The Expanded Program on Immunization (EPI) was introduced by the WHO in 1974 with the aim of vaccinating all children below the age of one year against six killer diseases. Since then, new vaccines against other severe vaccine-preventable diseases have been developed. South Africa is in the fortunate position to be able to include many of these new options into the national EPI and to adjust the EPI schedule according to the disease epidemiology of the country. The rationale behind some of these additions and changes to the national EPI is discussed.

Introduction

In the pre-vaccine era, epidemics were highly feared, as millions of people died from diseases about which there was little understanding. It is estimated that smallpox caused as many as 60 million deaths during the 17th century.

The vaccine era started in 1796, with Edward Jenner developing a vaccine against smallpox. The ultimate success of Jenner’s efforts, was finally realised in 1979, when the World Health Organization (WHO) certified that smallpox had been eradicated.

Since then, new targets have been set by the WHO; to eradicate poliomyelitis and measles, and to significantly reduce the burden of many other infectious diseases by means of successful immunisation programmes and other public health measures.

Prior to 1974, vaccination programmes in developing countries were restricted to the urban elite, and children of school-going age were the main target, in spite of the fact that younger children are often more vulnerable to the diseases. Less than 5% of children under the age of one year were being vaccinated against six killer diseases: polio, diphtheria, tuberculosis, pertussis (whooping cough), measles and tetanus.

In 1974, the WHO initiated the Expanded Program on Immunization (EPI) with the aim of making immunisation available to every child by 1990. Almost 80% of children below the age of one year were being vaccinated by 1990, and this is estimated to have prevented more than three million deaths per year. This article will look at the current EPI (SA) programme and the rationale behind it.

The EPI (SA)

The Expanded Programme on Immunisation in South Africa, EPI (SA) was introduced in 1995 and initially covered the six diseases mentioned above, but many additional vaccines have become available worldwide, and several of these could have a major impact on the burden of vaccine-preventable diseases in South Africa. The introduction of combination vaccines, as well as improved vaccines, contributes to a more successful programme. Immunisation schedules for developing countries also need to be adapted to suit the epidemiology of the diseases.

When attempting to add vaccines to the EPI, several factors need to be taken into consideration. These include the burden and significance of the disease within the country, whether there is a safe and effective vaccine available, what the cost-benefit of the vaccine would be and whether the country could afford to implement it and, finally, whether the vaccine could be incorporated practically into the national EPI.

Several milestones have been reached in the history of the EPI(SA):

- 1995: Hepatitis B vaccine was introduced.
- 1999: Haemophilus influenzae type b (Hib) vaccine was introduced.
- 2000: BCG vaccine was converted from percutaneous to intradermal route.
- 2002: Neonatal tetanus was eliminated.
- 2006: South Africa was declared polio-free. Last reported case was in 1989.
- 2008: Conjugated pneumococcal and rotavirus vaccines were introduced.
- 2009: Change from whole cell pertussis vaccine to acellular pertussis vaccine, which has a better side effect profile. Oral live polio vaccine (OPV) replaced by inactivated polio vaccine.
Vaccinology: The South African Expanded Programme on Immunisation schedule

Hepatitis B

In 1996, there were approximately 50 million chronic carriers of hepatitis B virus (HBV) in Africa, with a 25% mortality risk. In sub-Saharan Africa, carrier rates ranged from 9-20%. Many studies have suggested that HBV transmission in Africa occurs predominantly in childhood, by the horizontal rather than the perinatal route.8

Vardas et al carried out a study to determine the epidemiology of hepatitis B in South Africa and found that, overall, 10.4% of the children tested were HBsAg-positive. There was a high rate of positivity in the 0-6 and 7-12 month age groups, of 8.1% and 8.9%, respectively, suggesting a higher rate of early acquisition of this infection than previously reported in South Africa. This was the highest reported rate of HBV infection in community-based children, indicating a significant burden of this infection in South Africa.9 Of children who become infected with HBV between one and five years of age, 30% to 50% become chronically infected. By adulthood, however, the risk of acquiring chronic HBV infection is only 5%.10 This highlighted the need for vaccinating infants to reduce the burden of hepatitis B.

Since data showed that transmission in infants is predominantly horizontal, rather than perinatal, there is no need for a birth dose of hepatitis B vaccine and the vaccine is, therefore, currently only administered at six, 10 and 14 weeks of age.

The benefits of introducing this vaccine was studied by Heno et al.

- They prospectively studied two different cohorts of 12- to 24-month-old children in South Africa.
- These cohorts consisted of unvaccinated children (n=459), born before the introduction of universal vaccination, and vaccinated children (n=1 213) between one and two years, born after the introduction of the vaccination programme.
- The frequency of detecting HBV DNA was reduced from 6.5% in unvaccinated children to 0.3% in vaccinated children (P<0.00001).11

Ongoing surveillance is necessary to monitor efficacy and to determine whether the epidemiology will change with time, necessitating introduction of a birth dose of hepatitis B vaccine.

Haemophilus influenzae type b (Hib)

H. influenzae can cause serious invasive disease, especially in young children. Invasive disease is usually caused by the encapsulated strains of the organism, usually type b.12

- Hussey et al studied the epidemiology of Hib in Cape Town in 1994.
- 65.5% of invasive Hib occurred in children under the age of one year, and 23.2% were younger than six months.

- One in 250 children contract Hib in the first year of life, and one in 11 die.
- Meningitis cases due to this micro-organism peaked at 7-12 months of age, and pneumonia peaked at 0-12 months.

