Section 14 Immunology

Chapter 101

Adult Immunization

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INTRODUCTION

There is a common consensus among public health managers that disease prevention is the most cost-effective option to protect and promote health of populations and immunization is the key to achieve the same. Childhood immunization policies are primarily directed against six killer diseases, with hepatitis B added lately to the list. Protecting adults through vaccination has never been considered a preventive strategy likely to have a great impact on population health. Though adults are less susceptible to fall prey to traditional infectious agents, emergence of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) and re-emergence of malaria and tuberculosis worldover has complicated the prevailing fragile health scenario. Also, the probability of exposure to infectious agents have increased manifold owing to globalization and increasing travel opportunities both within and across countries. Though World Health Organization (WHO) considers childhood vaccination as first priority, it keeps on issuing lists of essential vaccines for adults as well. Thus, there is an urgent need to address the problem of adult immunization.

ADULT VACCINATION

The following discussion on adult vaccination is mainly based on: (1) "Expert Group Meeting for evolving Consensus Recommendations on Adult Immunization in India" which was jointly organized in December 2008 by the Association of Physicians of India (API) and the Department of Medicine, All India Institute of Medical Sciences (AIIMS) to address this issue and (2) the latest Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (CDC ACIP) guidelines 2012 (**Table 1**).

NEWER VACCINES IN THE PIPELINE

Dengue Vaccine[4]

- At present only one live attenuated chimeric tetravalent dengue vaccine is in phase III trial.
- This vaccine was found to be effective against three of the four dengue serotypes.
- The vaccine demonstrated 61.2%, 81.9% and 90% efficacy against dengue virus type 1, type 3 and type 4 respectively with impressive safety profile.

Malaria Vaccine[8]

- Vaccine for *Plasmodium falciparum* malaria has been invented. It consists of *P. falciparum circumsporozoites* protein from pre-erythrocytic stage of parasites.
- The RTS, S/AS01 vaccine (phase 3) provided protection against both clinical and severe malaria in African children (NEJM).

HIV Vaccine

- Currently over 60 and 30 candidate vaccines are in phase I and II respectively.
- Research is going on broadly neutralizing antibodies (bNAbs), a type of antibody that can be found in blood of HIV patient, capable of stopping the HIV virus from entering blood cells and replicating, thereby arresting HIV infected person's progression to AIDS. Though mutable, parts of HIV are relatively change resistant, this is a key to its ability to infect white blood cells and multiply, these are parts of HIV that bNAbs target.
- VaxGen gp120 protein subunit vaccine is in phase III trial at present.

Hepatitis C Vaccine

- It is at present in phase II trial.

Hepatitis E Vaccine[9]

- It was developed in China and was approved in June 2012.
- Recombinant HEV vaccine (HEV 239): 3 doses (30 μg of purified recombinant hepatitis E antigen per dose) of HEV 239 administered at months 0, 1 and 6 resulted in 100% efficacy at 1 year in a Chinese study.

CONCLUSION

We can conclude that adult immunization must become a fundamental part of routine patient care. Adult vaccination saves lives.

TABLE 1 | Adult vaccination

Cholera[1]

Oral cholera vaccine (WC-rBS/Dukoral) (monovalent inactivated killed whole cells of *Vibrio cholerae* O1 plus recombinant cholera toxin B subunit)	*Indications:* • Not for routine adult immunization • Not recommended for outbreak control or for prevention of outbreaking during emergencies	*Schedule:* • 1–6 weeks apart 2 doses

- BivWC (marketed as "Shanchol" and "mORCVAX") is a bivalent inactivated vaccine containing killed whole cells of *V. cholerae* O1 and *V. cholerae* O139. mORCVAX is only available in Vietnam.
- VaBiotech (bivalent killed whole cell oral cholera vaccine) not yet approved by WHO. Licensed for use only in Vietnam. The results of randomized controlled trial (RCT) Phase 3 conducted at Kolkata are still awaited.

