

Voice of the Expert

Adult Vaccination : Some Frequently asked Questions & Answers

Question : Why is HPV vaccine approved from 9 to 45 years in India whereas in many countries like USA it is approved from 9 to 26 years?

Answer— In many countries QHPV is approved from 9 to 26 years. In many countries the approval is sought up to 45 years based on the efficacy trials named FUTURE 3 trials in which efficacy for the age group 24 to 45 was shown to be around 90% (89% to be precise). Thus, based on the results of FUTURE 3 studies the ADULT WOMAN INDICATION (AWI) was granted. Currently QHPV is approved in 135 countries and in 54 countries for the age group of 9 to 45 i.e. AWI. India, Canada, Australia, New Zealand are examples of some countries where it is approved from 9 to 45 yrs.

In countries like USA, vaccines are given through either public or private insurer, which compels them to give it in best recommended age i.e. primary schedule and in catch up vaccination schedule for those missed during primary vaccination age. Also cost effectiveness would be more if it is given in age when you would get better immune response and ultimately clinical benefits.

Question : What is the maximum duration of protection that can be given with QHPV. Our patients ask us “will I be protected against cervical cancer forever”

Answer— QHPV was developed and launched in the year 2006. Mathematical models have predicted that protection (antibody titers) will last up to 32 years upon completion of 3rd dose.

In addition, many subjects from NORDIC countries (Denmark, Norway, Iceland & Sweden) are being followed up from 2003 till now. This data is called as NORDIC data or LTFU (Long term Follow up) data. The 14-year findings of this NORDIC data was presented at EUROGIN in 2018 and NO BREAKTHROUGH CASE was found. As of June 2020 the NORDIC data is published.

- Long term data from age of 9 to 26 yrs (NORDIC data) – 14 years no breakthrough (100% effectiveness)
- Long term data from age of 24 to 45 yrs – 10 years no breakthrough.

Question : I know there are 3 doses but what happens if someone misses the dose? What to do in such circumstances?

Answer— There are 3 doses of QHPV which has to be administered in the following schedule

- 1st dose – 0 months
- 2nd dose – 2 months
- 3rd dose – 6 months

ALTERNATIVE SCHEDULE

- 1st dose – 0 months
- 2nd dose – 1 month
- 3rd dose – 4 months

As long as all 3 doses are completed in one year it is fine. But it is best to complete the schedule in 0, 2 & 6 months.

Based on the post-hoc analysis, comparable efficacy will get if minimum gap between 1st & 2nd dose is 1 month and that of between 2nd & 3rd dose is 3 months.

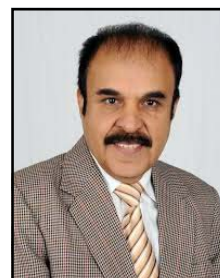
For girl's b/w 9 to 14 years – 2 doses 6 months apart is the schedule. If they, miss that schedule then you have to administer 3 doses.

Although approved in many countries – this vaccine is not approved for usage in Men/Boys in India as of now.

Question : When do I vaccinate. What age group? Which age group is best for vaccination?

Answer— HPV infection is sexually transmitted and is usually acquired within the first few years following sexual debut. Ideally, therefore, the vaccine should be administered before sexual debut, i.e. before any risk of exposure to HPV (age from 9 yrs. till 15 or 16 yrs.). Also, it is important to remember that antibody response to vaccine is much higher in younger age group. Thus, young age (9 to 15-17 yrs) is best age to vaccinate.

However, if one cannot vaccinate young and adolescent girls due to any reason then one must vaccinate at the next available opportunity as the



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window period to vaccinate is long (9 to 45 yrs.).

Another opportunity for vaccination is POST PARTUM period as QHPV is found to be safe in this period. There are studies which have indicated that women are also more receptive to the idea of vaccination, hence they listen to their OBGYNs for vaccination.

The whole idea is to improve practice patterns so that clinicians use every opportunity to recommend HPV vaccines and address questions from parents. This can help realize reductions in vaccine-preventable infections and cancers caused by HPV.

In "safe motherhood" programs of India, this vaccination may be included.

Question : What if a woman becomes pregnant after taking the vaccine? Or she was already pregnant and had taken the vaccine?

Answer — Vaccination Should NOT be done during pregnancy. The reason is that there not enough well controlled studies done in humans for pregnancy as getting approvals & subjects for studies during pregnancy is difficult.

However, if someone was pregnant or gets pregnant and vaccination does happen there is NO NEED for termination of pregnancy as the studies have indicated that vaccine does not cause any risk of additional fetal malformations or abortions or any harm. However as soon as pregnancy is confirmed the remaining dose/s should be deferred and can be administered after the delivery.

Reference - 6 years pregnancy registry data (Mary Ann Goss, 2014)

Question : Is there any use of protection against genital warts (GW)? I hardly see any cases of GW?

Answer — The prevalence of GW as done by a study in India was around 1%.

