

Adult Immunization – Need of the Hour

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ABSTRACT

Immunization is the process of making individuals immune. Childhood immunization is a common process for various ailments, but adult immunization in the Indian scenario is obscure. Officially, India has been declared polio-free, which is an achievement despite cultural, political, economic, geographic, and so many other factors. The changing demographics of adult, geriatric population and growing cost of health-care maintenance are a concern in developing countries like India. Thus, promoting healthy lifestyle needs prevention, early detection, and management of various diseases and disorders. Certainly, prevention in adults is yet to be tapped completely, so that goal of 100% prevention can be achieved. Various fraternities of medical association have come up with guidelines for adult immunization schedules in India. The present paper reviews infectious diseases such as anthrax, chikungunya, cholera, dengue, influenza, and malaria in this section of the review. We humbly request all health-care professionals and educators to educate the mass for adult immunization. So that, cost involved for treatment and workforce for the management of diseases can be better utilized in some other needed areas.

KEYWORDS: Anthrax, chikungunya, cholera, dengue, influenza, malaria

INTRODUCTION

In our previous review, adult immunization for HIV and hepatitis C virus was discussed thoroughly.^[1] In continuation, efforts have been made to give a comprehensive review on new guidelines and prevention of infectious and contagious diseases. In rural India, every household has animals and pets as a part of their routine daily life activities. Many of the diseases dealt in this section are zoonotic and transmitted through vectors.^[2] Therefore, it is important to understand the concept of spread, prevention, and treatment. The review enlightens very briefly about disease entity, but more on prevention and vaccination aspects, along with recent trends and developments.

ANTHRAX

Anthrax was known as Egyptian Plague caused by *Bacillus anthracis*. Anthrax estimated to occur worldwide and incidence reaches between 20,000 and 100,000 cases annually.^[2,3] Anthrax has gained its importance because of biological warfare.^[4,5] Transmission of anthrax is animal-soil-animal transmission.^[6] Usually, prevalence among Asian countries is much higher.^[6] Anthrax is a disease of animals, both domestic and wild. Transmission

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of infection will be through direct inoculation of spores in skin breach, inhalation of spores, and ingestion of contaminated food.^[2,6] Inoculation through contact occurs mainly among veterinary doctors, zookeepers, and butchers. Clinical features will be seen after 2–3 days of incubation.^[6,7] Patients will show small papules in the skin, vesicle around the central lesions. By the 3rd day, considerable local edema will be seen with lymphadenopathy. Lesions will resolve spontaneously in 80%–90% of the patients slowly over a period of 2–6 weeks.^[8] Usually, inhalation of contaminated spores from hides lead to disease. The risk is more in wool makers – shepherds; so, is called as a wool-sorter’s disease. Soon after a short incubation, patient will suffer with fever, chills, and feel short of breath and has higher mortality (95%). Prompt antibiotic therapy makes survival of patient possible.^[8-10] In African countries because of contaminated meat consumption, intestinal anthrax may develop; which is rare, elsewhere in the world.^[7] Many patients may present nonspecifically with diarrhea, vomiting, and fever but recover spontaneously.^[2,3] Sometimes, lesions occur in the oropharynx because of contaminated meat ingestion which causes severe, life-threatening edema and bacteriemia.^[6]

DIAGNOSIS OF ANTHRAX

It can be carried out through bacteriological (Sheep blood agar culture), serological, and immunological tests (titers of antibody to protective antigen and capsular components). New molecular diagnostic techniques use polymerized chain reaction specific to beta-anthraxes.^[7] Markers such as VrrA and Ba813 have been studied extensively for the diagnosis.^[11]

TREATMENTS

Penicillin remains proven drug; early antibiotic administration is essential in survivors. The antibiotic should be prolonged because nongerminated spores remain in alveoli for weeks. The regimen for postexposure and active disease can be read elsewhere.^[8]

GLOBAL SCENARIO OF VACCINATION FOR PREVENTION

In 1881, Louis Pasteur successfully developed anthrax vaccine. Later in 1935, Max Stern developed attenuated live vaccine, which is used in livestock; but it is not safe for human use because of virulence.^[12,13] At present, Advisory Committee on Immunization Practices recommends five doses of AVA (anthrax vaccine adsorbed) developed by Americans.^[10] Primary dose of 0.5 ml intramuscular (IM) at 0, 4 weeks and later 6, 12, and 18 months (preexposure prophylaxis) followed by annual booster dose. This vaccine is recommended for

unvaccinated people, but those exposed to anthrax should be given three subcutaneous doses.^[8,10] First one as soon as possible, second and third doses at 2nd and 4th week after the first dose. In pregnant women, the timeline will be same with subcutaneous administration.^[9]