These statistics motivated successfully for the vaccine to be introduced into the EPI in 1999, and South Africa was the first African country to introduce Hib into the EPI.13,14,15

In the first few years following the introduction of the Hib vaccine at six, 10 and 14 weeks of age, there was a significant decrease in the number of cases of invasive Hib disease in children under the age of five years, but especially in children less than one year of age. In recent years, however, there has been a steady increase in the number of cases in this young age group, and this needs to be carefully monitored and analysed.16,17 A booster dose at 18 months has now been introduced into the EPI schedule as one of the components of the combination vaccine, Pentaxim®.

Tetanus

In an attempt to provide lifelong protection from tetanus, the WHO currently recommends five doses of tetanus, with minimum intervals between tetanus toxoid (TT) doses for optimal seroconversion (see Table I).

The current primary series against tetanus in South Africa is administered at six, 10 and 14 weeks, which means that the interval between the second and third doses is too short and that the third dose, therefore, is not effective. The 18-month booster is thus considered the third dose, the school-going booster is the fourth dose and an additional dose has now been added to the schedule, given at 12 years of age. It is hoped that, if this schedule is maintained, it will no longer be necessary to vaccinate pregnant women to prevent neonatal tetanus in the future.18

Measles

South Africa set a goal to eliminate measles and interrupt the transmission of indigenous measles by the end of 2002. However,
the recent measles outbreak in Gauteng has dealt a major setback for measles elimination in South Africa.

The measles vaccine is most effective if given after the age of 12 months and is given at this age in developed countries. However, the WHO position paper on measles vaccine states that: “The optimum age for measles vaccination depends on the local epidemiological situation and, in countries with ongoing transmission in which the risk of measles mortality among infants remains high, the measles vaccine should be administered at nine months of age.”

According to the data collected in South Africa, almost 30% of cases occur in infants younger than 12 months of age and, for this reason, the first dose of measles vaccine is given at nine months, with a second dose given at 18 months of age.

Pneumococcal disease

Invasive diseases caused by Streptococcus pneumoniae are a major public health problem worldwide. These include pneumonia, meningitis and febrile bacteraemia. In 2005, the WHO estimated that 0.7–1 million children aged younger than five years, most of whom live in developing countries, die of pneumococcal disease every year.

Thanks to the development of the conjugated pneumococcal vaccine (PCV-7), many of these deaths can be avoided. The WHO has stated that: “It is a priority to introduce PCV-7 in national immunisation programmes, particularly in countries where the mortality among children less than five years is > 50/1,000 and where HIV prevalence is high, as the burden of pneumococcal disease is substantially higher among individuals who are infected with HIV.”

In South Africa, according to a study performed by Karstaedt et al, the minimum annual incidence for children younger than five years of age was 130 per 100 000 in 1996/7, and 349 per 100 000 for those < 12 months old. Collected data confirm that the age group at highest risk of disease in South Africa is infants under one year of age.

Although there are 90 different serotypes, 70% of invasive pneumococcal disease in children in South Africa under the age of five years is due to the serotypes contained in the current vaccine, Prevenar.

A trial in Soweto documented efficacy rates of 83% in HIV-uninfected children, and 65% in HIV-infected children. Although the efficacy is lower in HIV-infected children, they are at greatest risk of disease and, as the burden of HIV is high in South Africa, the vaccine has the potential to prevent a large number of disease episodes in this group.

Therefore, based on the background of a high disease burden in young children, especially amongst HIV-infected children, and the availability of a safe and efficacious vaccine, the conjugated pneumococcal vaccine has been introduced into the EPI. The vaccine was registered based on studies using a four-dose schedule:

- Three primary doses and a booster administered after the age of one year. The vaccine is given according to this schedule in the private sector.
- In the EPI, however, it is given as a three-dose schedule at six and 14 weeks and nine months (at the same time as the first measles vaccine).
- A three-dose schedule is used in some countries, but the third dose is usually given after the age of one year. In order for HIV-infected children to derive the most benefit from a three-dose schedule, and to fit in practically with the current EPI, the third dose is given at nine months in South Africa.

Rotavirus

In South Africa, diarrhoea causes more than 10,000 deaths a year, mostly in children under the age of five years, with a third to half due to rotavirus infection. The first infection is usually the most severe, with subsequent infections being milder. Sanitation and clean water have not had a significant impact on the epidemiology of this infection. An effective vaccine administered to infants could, therefore, save many lives. Once again, based on the burden of disease and the availability of an effective vaccine, a decision was made to include rotavirus in the EPI schedule. South Africa is the first African country to include both pneumococcal and rotavirus vaccines in the EPI.

Conclusion

When determining the most effective schedule for immunisation, various factors need to be considered, such as the age at which protection is required, the ability of the immune system to respond to the vaccine, the presence of maternal antibodies, the number of doses required to provide protection, the epidemiology of the disease and the need to ensure compliance. Taking all these factors into consideration, the EPI (SA) schedule has adopted a primary series of six, 10 and 14 weeks, ensuring protection at the earliest age, with boosters where applicable, and an early measles vaccine at nine months. The new EPI schedule attests to the commitment that the government has made to achieve the Millennium Development Goal 4, which aims, by 2015, to reduce by two-thirds the mortality rate among children under five.

References:

7. Introduction of Pneumococcal Conjugate (PCV-7) and Rotavirus Vaccines into the EPI – SA. Dr NJ Ngcobo Gauteng new vaccine training 2009.