Another study done in Denmark with a follow up of 30 yrs. involving around 50,000 subjects indicate that **Diagnosis of GW was strongly related to anal, vulvar, vaginal, cervical & sub sites of Head & Neck cancer with confirmed HPV association.** Hence if one can prevent GW then one must.

Question : I do screening regularly. Is screening better & more cost effective than vaccination or is vaccination a better tool?

Answer — Ideally both screening & vaccination should go hand in hand. Just because you are screened DOES NOT mean that you don't require vaccination and vice versa. Also, there is no need of doing screening just prior to vaccination.

Thus, it is best to vaccinate as well as follow the guidelines for screening of that country

Question : I understand that vaccination is good, but development of cervical cancer takes almost 10 to 15 years then how we know if the vaccine is going to prevent cancer in say a lady who got vaccinated just now or one year ago.

Answer — Since the vaccine was launched in 2006 many countries have adopted it in their NIP (National immunization program) and we are beginning to get good "REAL WORLD EFFECTIVENESS" data from such countries. Ex- Australia, New Zealand, Denmark, Sweden etc.

One recent and interesting data from Australia which is one of the first countries to include QHPV in their NIP indicates - "With data from a state-based cervical screening register, we have shown a decrease in high-grade cervical abnormalities in young women after the implementation of the vaccination program".

Also, since GW takes less time to develop as compared to Cancer there has been a substantial reduction in GW in both women & men.

Similarly, we have encouraging data from other countries too.

Question : What about cross protection. I heard that Bivalent offers cross protection against other HPV serotypes namely 31,33,45 etc. whereas QHPV does not?

Answer — It is worthwhile to remember that both QHPV & BHPV contains HPV 16 & 18 which are "High risk types" i.e. these are associated with cancer causation especially cervical cancer (Globally 16 & 18 are responsible for causing 70% of all cervical cancer case whereas in India they are responsible for causing around 82% of the cases). Hence, we should be focusing more on the serotypes which are by far predominantly responsible for causing most of the cancers i.e. 16 & 18.

As far as protection against other serotypes is concerned the cross protection with both the vaccines is inconsistent & short lived.

Direct protection & Long term follow up are the best

indicators for protection (NORDIC data with QHPV) rather than cross protection.

Merck has launched GARDASIL 9 (HPV serotypes 6, 11, 16, 18, 31, 33, 45, 52 & 58) this will take care of >90% of the HPV responsible for cancer. However, GARDASIL 9 is as of now not available in India.

Question : Is the vaccine safe? I have read on internet and media about stories doing the rounds? I am a bit concerned?

Answer — There is no denying that the vaccines have attracted a bit of negative publicity. However, it is important to remember that many international bodies like: - USCDC (Centre for Disease control), WHO, EMEA (European medicines agency) have conclusively said that vaccine is safe.

In almost all the cases the complaint filed due to or against the vaccine has not been found to be associated with the vaccine ie, CAUSALITY could not be attributed to the HPV vaccines.

In addition, surveillance is ongoing, and the vaccines will continue to be monitored.

Our own FOGSI & IAP (Indian Academy of Pediatrics) have recommended this vaccine.

One must not pay heed to online rumours.

Question : Is it true that antibody titers with QHPV falls after some time and we might need a booster?

Answer — It is important to note that both QHPV and BHPV induce antibodies and after some years that antibody levels fall. But it is equally important to note that this quantitative estimation of FALL in antibodies has no effect as far as protection against HPV is concerned because the level of antibodies required to provide protection against HPV is not defined. Thus, currently there is no need for any booster.

In addition, instead of going for indirect markers like antibody titers the best indicator of protection is *CLINICAL ENDPOINTS* ie, *ABSENCE OF DISEASE* that is where current NORDIC data of 14 years becomes important.

Question : I recommend the vaccination to almost everyone yet very few come forward for vaccination. What should I do?

Answer — Studies have demonstrated that the strongest recommendation comes from the physician/OBGYN/doctor

Some strategies are : -

- Strongly recommend adolescent vaccines to parents of your 9 year and older patients. **Parents trust your opinion more than anyone else's when it comes to immunizations.**
- Use every opportunity to vaccinate your adolescent patients. **Ask about vaccination status when they come in for sick visits.**
- **Use vaccine on Postpartum period/Post-delivery** – If the woman has not received HPV vaccination earlier.
- Patient reminder and recall systems such as automated **postcards, phone calls and text messages are effective tools for increasing office visits.**
- **Educate parents about the diseases that can be prevented by vaccines.** Parents may know very little about pertussis, meningococcal disease, or HPV.
- **Implement standing orders policies** so that patients can receive vaccines without a physician examination or individual physician order.

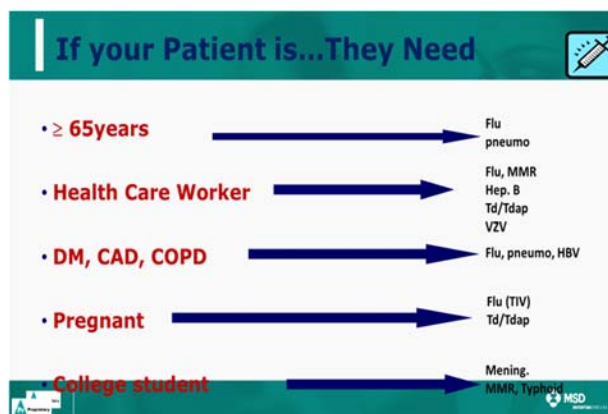
All branches of medical science must come forward for promoting HPV vaccinations.

