

In the name of Science and Public Health:
Concerns about the safety of Pentavalent Vaccine



People's Union for Democratic Rights

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Source of cover photograph : <http://dark.pozadia.org/wallpaper/Scalpel/>

Background

The introduction of the pentavalent vaccine in India in December 2011 as part of the immunization programme of the Government has had a chequered history. The pentavalent vaccine (a combination vaccine for protection against five childhood diseases- diphtheria, pertussis (whooping cough), tetanus, hepatitis B and pneumonia and meningitis (caused by *Haemophilus influenzae* type B (Hib)), seeks to replace the traditional DPT vaccine given to infants at 6, 10 and 14 weeks of age. At present the vaccines are procured from WHO pre-qualified manufacturers, by the UNICEF, through part funding from the Global Alliance for Vaccines and Immunizations, more commonly known as the GAVI alliance (GAVI is a public private initiative that provides financial support to developing country governments to purchase vaccines for their immunization programmes). The use of the vaccine has been associated with adverse events following immunization (AEFI) and deaths. The fact that globally at least 63 deaths of infants have been recorded post-pentavalent inoculation, and that even in India the number of recorded deaths have climbed to 54 since 2011, calls for some serious re-assessment of the decision to introduce pentavalent vaccine in the universal immunization programme in India.

Between September and October 2013, news reports from Kashmir reported 8 cases of deaths of infants at the G.B. Pant Hospital in Srinagar. Information obtained under RTI showed that there had been several deaths between June and December, specifically, 1 death in June; 1 in September; 11 in October and 1 in December 2013. Roughly between 1-3 months of age, all these infants had received the pentavalent vaccine 12-36 hours prior to their death. A Central Government team headed by Dr N.K. Arora of INCLEN (International Clinical Epidemiology Network), visited Srinagar to investigate into these deaths. Preliminary findings of the Central team as reported in the press in October 2013, indicated that the deaths were unrelated to the

pentavalent vaccine, and that the infants had died from septicemia and pneumonia. Since immunization is usually given only to healthy children, the explanation given by the Expert Committee, failed to explain why or how the babies were administered the vaccine in the first place if they were seriously ill with sepsis or pneumonia at the time of immunization. It suggests that there had been a serious programmatic error that the medical staff administering the vaccine did not recognize the child was seriously ill at the time of immunization. If the episode of sepsis and pneumonia had its onset after vaccination and rapidly evolved to death in the next 12 to 36 hours, it should at least prompt an investigation into the vaccine and the vaccination process that could have caused the episode of infection.

The doctors in the hospital who noted the sudden increase in infant deaths in October sent telephonic text messages to senior government officials in the central and state governments to apprise them of these events. However, the AEFI team came down heavily on them for sending these messages, saying it was as if it was some form of “breaking news”. Apparently the doctors were expected not to take notice of these deaths, not to alert anyone, and to continue with business as usual.

It was in this context that PUDR put together a team comprising public health experts, and clinicians, to look into these deaths. The team which was in Srinagar between 8th to 10th November 2013, visited some of the affected families and conducted a verbal autopsy of the infant deaths (as per the World Health Organization (WHO) guidelines) to look for antecedent illnesses as well as enquire about the adverse events as per the Adverse Events Following Immunisation (AEFI) guidelines. The team met doctors and medical staff of the G. B. Pant Hospital, civil society groups and representatives of the Doctors Association of Kashmir, Srinagar. To get access to more information, PUDR along with Jammu and Kashmir Coalition of Civil Society (JKCCS) filed

applications under the Right to Information Act 2005. On 5th February 2014, a PUDR team also visited a family in Jhajjar (Haryana) who had also lost their child in January 2013, a day after receiving this vaccine. This report presents and discusses the findings of the team.

The report is divided into four sections. Section I provides information on the policy and implementation of immunization in India. Section II gives the background information regarding introduction of the pentavalent vaccine in India. Section III describes the findings of the verbal autopsies gathered from the visits to Srinagar and Haryana, as also the replies obtained under from RTIs on the

situation in other states. Section IV discusses the findings and concerns regarding safety of pentavalent vaccine.

This report should not be interpreted as being critical of all immunizations *per se*. Rather it is an attempt to place in the public domain, to the extent possible, all the information and all sides of the discourse on adverse events following immunization and safety of vaccines. The objective is to enable a healthy public discussion on the merits, limits, and problems of medical interventions, and to contribute to the promotion of safe, rational and effective use of vaccines in specific, and of medical interventions in general.