TT/Td/Tdap (Diphtheria, pertussis, tetanus)[2]

Tdap (tetanus toxoid, diphtheria toxoid and acellular pertussis)	*Indications:* • In all adults not immunized earlier • Contacts with infants suffering from diphtheria or pertussis and last Td vaccine dose > 2 years ago • Adults who are in close contact with infants • Health care personnel • During pertussis outbreak • In pregnant patient: – Td within 10 years: Booster in immediate postpartum period – Td > 10 years: Booster in 2nd or 3rd trimester – Not immunized: 3 doses in 2nd or 3rd trimester • Postexposure prophylaxis: – Minor/uncontaminated wound: One booster dose of TT given if last dose taken > = 10 years back – Major/contaminated wound: One booster dose of TT given if last dose taken more than 5 years back	*Schedule:* • 0.5 mL intramuscular (IM) deltoid • Primary: 3 doses; 0, 1, 6–12 months • For contacts: Single dose 2 weeks before contact • Outbreak: Single dose if 2 years or more have elapsed from the last Td • Vaccination • Booster: Once every 10 years	*Contraindications:* • History of anaphylaxis • History of encephalopathy not attributable to an identifiable cause within 7 days of pertussis vaccine • Moderate to severe acute illness • Any unstable neurological condition *Precaution:* • Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of TT containing vaccine • History of Arthus reaction with previous dose of TT containing vaccine and/or DT containing vaccine, including MCV4**; defer vaccination until at least 10 years have elapsed since the last dose • Pregnancy

- For postexposure prophylaxis tetanus booster (TT) may suffice if complete primary vaccination with tetanus toxoid is done.
- But a wounded adult patient who cannot confirm receipt of primary vaccination or a tetanus booster during the preceding 5 years should be vaccinated with tetanus and diphtheria toxoids vaccine (Td) or tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap); adults aged > 64 years should receive Td instead of Tdap which is recommended for 19–64 years of age group.

Hepatitis A virus[1]

Inactivated vaccine (1) Havrix (2) Vaqta *Combination vaccines:* HAV and hepatitis B virus (HBV) (Twinrix)	*Indications:* • Universal immunization is not recommended – Adults at high risk are: – Illicit drug users – Hemophiliacs – Infected with other hepatitis viruses – Chronic liver disease (CLD) and not immune to hepatitis A virus (HAV) – Received or awaiting liver transplant – Food handlers – MSM* – Postexposure prophylaxis	*Schedule:* • *Vaqta:* IM 2 doses at 0, 6–18 months; 1–18 years: 0.5 mL (25 U); > 18 years: 1 mL (50 U) • *Havrix:* IM 2 doses at 0, 6–12 months; 1–18 years: 0.5 mL [720 enzyme-linked immunoassay unit (ELU)]; > 18 years: 1 mL (1440 ELU) • *Twinrix:* IM 3 doses 1 mL 0, 1, 6 months (> 18 years only)	*Precaution:* • Pregnancy

- Immune status to HAV should be checked prior to vaccination.

* Man who have sex with man

Hepatitis B virus[3]

Recombinant vaccine (Engerix-B/ Recombivax HB)	*Indications:* • All unvaccinated adults at risk for HBV infection and all adults seeking protection • Patients at risk are: – Intravenous (IV) drug users – Household contacts of persons with chronic HBV infection – Occupational exposure to HBV – HIV-seropositive – Chronic liver disease – Chronic kidney disease (CKD) – Diseases where blood products or multiple blood transfusions are required – Sexual exposure: Patients with sexually transmitted disease (STD), MSM*, CSW#, promiscuous partners, partners of HBsAg-positive persons – Postexposure prophylaxis: – Single IM dose of hepatitis B immunoglobulin (HBIG) 0.06 mL/kg as soon as possible, followed by full course vaccination	*Schedule:* • Engerix-B 20 µg (1 mL) IM (deltoid) at 0, 1, 2 and 12 months • For patients with CKD and other immunosuppressed patients, 40 µg (2 mL) is administered at 0, 1, 2, and 6 months • Routine boosters not recommended except in immunocompromised who have lost detectable antibodies and persons who are at high risk of repeated inoculation, e.g. CKD patients requiring hemodialysis

