

# A Brief Vaccine Update for the Busy GP

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There have been a number of new developments in the field of vaccine preventable conditions. These have ranged from the evolution of protein conjugate vaccines like Prevnar-13 to novel vaccines of which the zoster vaccine or Zostavax is an example.

## PNEUMOCOCCAL VACCINES (PREVNAR 13, PPSV23)

**I**nfections due to streptococcus pneumoniae continue to adversely impact morbidity and mortality especially among older adults. In Singapore, an attributable mortality of 21.4% was noted amongst 192 adult cases of invasive pneumococcal disease from 2000 to 2007<sup>1</sup>.

Incorporating capsular polysaccharide which is virulence determinant of streptococcus pneumoniae is the basis for pneumovax or PPSV23. This consists of capsular material from 23 pneumococcal types which account for 75.4% of invasive pneumococcal disease in Singapore in 2012<sup>2</sup>.

Conjugate vaccines offer a possible advantage of eliciting immunological memory, hence priming the immune system for either natural exposure or subsequent booster vaccination. Major reductions in the incidence of pneumococcal disease have been impacted by the use of these vaccines in childhood with resultant herd effect causing significant decrease in pneumococcal disease due to vaccine serotypes in unimmunised older children and adults. A pneumococcal conjugate vaccine, PCV13 is now available formed by linking capsular polysaccharides from 13 most common serotypes that cause disease to a nontoxic protein.

Preliminary results are available from a randomized, placebo-controlled, double-blind, single-centre trial in which subjects aged 65 years and older were randomly assigned to receive a single dose of either PCV13 or placebo<sup>3</sup>. Amongst almost 85,000 subjects, there were 45%

fewer first episodes of vaccine-type community acquired-pneumonia and 75% fewer first episodes of vaccine-type invasive pneumococcal disease among PCV13 recipients compared to placebo. While the results are encouraging, the study does not compare PCV13 with PPSV23. Available data however show that conjugate vaccines are more effective than polysaccharide vaccines in HIV-infected patients in Africa serving as a surrogate for immunocompromised populations<sup>4</sup>.

## PPSV23 or PCV13?

PCV-13 has been shown to be as safe as PPSV23. Unlike PPSV23, PCV-13 is antigenic in children under the age of two and can be used in this age group. A single dose of PCV-13 is recommended in at risk groups and revaccination is not required unlike PPSV23 which needs to be re-dosed in adults  $\geq 65$  years of age if they were vaccinated more than five years previously at a time when they were less than 65 years of age. Unlike PCV-13, PPSV23 cannot interrupt carriage or impact on herd effect. Their efficacy against invasive pneumococcal disease is unclear especially in older and high-risk individuals. Nevertheless, PPSV23 remains cost-effective for the low-risk elderly. The main drawbacks of PCV13 are its cost, lesser serotype coverage and the possible appearance of replacement strains. The United States Advisory Committee on Immunization Practices (ACIP)<sup>5</sup> endorses PCV13 over PPSV23 for adults with certain underlying medical conditions based on theoretical considerations and on results that some immunocompromised populations may show better responses.

For instance while patients who smoke, are alcoholic, or who have diabetes mellitus, and are more than 65 years should receive PPSV23, but persons with functional or anatomic asplenia, and who have immunocompromised conditions like HIV infection or malignancies like lymphoma should receive both PCV13 and PPV23 given sequentially.

## CONJUGATE MENINGOCOCCAL VACCINES

**2.** Apart from travelers to endemic areas, prevention of meningococcal meningitis is relevant to those with functional or surgical asplenia, complement component deficiencies, and overseas educational requirements.

Protein conjugate vaccines have also evolved for the prevention of meningococcal disease. The older quadrivalent meningococcal polysaccharide vaccine (Mencevax) has a good track record and is well tolerated. However repeated vaccinations may result in hyporesponsiveness. This is important as meningococcal vaccine boosters are recommended at 3 to 5 years intervals. As with other polysaccharide vaccines, they are not immunogenic in children under 2 years of age, and have little impact on clearing nasopharyngeal carriage and herd immunity.