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Immunization and Health

Immunization is the process whereby a person is made immune or resistant to germs that can cause an infectious disease by the administration of a vaccine. The vaccine stimulates the body's immune system to protect the person against disease subsequently when exposed to the germ. Immunization (or vaccination) has been promoted across the world by governments and institutions such as the WHO as an indispensable tool and one of the most cost-effective public health measures for reducing the burden of infectious disease and improving the health of populations. Although use of vaccines to control infectious diseases are projected as major public health success stories, available data establishes unequivocally the significant role of improved nutrition, better housing, improved sanitation, water supply and hygiene in reducing the mortality and morbidity due to infectious diseases. It is well acknowledged that historically a major decline in the incidence of infectious diseases had started taking place with improvements in living conditions and nutritional status from the latter part of the nineteenth century, well

before the arrival of modern medical tools such as vaccines and antibiotics by the mid-twentieth century.

While immunization is largely accepted as a useful preventive public health measure, yet it is not the case that it is without any problems or limitations. Several concerns prevail among sections of the public health community. These relate to: the exclusive focus and promotion of immunization by influential and dominant political and health institutions, especially in the developing and poorer countries, at the expense of more important factors causing mortality and morbidity among children, such as malnutrition, and lack of safe drinking water and sanitation. Apart from such distortions in public health that the emphasis on immunization leads to, there are unresolved issues and concerns about the safety, efficacy and effectiveness of vaccines, especially the new vaccines that are being promoted in the past decade.

Immunization Policy in India

Systematic efforts to immunize children

began in India in 1978 as the Expanded Program on Immunization (EPI), launched mainly in the urban areas for immunizing children during the first year. Through the subsequent years, more vaccines were included in the programme, e.g. oral polio vaccine (OPV) in 1979 and the vaccine to immunize pregnant mothers with tetanus toxoid (TT) vaccine in 1983. In 1985, the programme was universalized as the Universal Immunization programme (UIP) to cover all the districts in the country, and covered six vaccine preventable diseases, with the inclusion of the measles vaccine (tuberculosis, diphtheria, pertussis, tetanus, polio, and measles); by 1990, the programme had been expanded across the country.

It is important to be aware of the trends in child mortality in India and causes of death in the context of immunization policies. When the EPI was launched in 1978, the under-5 years mortality rate (U5MR) had been on a decline already. A recent ICMR-UNICEF report¹ gives some information regarding these trends.

Firstly, it shows that between 1960 and 2008, the U5MR had fallen continuously. The U5MR started declining during the late 1970s, even before introduction of the immunization program in the country, and was quite substantial till 1993. (See Figure)

Even though the UIP was launched for six childhood diseases, these were not the leading causes of death among children. Childhood mortality continues to be due to problems such as: perinatal conditions (46.3%), respiratory infections (21.8%), diarrhoeal diseases and other infections (9.7%) parasitic diseases (8.3%), congenital anomalies (3.1%), symptoms signs and ill-defined conditions (3%), nutritional deficiencies (2%), unintentional injuries (1.4%), malaria (1.1%), and fever of unknown origin (0.9%)².

POLIO ERADICATION INITIATIVE 1996

The polio eradication initiative (oral polio immunization) implemented as a vertical campaign targeted against a single disease forcefully brought to fore the pernicious effects of such campaigns, being promoted since the 1980s, on an already weak health service infrastructure. With the launch of the Polio Eradication Initiative in India in 1996, a disproportionately large amount of human and material resources have gone for immunization against this single disease – polio, as against that for routine immunization. At that time polio eradication was not a priority for developing countries, including India, and there were considerations other than its public health importance in adopting this strategy. However, it simply had to be implemented as part of the Global Polio Eradication Initiative. The NPSP (National Polio Surveillance Project) and a network of 148 polio laboratories were set up solely for identification and surveillance of polio. Tens of thousands of workers were trained to investigate cases of polio and manage pulse polio immunization activities. It is acknowledged in official circles and in review reports that there has been decrease in routine immunization and other services due to the concentration on the pulse polio programme.

