

By Dr Lam Mun San and Dr Wong Sin Yew

Adult Immunisations 2006: The Time is NOW



In Singapore, the success of our national childhood immunisation programme has resulted in the dramatic reduction in the incidence of vaccine-preventable diseases in the younger population. However, there remains a relatively high residual burden of vaccine-preventable diseases still observed in adolescents, adults and the elderly. There are common misconceptions regarding the circumstances that place adults at higher risk such as older age, chronic medical conditions, travel and sexual activity. There are several reasons for this 'increased susceptibility'; some adolescents and adults did not receive or did not complete their recommended primary vaccination schedule and booster doses. Other adults develop waning immunity as they age.

Many industrialised countries have now embarked on immunisation programmes for adolescents, adults and the elderly. Family

practitioners are in a unique position to enforce such programmes as they have first-line and extended contact with the public in the course of delivering basic medical care to them. A successful childhood immunisation programme should be complemented by an adult vaccination programme in order to close the gap for disease transmission by susceptible individuals.

Adult immunisations may be broadly categorised into the following:

1. 'universal' vaccines
2. occupational vaccines
3. vaccines for at risk individuals
4. travel vaccines

A vaccine that can be recommended to all to prevent a relatively prevalent infection that is associated with significant morbidity can be regarded as a universal vaccine. Ideally, the vaccine should be effective and inexpensive,

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making its use cost-effective. In the past, vaccines that have satisfied these criteria were oral polio vaccine, tetanus, diphtheria and measles vaccine. The present day closest equivalent is hepatitis B vaccine.

Occupational vaccines are for those who are at increased risk of certain infections by virtue of their occupation. These include rabies vaccine for veterinarians, veterinary students, taxidermists, dog handlers and so on, laboratory researchers working with viral and bacterial pathogens, as well as influenza vaccines for frontline healthcare workers, just to name a few examples.

Vaccines for high-risk persons include those who have underlying medical conditions and are at increased risks for complications from infection (example, pneumococcal and meningococcal vaccinations for patients with asplenia), and those who have behavioural risk factors that expose them to higher risks of infection (example, hepatitis A and B vaccinations for promiscuous individuals and illicit drug users).

Travel vaccines are recommended for individuals who travel to places that are endemic for diseases that are vaccine-preventable, example, typhoid, Japanese encephalitis, meningococcal meningitis and hepatitis A.

Certain vaccines may have a 'multi-purpose' function, example, hepatitis A vaccine may be recommended as a travel vaccine and also as an important vaccine for men who have sex with men.

INFLUENZA VACCINATION

Currently, there are several trivalent inactivated influenza vaccine registered in Singapore. These are either split virion or subunit vaccines (either adjuvanted or unadjuvanted).

There are widely accepted recommendations for influenza vaccinations:

- all adults who are 50 years or older
- chronic disorders of the cardiovascular or pulmonary systems including asthma
- chronic metabolic diseases like diabetes, renal dysfunction
- haematological disorder
- immunosuppression, HIV
- cognitive dysfunction or neuromuscular dysfunction predisposing to aspiration
- pregnant women

- caregivers or contacts of children 0 to 23 months
- healthcare workers
- care-givers of high-risk patients

A live attenuated influenza vaccine (LAIV) that can be given intranasally (FluMist®) has been registered in the United States for use in healthy, non-pregnant individuals between ages 5 to 49 who are not immunocompromised and not contacts of severely immunocompromised persons in special care units. This vaccine is not currently available in Singapore.

PNEUMOCOCCAL VACCINATION

Pneumococcal vaccination has been recommended for all adults above the age of 65. In many countries, the coverage has remained in the 20 to 30% range. This is unlikely to improve as long as the debate about the efficacy of the polysaccharide vaccine is not settled.

In contrast, the use of conjugate vaccine for young children targeting seven pneumococcal serotypes has reduced the cases of invasive pneumococcal disease in the vaccinated young population, and also in older adults. In a population-based surveillance of invasive pneumococcal disease in eight geographical areas (population of 18 million), the incidence in adults above 50 years was reduced by 28% from 40.8 cases/100,000 in 1998-1999 (pre-vaccination) to 29.4 cases /100,000 in 2002-2003. The incidence of invasive pneumococcal disease in this age group caused by the seven conjugate serotypes declined by 55%, whereas disease caused by any of the 16 serotypes found only in the polysaccharide vaccine did not change.