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			• Anti-HBs levels should be maintained above 10 mIU/mL *Contraindication:* • Hypersensitivity to yeast

• *Nonresponders with normal immunity:* Nonresponders who are HBsAg and anti-HBc-negative should receive a further full course of vaccination as fourth, fifth and sixth doses. Retesting should be done 1–2 months after the last dose. If there is no response, 40 µg of recombinant vaccine is administered at 0, 1 and 6 months.[1]

Human papillomavirus[2]

HPV4 quadrivalent vaccine against human papillomavirus (HPV) types 6, 11, 16 and 18 (Gardasil) HPV2 bivalent vaccine against HPV types 16 and 18 (Cervarix)	*Indications:* • For females, either HPV4 or HPV2 is recommended for routine vaccination at age 11 or 12 years, and for those ages 13 through 26 years, if not previously vaccinated • For males, HPV4 is recommended for routine vaccination at age 11 or 12 years, and for those ages 13 through 21 years, if not previously vaccinated. Males aged 22 through 26 years may be vaccinated. MSM* may especially benefit by prevention of condyloma (warts) and anal cancer	*Schedule:* • 3 doses of 0.5 mL IM at 0, 1 and 6 months for both HPV4 and HPV2	*Contraindication:* • Pregnancy • Hypersensitivity to yeast (Gardasil) or any other component of vaccine

• Screening for cervical cancer should be continued in spite of HPV vaccination.

Japanese encephalitis[4a]

Primary hamster kidney (PHK) cell-cultured, live attenuated vaccine (e.g. SA 14-14-2 vaccine)	*Indications:* • Primarily useful in the pediatric age group • Not recommended for routine use in adults	*Schedule:* • Subcutaneous (SC) as single dose of 0.5 mL and a booster may be given at 1 year

• Based on the recommendations of the Bi-Regional Consultation on Japanese encephalitis (WHO SEA/WPR and PATH, Thailand, March-April 2005), Government of India has decided on the following strategy for the introduction of the JE vaccine in the endemic districts in India:
  – A one-time mass campaign targeting all children in the age group of 1–15 years in the districts
  – Followed by integration of the Japanese encephalitis (JE) vaccine into the Routine Immunization Program to cover the new cohort (children attaining more than 1 year of age) in the districts covered previously under the JE vaccination campaign. These children would be administered the JE vaccine between 1 and 2 years of age along with the diphtheria, tetanus and pertussis (DPT) booster dose, under the Routine Immunization Program.

Measles, Mumps and Rubella[3]

Live attenuated vaccine	*Indications:* • All adults, except: – Those having suffered from all the three disease – Those who have received 2 doses of measles, mumps and rubella (MMR) vaccine in the childhood • Especially recommended for health care workers; in the setting of outbreaks; recent exposure to these infections; women who could become pregnant and college students	*Schedule:* • 0.5 mL SC in deltoid, 2 doses 28 days apart (2 doses for measles or mumps and 1 for rubella is sufficient)	*Contraindications:* • History of immediate hypersensitivity reaction to gelatin or neomycin • Pregnancy • Severe immunodeficiency • Patients with active febrile infections Precaution: • Recently received antibody-containing blood product • Avoid pregnancy for 3 months after vaccination

Meningococcal meningitis[1]

Polysaccharide vaccines: Bivalent (A and C) Quadrivalent (A, C, Y and W-135/MPSV4)	*Indications:* • During an outbreak, a single dose of vaccine (A and C) may be given • Health care workers, laboratory workers and close contacts of cases • Travelers, pilgrims, people attending fairs and festivals. Single dose of bivalent vaccine is recommended 10–14 days before the scheduled visit. As a national policy quadrivalent polysaccharide vaccine is given to the Haj pilgrims. Travelers to countries where meningococcal disease is hyperendemic or epidemic (e.g. the "meningitis belt" of sub-Saharan Africa) • During the interepidemic period, meningococcal vaccination may be given to personnel living in dormitories; military recruits; jail inmates; immunocompromised individuals, such as those suffering from terminal complement component deficiency • Anatomic or functional asplenia	*Schedule:* • 0.5 mL SC deltoid single dose • 2 doses at 0 and 2 months for functional or anatomical asplenia	*Contraindication:* • History of severe allergic reaction to dry natural rubber (latex)

