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# Controversies and Challenges in Pediatric Vaccination Today

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## Legacy of Jenner and Pasteur needs to be carried forward

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COMMENTARY

# Legacy of Jenner and Pasteur needs to be carried forward

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***Abstract:***
*Drugs control or cure a disease and provide relief in symptoms, but, vaccines prevent occurrence of the specific diseases, thus, development of vaccine was a landmark discovery. With advent of advanced technologies improved versions of some old vaccines and many new vaccines are available, but, these are very expensive vaccines. Development of new vaccines is not only a time consuming exercise, but an expensive venture also because studies regarding efficacy and safely are mandatory before a license to market the vaccine is issued. Overhead expenditures are incurred on transportation, storage and sale of the product. The governments also impose different taxes on the vaccines. All these expenses raise further the cost of vaccines. The great irony is that people belonging to low socio-economic strata are most vulnerable to contact infectious diseases, thus need vaccines most, but may not be in a position to afford these. The drug industry, the governments and medical professionals should device strategies to bring down the prices of the vaccines. Edward Jenner and Louis Pasteur developed Smallpox and Rabies vaccines respectively to provide benefit to the mankind, same principle or motive needs to be carried forward.*

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## Introduction

Development of vaccines is a priceless gift from man to the mankind. Drugs control or cure the diseases whereas a vaccine prevents the disease. Death and morbidity in millions have been prevented by vaccines. It is very important to remember that rabies and tetanus cause painful death, because, the patient remains conscious and repeatedly gets spasms of the muscles. It should be realized that unlike Smallpox viruses Clostridium tetani and Rabies viruses can not be eliminated.

Smallpox vaccine was developed in 1798 by Edward Jenner and Louis Pasteur developed Rabies vaccine in 1885, and Cholera vaccine was developed in 1892. Thus, in the eighteenth century one vaccine was developed, in nineteenth century two vaccines were developed. In the twentieth century BCG was developed in 1921, followed by development of Pertussis and Diphtheria vaccines in 1923. Then followed the spate of new vaccines which has continued unabated.

In the latter half of the eighteenth century many had noticed that milkmaids did not generally get smallpox, and some people had successfully provided protection to many against smallpox by inoculating material from blisters on cows[1] Credit for smallpox vaccine goes to Edward Jenner on two counts: (i) he took material from a blister from milkmaid and not from the cow and inoculated it on both arms of a boy, and (ii) later injected material taken from smallpox blister to the child, but, that child did not develop smallpox. He had carried this procedure on 23 subjects, providing evidence that inoculums could be taken from human beings and inoculated to people; and it provided protection against smallpox if exposure occurs later.

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Louis Pasteur was a chemist, while working on Chicken cholera, a culture of the bacteria had spoiled and failed to induce the disease in some chickens, and these chickens did not develop disease when infected again with fresh bacteria. This observation suggested that the weakened bacteria given earlier had provided some protection against subsequent infection [2]. This laid the foundation for vaccines. Thus, the principle of immunization was discovered by accident or default and not by design or planned strategy. Similarly Pencillin was discovered by a stroke of luck or accident and Alexander Fleming won and shared Nobel prize with Howard Walter Florey and Ernst Boris Chain in 1945. Stroke of luck or comedy of errors played a role in the institution of Nobel Prizes. The erroneous publication in 1888 of a premature obituary of Alfred Nobel by a French newspaper is said to have played a role in the decision made by Nobel to leave a better legacy after his death. The French paper had captioned "Le marchant de la mort est mort" (The merchant of death is dead), and stated: "Dr. Alfred Nobel, who became rich by finding ways to kill more people faster than ever before, died yesterday." On 27 November 1895, Nobel signed his last will and testament and set aside the bulk of his estate to establish the Nobel Prizes, to be awarded annually without distinction of nationality[3]. Peace Award happens to be most coveted award. He died more than a year later, on 10 December 1896.

Earlier the vaccines were developed by individuals or groups of individuals, now a days the vaccines are developed, produced and marketed by the drug industry. Some people in England and Germany had probably provided protection to few closed group persons against smallpox through inoculation of cowpox exudates. Jenner being a medical practitioner had carried his experiment on 23 persons and provided protection against smallpox - perhaps the first small scale mass vaccination. As has been seen during the Global Polio Eradication Program undertaken by WHO, many people or groups of people have shown resistance to OPV administration to their children with the wrong notion that OPV may cause infertility in their children. Similarly during the early phase of Jenner's 'campaign' many people were afraid that vaccine derived from blisters of cowpox may result in growing cowlike appendages. Jenner's continuing work on vaccination adversely affected his medical practice. But, he was supported by his colleagues and the King in petitioning parliament and was granted £10,000 for his work on vaccination.