Secondly, the decline of neo-natal mortality (death in the first 28 days after birth) rate has been slower than the rate of decline in post-neo-natal mortality, resulting in increasing contribution of neo-natal mortality to infant mortality. Within the neo-natal period, decline in early neo-natal period (death within 7 days of birth) has been even slower, and has stagnated in recent years. The fact that perinatal

¹ NIMS, ICMR and UNICEF, 2012, *Infant and Child Mortality in India: Levels, Trends and Determinants*; National Institute of Medical Sciences (NIMS), Indian Council of Medical Research (ICMR) and UNICEF India Country office, New Delhi, India.

² Registrar General of India, Centre for Global Health Research. *Causes of death in India, 2001-2003: Sample Registration System*. New Delhi: Government of India; 2009

conditions result in 46% of the deaths among children below 5 points to the pressing need for improving quality of perinatal care (namely care during pregnancy and immediately following birth).

Thirdly, between 1981 & 2005 infant mortality rates (death before 1 year of age) and U5MR rates were consistently lower among children living in families who accessed drinking water from a safe source as compared to those who consumed water from an unsafe source, pointing to the need for improving living conditions for improving child survival. So, although the need for immunisation has been emphasised since very long, there are other equally important causes of death that demanded equal attention in the child protection strategies, but not given due attention.

The Universal Immunization Programme (UIP) in India is considered to be one of the largest immunization programmes in the world, in terms of quantities of vaccine used, number of beneficiaries, number of immunization sessions organized, and the geographical spread

and diversity of areas covered. But according to coverage evaluation surveys, as of 2009 India had achieved full immunized coverage of 61%. There is, however, a large variation in the immunization coverage across states, ranging from 24.8% to 87.9%. Coverage with three doses of DTP by age 12 months is used as a major indicator of immunization program performance. India had achieved 72% coverage with the three doses of DTP as of 2012.

The UIP was given the status of a National Technology Mission in 1986. In 1992, UIP became a part of Child Survival and Safe Motherhood (CSSM) programme and of the Reproductive and Child Health (RCH) programme in 1997. It continues to be part of this RCH programme, now placed under the National Rural Health Mission (NRHM).

The UIP is managed by the Immunisation Division of the Department of Family Welfare (DFW) under the Ministry of Health and Family Welfare of the Government of India. The functional responsibility is shared between the Central and State Governments, with the

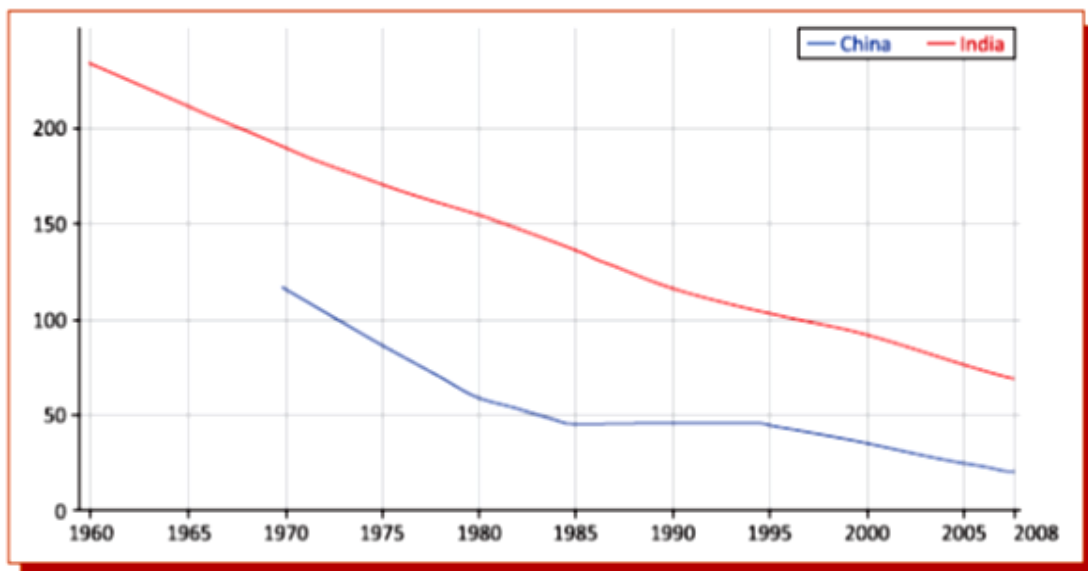


Figure: Trends in under-five mortality rate in India and China (Data Source: World Bank, World Bank Indicators)³

³ Same as in foot note no. 1

Centre providing funds, policy formulation, training of staff, cold chain support, and procurement and supply of vaccines and injection equipment; while the states are responsible for the implementation of the program through the district health system. Technical advice to inform decision making on both technical and operational matters pertaining to immunisation and choice and scheduling of existing and planned vaccines, is taken by the National Technical Advisory Group on Immunization (NTAGI) established in 1991.