OTHER QUESTIONS

Vaccination Related :

1. Should Health care workers and doctors also take Pneumococcal and Influenza vaccination during this COVID times?

Answer — yes, everyone should be protected as per their age and indication



2. What will be the pneumococcal Vaccine schedule for a 50+ healthy HCP (Health Care provider)?

Answer — As per the latest ACIP (Advisory Committee on Vaccines and Immunization practices)-2019 guidelines if there is no underlying medical condition ie, person is healthy b/w age of 19 to 64 years no Pneumococcal vaccine is recommended.

3. What is the relevance of Pneumococcal vaccination during this COVID pandemic times?

Answer — As per the NFID (national Foundation for Infectious Diseases) Although there is no vaccine available to prevent COVID-19 at this time, ensure that other vaccinations are up to date, including influenza and pneumococcal vaccines. This will help reduce the

pressure on the healthcare system by reducing vaccine-preventable diseases.

Physicians of today must discuss adult vaccinations with their patients. There are many studies which have proved the efficacy of these vaccines in reducing mortality.

For example, Meningococcal Vaccine may be given to inmates of prisons or crowded hostels to reduce mortality.

Similarly, people going on trekking or jungle safaris must take Typhoid Vaccine.

Thank you Dr. A. Muruganathan for your answers. We appreciate the time taken by you and we are sure that our readers will be benefited immensely.

VACCINE TABLES

RECOMMENDED VACCINATION SCHEDULE FOR HEALTHY ADULTS

Vaccine	Recommended age of vaccination
Influenza (flu)	Yearly
Tetanus, diphtheria (Td) Or Tetanus, diphtheria, pertussis (Tdap)	Td every 10 years Replace one dose with Tdap
Varicella (chickenpox)	Two doses (unless had documented disease or immunized as a child or adolescent)
Human papillomavirus (HPV)	Three doses before 26 years of age (unless already immunized as an adolescent)
Measles, mumps, rubella (MMR)	One or two doses (unless immunized previously with two doses after the age of 1 year, known to have been previously infected)

VACCINES THAT MIGHT BE INDICATED FOR ADULTS BASED ON MEDICAL AND OTHER INDICATIONS

	Pregnancy	Splenectomy	Diabetes	Kidney disease and hemodialysis	Heart disease, HIV lung disease and chronic alcoholism	Liver disease	
Influenza	Yes	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	
Tdap	One dose for every pregnancy	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	Similar to healthy adults	
Hepatitis B	If there is no immunity	-	Yes	Yes	-	Yes and Hepatitis A if no immunity	
Pneumococcal vaccine	-	PCV 13 PCG 23	PCV 23 (Preferred)	PCV 13 PCV 23	PCV 23 (Preferred)	PCV 13 PCV 23	PCV 23 (Preferred)
Meningococcal vaccine	-	Either conjugated or polysaccharide	-	-	-	-	-
Haemophilus influenzae type B	-	One dose	-	-	-	-	-

VACCINATION FOR HEALTHCARE WORKERS

Influenza	One dose annually
Tdap	Similar to healthy adults
Hepatitis B	3 doses if no immunity followed by booster dose once in 5 years
Varicella	Two doses (unless had documented disease or proof of immunity)
MMR	One dose at the time of joining health care job
Typhoid	For food handlers in the hospital kitchen and microbiology laboratory personnel once in 3 years

VACCINE TABLES			
TRAVEL VACCINATION			
	Visitors travelling India	Indians travelling to USA	Travel vaccines
Typhoid	2 weeks before the travel		
Hepatitis A	2 weeks before the travel		
Hepatitis B	2 months before travel	Similar to healthy adults	
Rabies	3 doses (0,7,21) 1 month before travel		
Japanese B encephalitis	2 doses at 4 week interval, 1 month before travel		
Influenza	1 dose annually	1 dose annually	
Tdip		Students and visitors above the age of 65 years going to handle children	
MMR		One or two doses for students going for higher studies	
Polio			Travelers to Afghanistan, Cameroon, Equatorial Guinea, Ethiopia, Iraq, Israel, Nigeria, Pakistan, Somalia and Syria
Meningo-coccal vaccine		One or two doses for students going for higher studies	To persons going for Haj pilgrimage
Yellow fever			Africa : Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Coted' Ivoire, Democratic Republic of Congo, Equatorial Guinea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea Bissau, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Rwanda, Senegal, Sierra Leona, Sudan, South Sudan, Togo, Uganda South America : Argentina, Bolivia, Brazil, Colombia, Ecuador, French, Guyana, Guyana, Suriname, Trinidad (Trinidad only), Venezuela, Panama, Paraguay, Peru