CHIKUNGUNYA

It is remerging viral disease (caused by Chikungunya [CHIK] RNA virus belongs to family Togaviridae, genus Alphavirus) with abrupt fever, arthralgia followed by a rash.^[14-16] The name derives from Makonde (means “which bends up”) results of arthritic symptoms; even though it is self-limiting, but rarely fatal. Patients affected show abrupt and sudden onset of high degree fever and chills, severe myalgia, arthralgia, and skin rash for 1–7 days,^[17-22] the incubation period is usually 2–3 days with a range of 1–12 days; temperature will remit for 1–2 days after a gap of 4–10 days.^[14-16] Swollen joints and tender crippling arthritis are evident, involving more than 10 joint groups and usually radiological findings are normal.^[22,23] Pregnant patients if affected may abort during the first trimester and transmission to child may happen during term.^[24-26] Cardinal features such as encephalitis, neuropathy myoclonic seizures, acute flaccid paralysis multiorgan involvement, and ocular involvement were reported.^[17-21] In some cases, sensorineural hearing loss hypokalemic periodic paralysis and hemorrhagic manifestations were documented.^[14-17] It may unmask rheumatoid arthritis, CHIK virus (CHIKV) infection thought to confer lifelong immunity.^[22,23] It is mostly transmitted through a bite of infected mosquito Aedes genus. In the recent past in India, 2008–2009, there was an outbreak.^[24,27]

MANAGEMENT CHALLENGES

The specific antiviral drug is available for management. Many times dengue and CHIK fever occur frequently, which needs to be distinguished from diseases such as other viral fevers and malaria. The gold standard for diagnosis is viral culture,^[14-17] but facilities are not widely available in India. Reverse transcriptase polymerized chain reaction is a useful molecular tool for rapid diagnosis.^[28,29] More frequently, ELISA and indirect immune fluorescent heme agglutination inhibition techniques are used.

TREATMENT CHALLENGES

It is symptomatic and supportive only.^[30] Adequate fluid intake should be ensured. nonsteroidal anti-inflammatory drugs may be used and antirheumatic drugs also shown effective in the treatment of chronic arthritis.^[31] There is a need for CHIK vaccine as the burden of disease is tremendous and infection rates are significant in

developing countries.^[32-34] As of now, no commercial vaccines are available to prevent the occurrence of infection. Many vaccines have tried in preclinical and Phase-I, II trial; like inactivated live-attenuated genetically engineered DNA, virus-like particles vaccine are under trial.^[31-36] CHIKV is an old virus, but now it has become a global disease.^[36] This leads to socioeconomic impact, so there is an urgent need of safe and effective CHIK vaccine.^[36]

CHOLERA

Cholera is caused by *Vibrio cholerae* leading to acute enteric infection. Route of transmission is feco-oral contamination or ingestion of contaminated food and water. It is characterized by dehydration due to a rigorous form of acute, severe watery diarrhea, which may lead patients to deathbed.^[37] Two-third of the patients will be asymptomatic, but 80%–90% of symptomatic patients develop acute-onset diarrhea. If it is untreated, the fatality may raise up to 40%.^[37,38] Recently, massive outbreaks of cholera, killed more than one lakh people.^[37] Diagnosis depends on the isolation of *Vibrio cholerae* from feces.

According to WHO, the patient aged 5 or more and develops severe dehydration or watery diarrhea or vomiting in the cholera epidemic area should suspect infection.^[37] The majority of patients may be treated for dehydration. Antibiotic therapy for 3–5 days will suffice. The single dose of tetracycline, doxycycline, or ciprofloxacin has been shown effective in reducing duration and volume of diarrhea.^[38] Cholera vaccine first developed in 1980 as an injectable, later as oral form. Injectable vaccines are effective in cholera endemic areas.^[39-43] It offers protection up to 2 years after single-dose administration. In addition, 3–4 years with annual booster dose, this will reduce 50% of the risk of death. Because of low efficacy and severe adverse reactions, the WHO never recommended the use of this vaccine, except some specific epidemiological sequences like Kumbhmela.^[44]

Currently, whole-cell-cholera toxin recombinant B subunit vaccine and bivalent killed whole-cell vaccine are available with trade names Dukoral, Shanchol, and Morcvax.^[37] In the global scenario, the WHO recommends available cholera vaccine can be considered at risk areas for outbreaks and should be utilized as compliments to traditional control and preventive measures.^[38,39] Vietnam has incorporated cholera vaccine in public health program. However, an oral cholera vaccine does not provide 100% immunity from disease.