As stated earlier Pasteur had observed that weakened bacteria had failed to manifest the disease and on the other hand exposure to fresh infection also failed to cause the disease, thus weakened bacteria had infact provided protection against subsequent infections, Pasteur gave these artificially weakened organisms the generic name of vaccines, to honour Jenner's discovery. Pasteur produced the first vaccine for rabies by growing the virus, and then weakening it by drying the affected nerve tissue. This vaccine was first used on 9 years old Joseph Meister, on July 6, 1885, after the boy was badly mauled by a rabid dog. This was done at some personal risk as Pasteur was a chemist and not a licensed physician and could have faced prosecution for treating the boy. As without treatment the boy faced almost certain death, so after consulting some of his colleagues Pasteur decided to conduct his experiment, which infact proved treatment and the boy survived. As the boy did not develop the disease Pasteur was hailed as a hero and the legal matter was not pursued.

The above narrations look like saga, stories of bravery and dedication. During these two hundred plus years lot of water has flown down the rivers Thames and the Ganges. Now a days the vaccines are researched, developed and marketed by drug industry, profit being a big motivating force. It is a reality and has to be accepted. The other reality also needs to be understood and accepted to understand the present day ground reality. Over crowding, poor sanitation and poor hygienic habits help in rapid spread of infectious diseases; malnutrition affects the severity of the diseases. People belonging to low economic group are thus more prone to catch infectious diseases, resistance to diseases may be low because of malnutrion and means to provide treatment may be meagre. Such populations need protection on priority basis. All the new vaccines are very expensive, because the manufacturers have invested millions of dollars in research and development of vaccines, and have to recover their investment.

What is the way out? World Health Organization (WHO) has aptly stated in one sentence: "Stewardship of health system is a responsibility of national governments [4]. There is nothing new in the

concept. Even during the olden times the Sovereign rulers like Monarchs, Kings, Maharajas, Rajas or Tribal leaders used to provide facilities like education, medical, protection in form of police and army, drinking water etc. to their subjects. As mentioned earlier that Jenner had been provided financial aid by the Parliament. In 1840 the British government passed Vaccination Act and provided vaccination using cowpox free of charge, launching National Immunization Program.

Health care systems cannot be of uniform standard in all the countries. Though primarily it is the responsibility of the national governments, but in some countries specially developed and rich nations insurance companies play a big role in health care system. But, the author intends to keep discussion to the underdeveloped and developing countries. In these countries two issues of main concern are: (i) limited resources, and (ii) large vulnerable populations.

No disease is a good disease so every disease should be avoided by all the means. All the vaccine preventable diseases should be prevented by prior vaccination, but limitation of resources may pose some problems. Thus, there is a need to enlist the diseases which need to be given priority. This list would vary from country to country depending on socio-economic and environmental factors. In general, for underdeveloped and developing countries the diseases which should be on top priority are tuberculosis, polio, pertussis, diphtheria, measles and typhoid. The vaccines against these diseases should be included in the National Immunization Program.

Currently vaccines against other diseases are expensive, and provide protection against specific diseases which also need to be prevented. Public health interventions are for population at large or some specific groups e.g., polio eradication campaign targets children up to five years of age. Public health interventions cover many aspects of civic life which include sanitation, clean drinking water, good quality food etc., medical aspects include providing protection against vector borne diseases by preventing mosquito breeding etc., and providing protection against vaccine preventable diseases. An individual visits or is taken to health provider for sickness whereas preventive care initiative is taken by the health providers like time to time disinfection programs being carried out to stop mosquito breeding and conducting immunization programs.

Vaccines provide benefit to the recipient, but community also gets some indirect benefit because the immune individuals act as barriers in the spread of diseases where causative organism spreads from man to man. Higher the vaccine coverage and immune population, lower are chances of occurrence of epidemic. This phenomenon is called herd protection [5]. Such benefit occurs in polio, tuberculosis, diphtheria, pertussis, measles etc., but, does not occur in tetanus, rabies, Japanese encephalitis etc. Thus, vaccines become a tool to provide public good.

The vaccines are administered to people to protect against specific diseases, thus are administered before getting infection, but, also in some cases soon after getting exposure to infection especially after dog bite. But, every unvaccinated person may not develop a disease so vaccination is administered on voluntary basis or with consent of care providers in children, and is not forced upon. In author's opinion in some situations the voluntary clause may be overlooked. The author would like to cite two situations. Every abandoned newborn or young child whose mother's status regarding hepatitis B disease is not known should be provided hepatitis B vaccine as per post exposure schedule [6]. Typhoid vaccine should be mandated for all food handlers because these people may act as source of infection for typhoid disease [7].

Advice regarding the immunization should be given with full considerations to the financial status and circumstances of the family, but, in the best interest of the individual concerned. Similarly, the drug industry should cater to the needs of the masses too while continuing their research and production of new and costly vaccines. The author would like to highlight the need of protection against pertussis and diphtheria for adolescents and young adults from poor economic group.