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Meningococcal conjugate vaccine (MCV4**)			*Contraindications:* • Age > 55 years • History of severe allergic reaction to dry natural rubber (latex) or to DT containing vaccines *Precaution:* • History of GBS

Pneumococcal

Pneumococcal polysaccharide vaccine [pneumococcal capsular types (PCV23)]: 23 serotypes Conjugate pneumococcal vaccine (heptavalent)	*Indications:*[1] • Recommended in patients undergoing splenectomy (preferably at least 2 weeks prior to splenectomy) and one-time revaccination is indicated after 5 years in these patients	*Schedule:* • 0.5 mL IM/SC 1 or 2 doses

• Indications according to CDC ACIP guidelines:[3]
  – Adults aged 19–64 years with (one-time revaccination after 5 years)
    i. Chronic medical illness, functional or anatomic asplenia, immunocompromising conditions
    ii. *Other:* Residents of nursing homes or long-term care facilities and persons who smoke cigarettes
  – At age 65 years, all persons should receive vaccination (single dose).

Typhoid

Live oral Ty21a vaccine: Liquid suspension/enteric-coated capsule	*Indications:*[1] • Typhoid vaccine is recommended as part of routine immunization in adolescents. Either Ty21a or Vi vaccine may be used as both have comparable efficacy (51% vs 55% at 3 years) and both are safe • Vaccination of the entire community at risk during an outbreak situation • Due to insufficient data, *currently routine immunization of adults is not recommended* • It is recommended for travelers to areas where there is a moderate to high risk of exposure to *Salmonella typhi*, lab workers and household contacts of *S. typhi* carriers[5] • Not recommended for adults residing in typhoid-endemic areas or for the management of persons who may have been exposed to a common source outbreak[5]	*Schedule:* • 3 doses on alternate days • Repeated once in every 3 years as a booster dose • Liquid formulation is recommended over enteric-coated capsule	*Contraindications:* • Pregnancy • Immuno-compromised state • Age < 6 years
Vi capsular polysaccharide vaccine (Vi CPS)		• A single SC/IM dose of 0.5 mL • A booster is recommended once in every 3 years	• Age < 2 years

• Despite efficacy of whole-cell vaccine (73%), it is no longer used as it is associated with a much higher incidence of side effects (especially fever: 16% vs 1–2%) than the other two vaccines.[5]

Influenza[6]

Trivalent inactivated influenza vaccine (TIV)	*Indications:* • All people 6 months of age and older Especially: – Persons with chronic medical illness, immunocompromised individuals having high risk of severe influenza – Pregnant women – People 65 years and older	*Schedule:* • Single dose IM/ intradermal (ID) 0.5 mL annually	*Contraindications:* • Moderate-to-severe illness with fever • History of GBS following influenza vaccine • History of immediate hypersensitivity reaction to eggs (TIV/LAIV) • Allergic to any of the ingredients or formaldehyde, gentamicin sulfate or sodium deoxycholate
Live attenuated influenza vaccine (LAIV)	• Healthy nonpregnant individuals ages 2–49 years	• Intranasal (IN)	*Contraindications:* • Age ≥ 50 years or below 2 years • Pregnancy • Immunosuppression • Chronic medical conditions • Close contact with severely immunosuppressed