Other at risk individuals between 2 to 64 years old who should receive the polysaccharide vaccine are:

- persons with chronic cardiac or pulmonary disease
- chronic liver disease
- alcoholism
- diabetes
- CSF leak
- anatomic/functional asplenia
- sickle cell anemia
- HIV
- leukemia/lymphoma/multiple myeloma
- immunosuppressive or chemotherapy
- chronic renal failure or nephritic syndrome
- organ/bone marrow transplant

HEPATITIS B VACCINATION



Singapore was one of the first countries to adopt hepatitis B vaccination. This has certainly paid significant dividends with rise in hepatitis surface antibodies in the population, and reduction in hepatitis-related chronic liver disease and liver cancer incidence. With reduction in vertical transmission, sexual transmission is now the most common mode of transmission of hepatitis B in industrialised countries including Singapore.

For those who had not been vaccinated in infancy, many industrialised countries recommend 'catch-up' vaccination for all adolescents and adults who have an increased risk of exposure. The introduction of hepatitis B vaccination into the childhood vaccination programmes in many Asian countries have seen a dramatic decline in the incidence of hepatitis B associated hepatocellular carcinoma over the last two decades.

The vaccine should also be given to all non-immune adolescents and healthcare workers. It is also indicated in other older adults with risk factors:

- chronic renal failure on hemodialysis
- recipients of clotting factors and other plasma-based products
- men who have sex with men
- multiple sexual partners
- intravenous drug abusers
- contacts and sex partner of person with chronic hepatitis B infection

HEPATITIS A VACCINATION



Hepatitis A was initially touted as a travel vaccine for travellers outside of the US, Western Europe, Canada, New Zealand, Australia and Japan. However, this vaccine is also recommended for patients with underlying medical indications viz persons with chronic liver disease like hepatitis B and C. There are also indications for persons with behavioural risks, like men who have sex with men, illicit drug users, as well as occupational risks, like laboratory workers working with hepatitis A virus, primates, and exposure to infectious hepatitis A patients.

MEASLES, MUMPS AND RUBELLA (MMR)



In the past, a single dose of MMR II vaccine in childhood was recommended. This was revised

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to two doses in the childhood immunisation programme to increase the herd immunity when numerous outbreaks of measles and mumps occurred. Whilst many school children have been vaccinated with two doses of MMR II, many adults have only received one dose of MMRII and small outbreaks of measles and mumps continue to occur.

In an observational serological study of women presenting for prenatal care in North Carolina, Haas et al reported that 9.4% were susceptible to rubella, 16.5% to measles and 16.3% to mumps. Clearly, the current vaccine programme in many developed countries that has primarily focused on childhood immunisation has left many reproductively aged women (and by implication, much of the adult population) susceptible to these viral infections. Adults born before 1957 are considered immune to measles. Adults born after 1957 who have never received MMR II before should receive at least one dose of MMR. In these adults, a second dose is indicated if they are in the high-risk groups, example, healthcare workers, students entering college and international travellers. As a rule, all women and adolescent girls of child-bearing age should be immunised against rubella. They should be counselled regarding congenital rubella and to defer pregnancy planning for four weeks after immunisation due to theoretical risk of infection of the foetus from the live vaccine virus.

DIPHTHERIA – TETANUS



All adults with an uncertain history of immunisation should complete a primary series with Td vaccine. A booster is recommended for those who had completed the primary series more than 10 years ago. A booster dose as early as 5 years may be given for wound management.

PERTUSSIS



Pertussis is a highly contagious, vaccine-preventable bacterial illness characterised by paroxysmal cough, posttussive vomiting and inspiratory whoop. In the past, most cases occurred in infants less than 6 months of age. With improvements in childhood coverage, morbidity and mortality in infancy has dramatically reduced by the 1970's. Interestingly in the United States, reported pertussis cases increased tenfold from 1010 in 1976 to 11,647 cases in 2003. A substantial number of cases occurred among adolescents who had become susceptible to pertussis because of waning immunity. Until recently, there was no booster vaccines for pertussis in adolescents and adults. Recently, a combined vaccine containing tetanus, diphtheroid toxoids and pertussis antigens (Boostrix®) became available for use by adolescents and adults. This vaccine elicited robust immune responses in adolescents and adults while exhibiting a safety profile similar to that of currently available Td vaccines.

Health authorities in the US now recommend that adolescents should receive a booster dose of pertussis vaccine to combat waning immunity and it is often administered as a combined vaccine with tetanus, diphtheria toxoids together with pertussis antigens.

