. The anticoagulant activity of the heparins resides in a unique pentasaccharide sequence which is randomly distributed along the heparin chains and binds with high affinity to antithrombin. Any heparin (no matter how long the molecule), containing this pentasaccharide sequence, inactivates factor Xa simply by binding to antithrombin and thereby accelerating the interaction between factor Xa and antithrombin. In contrast, the inactivation of thrombin by unfractionated heparin requires heparin to bind to both antithrombin and thrombin. This complex can only be formed if the heparin chains are at least 18 saccharide units long and also include the pentasaccharide sequence (most molecules of unfractionated heparin are at least 18 saccharide units in length). As a result, unfractionated heparin has equivalent inhibitory activity against both factor Xa and thrombin, while LMWHs preferentially inactivate factor Xa.

2. Unlike unfractionated heparin, LMWHs can inactivate platelet-bound factor Xa and can resist inhibition by platelet factor 4, which is released during clotting.