• On February 23, 2012 the WHO recommended that the Northern Hemisphere's 2012-2013 seasonal influenza vaccine be made from the following three vaccine viruses:
  – An A/California/7/2009 (H1N1)pdm09-like virus
  – An A/Victoria/361/2011 (H3N2)-like virus
  – A B/Wisconsin/1/2010-like virus (from the B/Yamagata lineage of viruses).
• While the H1N1 virus used to make the 2012-2013 flu vaccine is the same virus that was included in the 2011-2012 vaccine, the recommended influenza H3N2 and B vaccine viruses are different from those in the 2011-2012 influenza vaccine for the Northern Hemisphere.
• In the absence of epidemiological surveillance regarding the influenza serotypes in our country, the Expert Group observes that *presently the use of influenza vaccine in India is not recommended*.[1]
• Efficacy of TIV is 70–90% and 30–70% among healthy young people and elderly population respectively when the "match" between the vaccine and the circulating strains is close.

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Rabies

Purified vero cell rabies vaccine (PVRV) Purified chick embryo cell vaccine (PCECV) Human diploid cell culture vaccine (HDCV) Purified duck embryo vaccine (PDEV)	*Indications:* • Postexposure prophylaxis: – Bites by dogs – Bite by rats and rodents may be considered • Pre-exposure prophylaxis: – For risk groups like veterinarians, laboratory personnel, health care personnel	*Schedule:* • Postexposure prophylaxis: – IM deltoid (1 mL): Days 0, 3, 7, 14, 28 and 90 (optional) – ID (0.1 mL): Two sites: 0, 3, 7 and 28 Eight sites: 0, 7, 28 and 90 • Pre-exposure prophylaxis: – IM or ID single dose on days 0, 7 and 28 • Re-exposure: – IM or ID Booster on days 0 and 3

• The animal in question is to be observed for 10 days. Postexposure vaccination can be discontinued if the animal is healthy after 10 days.
• Rabies vaccines and rabies immunoglobulin are safe during pregnancy, lactation and in immunocompromised states including HIV.
• Only modern tissue culture vaccines must be used for pre-exposure prophylaxis.

Varicella (Chicken pox)[7]

Live attenuated (Oka strain)	*Indications:* • Persons aged over 13 years without evidence of varicella immunity • Strongly recommended in those having: – Close contact with persons at high-risk for severe disease (e.g. health care personnel and family contacts of persons with immunocompromising conditions, nonpregnant women of childbearing age) or, – High-risk for exposure or transmission (e.g. members of institutional settings, military personnel; living in households with children; nonpregnant women of childbearing age and international travelers) • Recommended for outbreak control • Recommended for postexposure administration within 3 days of exposure to varicella rash and can be given up to 5 days of exposure to rash	*Schedule:* • 2 doses (0.5 mL) SC over deltoid 4–8 weeks apart	*Contraindications:* • Pregnancy • Severe immunodeficiency • History of hypersensitivity reaction to gelatin or neomycin • Seriously ill people • Received blood products or transfusions during the past 5 months *Precaution:* • Recent (within 11 months) receipt of antibody-containing blood product

• 70–90% effective for preventing varicella and more than 95% effective for preventing severe varicella.

Zoster (Shingles)[7]

Live, attenuated varicella-zoster virus (VZV) (Oka strain)	*Indications:* • Adults aged 60 years and older regardless of whether they report a previous episode of herpes zoster • Persons with chronic medical illnesses	*Schedule:* • Single 0.65 mL dose SC in the deltoid region	*Contraindications:* • Age < 60 years • Pregnancy • Known severe immunodeficiency • History of immediate hypersensitivity reaction to gelatin or neomycin

• Expert Group observes that presently herpes zoster *vaccine is not recommended for use in adult population*, with or without comorbid conditions as reliable epidemiological data are not available from India regarding the burden of herpes zoster.[1]
• Zoster vaccine with 18 times the viral content of the varicella vaccine decreases the incidence of shingles by 51%, the burden of illness by 61% and the incidence of postherpetic neuralgia by 66%.