VARICELLA



Varicella vaccine has been registered in Singapore for almost ten years. We continue to have a significant number of chickenpox notifications in Singapore. The age group most affected are young adults and adolescents. All susceptible adults and adolescents should be vaccinated. In particular, the following groups should receive vaccination:

- healthcare workers
- care-givers of immunocompromised patients

- teachers of young children, day care workers
- workers in correctional institutions, colleges, long-term care facilities
- military personnel
- international travellers

MENINGOCOCCAL



Except for the meningitis belt in Sub-Saharan Africa and Saudi Arabia, most parts of the world have sporadic meningococcal disease with occasional outbreaks. Meningococcal vaccination is indicated in the following situations:

- mandatory for travel to Saudi Arabia for Hajj and Umrah (mini Hajj)
- travel to Sub-Saharan Africa meningitis belt during transmission season
- first year college students living in dormitories
- laboratory workers working with meningococcus
- military recruits

Meningococcal conjugate vaccine is preferred although the polysaccharide vaccine is an acceptable alternative.

BARRIERS TO IMPLEMENTATION OF ADULT IMMUNISATION



In a Swiss survey of 1166 physicians, the majority (75%) considered immunisation of adults a public health priority and an important asset for reducing healthcare costs. However, some factors were identified as barriers. Lack of time to convince a patient or to verify his immunisation status were associated with lower use of vaccination. Patients' refusal was frequently reported as a barrier to implementation. Vaccine safety was cited as an important factor for patient refusal. Lack of reimbursement has also been reported by others as an important barrier to successful implementation.

To have a successful immunisation programme for adults, these factors will need to be addressed, including reimbursement, education materials, public education and governmental support.

FUTURE VACCINATION



Two new promising vaccines will be discussed. These are not registered for use as yet but will hopefully be available in Singapore in the near future.

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Human Papilloma Virus Vaccine

Two vaccines against human papilloma virus (HPV) which target the most oncogenic strains of HPV have been studied separately in Phase 3 trials. One vaccine (Gardasil®, Merck) was found to be 95% effective in preventing development of vulvar or vaginal lesions that can be precursors of cervical intraepithelial neoplasia. In a separate study by GlaxoSmithKline using their candidate vaccine with an investigative adjuvant AS04, it was found to be 100% effective against both persistent infection with HPV types 16 and 18 and the virus' associated cervical lesions in women.

The two vaccines represent an important step forward in preventing a key factor for development of cervical cancer. Young adolescent females and young women are the targets of vaccination to prevent HPV infection before they become sexually active. Trials of the vaccine to see if they are equally effective in men are ongoing.

Herpes Zoster

A randomised double blind trial of a live attenuated zoster vaccine which was effective in reducing the burden of herpes zoster and post-herpetic neuralgia in older adults was

published in the *New England Journal of Medicine* (NEJM), 2 June 2005. The incidence of herpes zoster and post-herpetic neuralgia increases with age in association with a decline in cell-mediated immunity to varicella zoster virus (VZV). A zoster vaccine can elicit a significant increase in cell-mediated immunity to VZV and reduces the incidence and severity of herpes zoster in older persons.

“It is hoped that the use of a zoster vaccine would eradicate zoster and its related complications just as measles vaccine has wiped out not only measles but also measles-associated post-infectious encephalomyelitis and sub-acute sclerosing panencephalitis in regions where the vaccine is used.” (Donald Gilden, University of Colorado Health Science Centre, editorial in NEJM)

CONCLUSION

In Singapore, we have made some inroads where adult vaccination is concerned. We have success with the various travel clinics in the restructured hospitals as well as polyclinics offering influenza vaccination, hepatitis vaccination and other travel-related vaccinations. Hospitals are offering infection control programmes with an emphasis on the well-being of healthcare workers, and this includes hepatitis B and influenza vaccinations package. Family practitioners are also more aware of the importance of prevention, and proactive in offering immunisations.

Finally, we hope to be able to see a consensus statement/guideline on adult vaccination in Singapore in the near future so that this can be propagated to our medical community. ■

Suggested Reading:

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4. Haas DM, Flowers CA, Congdon CL. Rubella, Rubeola and mumps in pregnant women: susceptibilities and strategies for testing and vaccinating. *Obstet Gynecol* 2005;106:295-300.
5. CDC Guidelines : MMWR. Recommended Adult Immunisation Schedule – United States, October 2005 – September 2006.