By conjugating neisserial polysaccharides to carrier proteins a T-cell-dependent immune response can be elicited and is the basis for the new quadrivalent meningococcal conjugate vaccines (Menactra, Menveo, and Nimenrix) currently available.

The pendulum appears to be swinging more in favor of these relatively new protein conjugates vaccine over the older polysaccharide type. Expert opinion and major health bodies in the European Union, Canada, and Australia recommend the use of quadrivalent conjugate vaccines for travelers.

A recent study<sup>6</sup> showed that Menveo and Menactra show good antibody responses against all 4 serogroups. Three years after primary immunization the proportions of vaccine recipients with protective titres were higher in persons vaccinated with Menveo than with Menactra for serogroups W135 and Y, but were no different against serogroups A and C.

A single dose of Menveo booster led to excellent response to all serogroups.

These vaccines are generally well tolerated. Those with past cutaneous reactions involving skin necrosis (Arthus-type reaction) may need deferment of vaccines for a minimum of 10 years after the last dose. Although no clear link was established in previous rare reports of Guillain-Barre Syndrome (GBS) post vaccination, GBS continues to be listed as a precaution in the drug inserts. However since 2010 ACIP had removed a history of GBS as a precaution for Menactra.

### VARICELLA ZOSTER (ZOSTAVAX)

**3.** Up until recently herpes zoster was an unpreventable malady. However data from a landmark study<sup>7</sup> showed that a onetime subcutaneous injection of a novel vaccine, Zostavax reduced the incidence of herpes zoster by 51% compared with placebo in adults 60 years of age or older. It paved the way for the approval of this live attenuated vaccine in persons  $\geq 60$  years of age including those with previous episodes of zoster. In some countries like the United States, it is approved for adults  $\geq 50$  years. It is well tolerated with injection site pain being the most common side effect.

Being a live vaccine, Zostavax is contraindicated in immunocompromised conditions including leukemia, recipients of cancer chemotherapy and immunomodulatory therapy, post-transplant recipients, HIV infected individuals with a CD4 cell count of  $< 200$  cells/ul, and those who receive a dose  $\geq 20$  mg/day of prednisolone for  $\geq 14$  days.

### HUMAN PAPILLOMA VIRUS VACCINE (HPV) (Gardasil / Cervarix)

**4.** Safe and effective vaccines<sup>8</sup> are now available for the prevention of infection due to HPV 16 and 18 which are implicated in cervical cancers and HPV 6 and HPV 11 causing genital warts. The quadrivalent vaccine (Gardasil) includes HPV types 6, 11, 16, and 18, while the bivalent vaccine (Cervarix) includes HPV types 16 and 18. Gardasil is given as 3 doses at time 0, 2 and 6 months of follow-up. Cervarix is administered in 3 doses at time 0, 1 and 6 months of follow-up.

Immunization is most effective prior to acquisition of HPV hence before sexual debut. Those who are already sexually active may still benefit from immunization because they may not yet be exposed to HPV subtypes covered by the vaccine. Immunization of females should be offered to girls 9 years through to 26 years.

The quadrivalent but not the bivalent HPV vaccine is effective in preventing both genital warts in young males and anal intraepithelial neoplasia among men who have sex with men. In many countries, immunization is also offered to boys aged 9 to 26 years.

### TETANUS/ DIPHTHERIA/ PERTUSSIS (Tdap - BOOSTRIX)

**5.** Booster immunization with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine is rarely followed up in adults. Being part of routine childhood vaccination in children, DTaP is followed by a booster dose of Tdap at 10 to 11 years of age. It is not often practiced but subsequent tetanus doses, in the form of Td, should be given at 10-year intervals throughout adulthood. It is imperative to note that tetanus immunization should be reviewed in the context of acute traumatic wounds especially if heavily contaminated regardless of prior tetanus and diphtheria immunization.