PRESENT STATUS OF VACCINES

Dukoral™ approved for the age group of more than 2 years (2–6 years); administered in three doses

1–6 weeks apart; and two doses for the age group of more than 6 years, 1–6 weeks apart. Each dose of vaccine should be administered in 150 ml of water. The protection starts approximately 1 week after ingestion of the second dose and gives protection of 85%–90% at 6 months. However, Dukoral should be stored 2°–8° and will be stable for 1 month at 37°. The volume of a single dose is 15 times the volume of other vaccine.^[43,44]

Shanco™ is the second type of vaccine licensed in India in 2009; it is administered in two doses between a minimum of 1 and maximum of 6 weeks apart. In the Indian scenario, drinking water sanitation is an important cornerstone to improve the situation.^[40] Two-dose product should be immunized cost effectively for the target population, for example, Kumbh Mela pilgrims. The cost involved with Shanco is approximately Rs. 12 whereas Dukoral is Rs. 300–600.^[43,44]

DENGUE

Dengue is an important arthropod-borne viral disease. Around 40% of population in the world is at risk of dengue transmission. It is endemic in at least 100 countries.^[45-48] The WHO estimates 50–100 million infections, including 5 lakh dengue hemorrhagic fever and 22,000 deaths happen among children. Dengue fever is caused by four viral serotypes, den V1–V2.^[47] Dengue is transmitted by vector mosquitos *Aedes aegypti*, and *Aedes albopictus*. Symptoms will begin 3–7 days after the bite and last for typically 3–10 days. The transmission occurs if mosquito fed with an infected person during a 5-day period of viremia.^[46] Sometimes, the patient may not be symptomatic but can infect mosquito after entry into the blood meal.^[48] It requires 8–10 days for transmission to another host.^[49] In rare cases, it can be transmitted by organ transplant or blood transfusion and vertical transmission.

In tropic and subtropic, it is endemic, often when the rainfall is optimum for breeding. Severe disease is common in babies and young children.^[46] Other risk factors include female gender, high body mass index, and viral load.^[47] It can be life-threatening with chronic disease.^[49] The person infected with one serotype may have lifelong immunity to that particular serotype. But develop only short-term immunity against other serotypes. Clinical manifestation will have 3–14 days incubation and will experience prodrome of chills, erythematous mottling and facial flushing which may last for 2–3 days.^[45,46] Classic dengue fever begins with sudden-onset fever, chills, and severe aching of the head and back extremities. The fever lasts for 2–7 days may reach 41°C.^[47] The rash typically begins on the 3rd day and persists 2–3 days. Sometimes, 2nd rash may occur

within 1–2 days of defervescence lasting for 1–5 days. It is morbilliform and maculopopular, occasionally desquamates.^[47] Recovery is slow but complete.^[50,51] Convalescent phase may last for 2 weeks. It has become the leading cause of morbidity and mortality, which requires vaccine against such a life-threatening virus.^[52]

PRESENT STATUS OF DENGUE VACCINE

Even though the dengue virus was isolated in 1945 in Calcutta. However, no vaccine is available yet in the market.^[52-55] At present, live attenuated chimeric yellow fever, dengue virus tetravalent dengue vaccine (CYTDV) has progressed to Phase III. Whereas the live attenuated vaccine has reached up to Phase II clinical trials.^[56] Chimeric dengue vaccine has shown to be genetically and phenotypically stable and immunogenic.^[57] CYTDV Phase III studies are underway in 10 countries of Asia and Latin America.^[58] In India, at the International Center for Genetic Engineering and Biotechnology supported by Government of India has developed a noninfectious dengue vaccine from yeast *Pichia pastoris*. Preliminary animal trail in mice has yielded good results. In conclusion, CYTDV remains a public health value, which needs further studies for licensing by national regulatory agencies.^[58]

INFLUENZA

Influenza commonly referred as flue; caused by Orthomyxoviridae. Influenza A and B are two common types of virus.^[59-61] Further, Influenza A classified based on two surface antigens as hemagglutinin (H) and neuraminidase (N). Most infections globally caused by influenza A H1N1, H3N2, and influenza B. Antigenic drift results in seasonal epidemics due to point mutations that occur during viral replication.^[62,63] Globally, 5%–10% and 20%–30% attack rate is estimated among adult and children, respectively.^[60,61] The incidence of respiratory infections in urban area is 23% and 17.7% in a rural area per month.^[61,64] Respiratory syncytial virus, Influenza A, and Para A influenza virus are the most common causes leading to acute respiratory tract infections among children in rural India.^[60] The mortality rate is more in aged patients (65 years and above).^[59,61] The most effective prevention is annual vaccination, which can be routinely done in certain groups with associated risks.^[65,66] In addition, improvement of respiratory hygiene is economic strategies to reduce respiratory diseases.^[65]