Anthrax[3]

Anthrax vaccine	*Indications:* • Anthrax vaccine is recommended for people 18 through 65 years of age who might be exposed to large amounts of *Bacillus anthracis* bacteria, e.g.: – Laboratory workers – People handling animals or animal products – Some military personnel	*Schedule:* • 5 doses IM: 0 and 4 weeks and 6, 12 and 18 months • Postexposure prophylaxis: 3 doses SC 0, 2 and 4 weeks • Annual booster doses are recommended for ongoing protection	*Contraindications:* • Allergic reactions • History of GBS • Moderate or severe illness

Plague[3]

Killed whole cell plague vaccine Live attenuated vaccine	*Indications:* • All laboratory and field personnel who are working with *Yersinia pestis* • Persons engaged in aerosol experiments with *Y. pestis* • Persons engaged in field operations in areas with enzootic plague	*Schedule:* • IM 3 doses: 0 (1 mL), 1 (0.2 mL) and 6 (0.2 mL) months • Accelerated dose: 0.5 mL 3 doses 1 week apart • Booster: 3 doses at 6 monthly intervals	*Adverse effect:* • Local reactions • Hypersensitivity

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- A subunit vaccine based on the F1 and V antigens is being developed.
- Field experience indicates that vaccination with plague vaccine reduces the incidence and severity of disease resulting from the bite of infected fleas. The degree of protection afforded against primary pneumonic infection is not known.

Yellow fever[3]

Live attenuated virus	*Indications:* • Persons 9 months through 59 years of age traveling to or living in an area where risk of yellow fever is known to exist, or traveling to a country with requirement to vaccinate before entry • Laboratory personnel who might be exposed to yellow fever virus or vaccine virus	*Schedule:* • Single shot 0.5 mL SC • Booster dose is recommended every 10 years	*Precautions:* • Allergy to any component of the vaccine, including eggs, chicken proteins, or gelatin • < 6 months of age • Immunocompromised • Pregnant and nursing mothers

- "International Certificate of Vaccination or Prophylaxis" (yellow card) is issued after vaccination. This certificate becomes valid 10 days after vaccination and is good for 10 years.

***Haemophilus influenzae* Type b (Hib) vaccine[2]**

Hib (polysaccharide vaccine) Hib (polysaccharide-protein conjugate vaccine)	Indication: • Dose should be considered for persons who have sickle cell disease, leukemia or HIV infection, or who have had a splenectomy, if they have not previously received Hib vaccine

*Man who have sex with man
#Commercial sex worker
**Meningococcal conjugated vaccine quadrivalent

REFERENCES

1. API Guidelines "Executive Summary The Association of Physicians of India Evidence-Based Clinical Practice Guidelines on Adult Immunization" Expert Group of the Association of Physicians of India on Adult Immunization in India JAPI. 2009;57:345-56.
2. Schuchat A, Jackson LA. Immunization principles and vaccine use. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (Eds). Harrison's Principles of Internal Medicine, 18th edn. New York: McGraw-Hill; 2011. pp. 1031-41.
3. Centers for Disease Control and Prevention (2012). Recommended adult immunization schedule—United States – 2012. [online] CDC website. Available from www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf [Accessed December 2012].
4. Dengue Vaccine Initiative (2012). [online] DVI website. Available from www.denguevaccines.org [Accessed December 2012].

4a. Operational Guide Japanese Encephalitis Vaccination in India, September 2010 ministry of health and family welfare.

5. Pegues DA, Miller SI. Salmonellosis. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (Eds). Harrison's Principles of Internal Medicine, 18th edn. New York: McGraw-Hill; 2011. pp. 1277-8.
6. Centers for Disease Control and Prevention (2012). What you should know for the 2012-2013 influenza season. [online] CDC website. Available from www.cdc.gov/flu/about/season/flu-season-2012-2013.htm [Accessed December 2012].
7. Whitley RJ. Varicella-zoster virus infections. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (Eds). Harrison's Principles of Internal Medicine, 18th edn. New York: McGraw-Hill; 2011. pp. 1465-6.
8. PATH Malaria Vaccine Initiative (2012). [online] MVI website. Available from www.malariavaccine.org [Accessed December 2012].
9. Hepatitis E vaccine: why wait? Lancet. 2010;376(9744):845.