Many practitioners also do not associate pertussis as a cause of protracted cough in adults. It is also not commonly appreciated that without boosting protection after childhood vaccination is insignificant after 10 years. A recent study in Singapore<sup>9</sup> highlighted the dichotomy between the seroprevalence of 97% amongst adults as compared with a historical seroprevalence of 50% amongst adolescents suggesting acquisition of natural infection. This argues for booster vaccine for adolescents and young adults in Singapore. The ACIP recommends a single booster administration with Tdap for adults aged 19 and above, those with obesity and pre-existing asthma and persons having close contacts with young children.

### OTHER VACCINES

**6.** Sporadic cases of measles, and mumps continue to appear in Singapore. Recently there was also an outbreak of measles in the Philippines. It is important to know that **2 doses of MMR** (measles, mumps, and rubella vaccine) are required for adequate protection.

There is a relatively new purified, inactivated vaccine for **Japanese encephalitis** (Ixiaro) for travelers at risk to rural agricultural endemic areas in Asia and the Western Pacific.

There are still several areas in the world which continue to report cases of **polio**. A booster dose of OPV or IPV between 4 weeks and 12 months is recommended prior to travel for long term travelers to countries like Nigeria, and but should be given for long term travelers to Pakistan, Cameroon, or Syria.

Last but certainly not least, as we strive to protect our patients, we must remember to keep our own vaccine record updated. The annual seasonal **influenza** vaccine should not be forgotten.

**In summary**, the newer vaccines to consider for adults include:

- 1. Pneumococcus** – All people age 65 years or older should receive a one-time dose of PCV13 (if previously unvaccinated) followed 6 to 12 months later by 1 dose of PPSV23. In adults younger than 65 years who smoke cigarettes, or have chronic cardiac or pulmonary disease (including asthma), chronic liver disease, alcoholism or diabetes, administer at least PPSV23. Those with more immunocompromising conditions like HIV infection should receive the PCV-13 first followed at least 2 months later by PPSV23
- 2. Meningococcus** – Recommended for travellers to endemic regions (e.g. for the Haj - the polysaccharide vaccine e.g. Mencevax may be given), and for college students living in student housing and for those requiring future

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repeat doses of the meningococcal vaccine (the new quadrivalent meningococcal conjugate vaccines e.g. Menactra/ Menveo / Nimenrix preferred)

**3. Human Papilloma Virus (HPV)** – HPV vaccine should be offered to girls and boys aged 9 – 26 years. In girls, the bivalent or quadrivalent vaccines may be administered, and in boys only the quadrivalent vaccine.

**4. Herpes Zoster** – Zostavax recommended for all adults above 60 years. May be given after 50 years age.

**5. Tetanus, Diphtheria, Pertussis** – All adults who have not already received Tdap or whose Tdap history is not known should receive a single dose of Tdap, followed by Td booster every 10 years. (A dose of Tdap should be given regardless of interval since previous Td). In each pregnancy, the Tdap should be administered during the 3rd trimester.

College Mirror asked Dr Asok Kurup for advice on the following scenarios:

**Scenario 1:**  
**In advising a 50 year old healthy adult about routine vaccinations, unrelated to travel, which vaccinations are recommended?**

Dr AK: The following routine vaccinations are to be considered: Influenza, Pneumococcal (specific indications), Hepatitis A & B, Zostavax, Tdap, Hemophilus Influenza.

**Scenario 2:**  
**What is the recommended timing of Zostavax vaccination following herpes zoster (shingles) infection?**

Dr AK: There is no specific guideline on this, but as a rule, it may be prudent to wait 6 to 12 months after resolution because zoster itself can induce some immunity. By deferring the vaccine we can potentially boost immunity better.

**Scenario 3:**  
**Use of Tdap instead of tetanus toxoid (TT) to a patient with a contaminated wound.**

Dr AK: What is relevant here is TT; if the Tdap has already been given once to an adult then subsequent regular boosters every 10 years is with Td; however in the case of a contaminated wound proceed with TT.

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