INFLUENZA VACCINE CURRENT SCENARIO

It offers an important preventive tool to prevent death and substantially reduces health-care expenses. Immunization can be carried out using trivalent

inactivated influenza vaccine (IIV) or live attenuated influenza vaccine (LAIV).^[67,68] Present Quadrivalent IIV approved along with LAIV.^[69] A trivalent cell culture based on activated influenza vaccine and trivalent recombinant influenza vaccine (RIV). Annual vaccination is recommended for adults who want to reduce the risk of transmission and becoming ill.^[70]

Center for disease control advisory committee (USA) on immunization practices indicates vaccination for women of childbearing age during influenza season,^[71] patients with systemic illness including chorionic villus sampling, renal, hepatic, hematologic metabolic and chronic pulmonary disorders;^[72] persons above the age group of 50 years and with immune suppressions, and conditions that may compromise respiratory function should be considered for immunization.^[73-75] Residents of nursing homes, health-care personnel, and caregivers should undergo vaccination regime.^[76,77] LAIV given intensely for 2–49 years age group. Trivalent influenza vaccine and IIV can be given IM with persons aged more than 6 months, up till more than 65 years and older.^[78] In India, LAIV and RIV3 vaccines free from egg are not yet available. Indian studies are needed to assess the cost-effectiveness of the vaccine among children, adults, and aged.^[79] Antiviral drugs used for chemoprophylaxis are to treat influenza can be used as adjuncts, but not substitute for animal vaccination.^[80]

AVIAN OR SWINE INFLUENZA

Swine or Avian influenza is fatal infection. H5N1 is highly pathogenic virus seen in Asia, Africa, Europe and Middle East. It will be contracted through direct contact with sick or dead birds.^[70] Associated with H5N1 is panzootic among birds. H5N1 circulating among poultry caused outbreaks of Avian Influenza. Occasionally, infected humans are potential to recombine with human Influenza A virus.^[60,61] In recent years (in 2006) outbreak of H5N1 occurred in Nandurbar, Jalgaon District of Maharashtra, Gujarat, and Madhya Pradesh.^[81] National Institute of Virology suggested the introduction of viruses might be due to migratory birds.^[81,82] However, reducing seasonal influenza risk through vaccination might reduce risk of recombination of animal origin virus and human virus theoretically.^[83]

MALARIA

Malaria is mosquito-borne parasitic disease.^[84] Clinical features, diagnosis, and treatment can be read elsewhere in medical literature.^[85] Development of a vaccine is a complex affair because complex cycle of parasite in human and mosquito as well as antigenic diversity.^[86-89] Currently, no malaria vaccine is commercially available. But during the last decade in the global scenario, they developed

first-generation malaria vaccine by GlaxoSmithKline.^[90] Few Phase I and Phase II trials have been carried out in Tanzania which prevented quarter of Malaria cases in the study population.^[91] American Biotech Company (Sanaria) developed PfSPZ vaccine, which contains weakened live form parasite of *Plasmodium falciparum*.^[92] The vaccine safety has been tested in Phase III trial in 2011 African Sub-Saharan countries.^[90,91] Indian Institute of Malaria Vaccine targeted both *P. falciparum* and *Plasmodium vivax*. International Centre for Genetic Engineering and Biotechnology developed JAIVAC-1 first Indian Malaria vaccine underwent trial in humans.^[91,93] Efficacy was evaluated in Papua New Guinea, but in India, efficacy is still not clear as of now and it is difficult to comment on the cost-effectiveness because no commercially available vaccine is present.^[93]

CONCLUSION

Many of these infections encountered during traveling. Few of the diseases can be prevented because of childhood vaccination. However, the adults often neglect the recommendations of booster dose. In addition, some adults have never been vaccinated at all. To prevent burden of disease and treatment cost; it is essential to have knowledge of adult immunization. Adult immunization makes difference for developing countries to combat infectious diseases epidemics. Due to emerging and reemerging infectious diseases worldwide, everyone should have booster doses of vaccination, along with scheduled vaccination. Travelers are at risk of acquiring travel-associated infections, and they may transmit the same to their home country after return. Hence, it is necessary to have travel vaccine list with booster doses to prevent disease epidemic and pandemic.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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