Surveillance studies from the developed world, chiefly US have shown a gradual increase in adolescent and adult pertussis cases over the past decades [8]. Henceforth, several developed countries have instituted routine booster immunization of adolescents and adults with standard quantity tetanus toxoid and reduced quantity diphtheria and acellular

pertussis vaccine instead of tetanus and reduced quantity diphtheria (Td) vaccine [8, 9]. Need for protection of adolescents and young adults in India was realised and the author along with a colleague had stated: "Studies should be done on Indian children to evaluate antibodies against tetanus, pertussis and diphterhia around 10 years of age to find if the adolescents in India would need Td or new vaccine where pertussis and diphtheria components in reduced quantity with normal quantity of tetanus toxoid be made available [10].

In 2008 Indian Academy of Pediatrics in the Consensus Recommendations on Immunization, 2008 stated: There is no reason to believe that the disease burden of pertussis is low in adolescents in India. A safe and efficacious vaccine is available. The IAPCOI therefore recommends offering Tdap vaccine instaed of Td/TT vaccine in all children/adolescents who can afford to use the vaccine [11]. Tdap contains acellular pertussis antigen, and is very expensive. In India Tdap and TDaP cost Rs. 699/- each (approximately $15), while TDP along with a syring costs Rs. 15/- (approximately $ 0.33) i.e. vaccine with acellular pertussis component is about 46 times costlier than vaccine with whole cell pertussis component. In 2006 the author had suggested use of reduced quantity of whole cell pertussis component [10]. Whole cell pertussis component may be reactogenic in adolescents, but in reduced quantity may cause some pain and local swelling which can be relieved by analgesics.

Adolescents and young adults belonging to low economic groups are more prone to get infections because of overcrowding, but, because of the cost factor may not be able to get any benefit from this costly vaccine. On November 5, 2008 the author had written to the Serum Institute of India, a leading vaccine manufacturer with copies to the Convener, Committee On Immunization of the Indian Academy of Pediatrics and other functionaries of the Indian Academy of Pediatrics "to take an initiative and come out with a combination vaccine of tetanus with reduced quantity of diphtheria and whole cell pertussis components. This is needed for masses that also need protection against pertussis but can not afford the current Tdap vaccine". There was no response from any one.

But, the drug industry alone can not be blamed for this; the system also plays a big role. Tetanus toxoid with reduced quantity of diphtheria antigen as Td and tetanus toxoid with reduced quantities of diphtheria antigen and acellular pertussis antigen as Tdap are being administered. But, tetanus toxoid with reduced quantities of diphtheria antigen and whole cell pertussis antigen will be considered a new molecule and to be licensed fresh studies need to be conducted and results regarding the safety and efficacy have to be presented to the licensing authorities. This exercise is not only time consuming, but, needs heavy expenditure. Moreover such combination vaccine can not be sold at a price higher than that of DTP. These problems will discourage any manufacture to go for such a vaccine which may be the need of the hour but, is bound to act as a loss incurring venture. The solution to bail out industry should come from the authorities and the medical profession. Ministry of health can conduct or sponsor such studies and if found feasible, invite some manufacturer(s) to produce such vaccine.

As compared to the Soverign rulers' time presently welfare of people is on higher priority. Education and health sectors should be given higher priority, but are put in low priority section. The lack of political commitment to population health can be seen in the allotment of relatively low public health expenditure in many national budgets. This mind set needs to be changed.

Vaccines can be divided in two broad groups: (i) vaccines under national immunization program which are provided by the government, and (ii) vaccines outside national immunization program which have to be purchased by the people. The government should make every endeavour to make these affordable, so that higher vaccine coverage provides some benefit to the community also. The governments should exempt import duty on imported vaccines and local taxes on all the vaccines. There should be some mechanism in place to regulate the prices of vaccines, specially the difference between the maximum retail price (MRP) and price to the doctors and retailing chemists. Huge margin between MRP and the cost to the doctors may act as enticement to recommend a vaccine even where it is not strongly indicated or may not be cost effective for that person or family.

No disease is a welcome entity and chickenpox is no exception. In developing countries especially for poor people prevention of chickenpox by vaccination is not cost effective, except in high risk children. Medical profession needs to be sensitized to the needs of the society.

W.H.O. and other international agencies should make some interventions like differential price structure of vaccines for rich and poor countries. All the governments have to spend huge money on defense of their countries which cannot and should not be ignored. Lot of money is spent on research also, which is also necessary, but may need rethink about striking a balance between money spent on certain projects especially like space research etc., and money spent on health projects which provide direct visible and desirable benefit to the people.

We should first bring moon on the earth in form of happiness, reduction in mortality specially of young children, and good health facilities and education for the people, and then plan to go to the Moon or other celestial bodies for scientific discoveries.

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