The NTAGI is the primary advisory committee on all immunisation-related issues. This Group comprises bureaucrats and experts from national organizations involved in health-care policy and research, such as the Indian Council of Medical Research and the National Institute of Health and Family Welfare; professional organizations such as the Indian Academy of Paediatrics and the Indian Medical Association; representatives of government bodies such as the Child Health Division, Department of Biotechnology, Planning Commission, and the National Regulatory Authority (Drugs Controller General of India); representatives of five State Governments (Madhya Pradesh, Maharashtra, Orissa, Tamil Nadu and Uttar Pradesh); and five independent experts. Although not as formal members, representatives of UNICEF, the World Health Organization (WHO) and the World Bank are invited to attend committee meetings. Industry representatives may also be invited to present data but they do not participate in other discussions. The NTAGI meets annually to discuss the technical and policy issues pertaining to immunization, and to advise on the introduction of newer vaccines, based on the available disease burden data. Any major immunization decision is first discussed by the NTAGI and the recommendations are then operationalised by the Program Division within the Ministry.

Safety of vaccines - Monitoring and Surveillance of Adverse Events

It needs to be kept in mind that vaccines are administered to healthy individuals, mostly infants and children, and hence safety of immunization is of utmost concern. As immunization involves inducing an immune system response, most vaccines may cause side effects. There are increasing concerns about safety of newer vaccines. Hence most governments are setting up mechanisms for monitoring and treating adverse events following immunization (AEFI). An adverse event following immunization is defined as a medical incident that takes place after immunization, causes concern and is believed to be caused by immunization.

A surveillance mechanism has been instituted under the UIP for recording and reporting of all cases of AEFI. The AEFI guidelines provide information for immunization program managers at national, state, district, block and PHC level for establishing a sensitive system for detecting, notifying, investigating and responding to AEFI for vaccines supplied by the government. From 2007 onwards State & District Level AEFI Committees have been formed and in 2008 a National AEFI Committee was constituted. In 2010, the AEFI operational surveillance guidelines were revised and widely circulated. These guidelines are applicable to private practitioners also; as also for vaccines outside UIP. All *serious* AEFI cases – defined as those events that are life-threatening and those that result in hospitalization, disability or death - need to be investigated by District AEFI committee within a prescribed time frame. Timely reporting of AEFI followed by appropriate and detailed investigation is, thus, the key to successful causality assessment and signal detection.

In 2012, a National AEFI Secretariat was set up in the Immunization Technical Support Unit, which has been established at the Public Health Foundation of India by the Ministry of Health. The Immunization Handbook for

"In keeping with the Hippocratic oath, "First Do No Harm", any medical intervention including vaccines should be shown to be safe and effective prior to widespread adoption. However, interventions are rarely 100% safe. The decision to immunize must therefore balance the risks versus the benefits within an appropriate context. For preventive public health interventions like immunizations this context includes factors such as the incidence and severity of the target disease, as well as real and perceived adverse events following immunization".⁴

Medical Officers prepared by the Ministry of Health & Family Welfare directs Medical Officers to encourage Field workers to report AEFIs without fear of penalty, with the aim of improving systems to prevent/minimize further AEFI. It also says that anaphylaxis – one of the most serious adverse events and potentially fatal – is treatable without leaving long-term effects.

To enhance the safety data collection, another level of monitoring under the Pharmacovigilance Programme of India (PvPI) of the Central Drugs Standards Organisation (CDSCO) has been instituted. Under this Adverse Drug Reaction (ADR) Monitoring Centres have been set up to monitor ADR following immunization. This mechanism analysed 581 individual case safety reports received between April 2011 and December 2012. This analysis shows that largest number of ADRs were reported for DPT vaccine (297, of which 24 were serious and 282 non-serious) and for polio vaccine (198 of which 2 were classified as serious)⁵.

Production of vaccines

The basic vaccines for the national immunization programmes were being manufactured largely by public sector institutions and companies, such as the Central Research Institute- Kasauli, King's Institute- Chennai, Haffkine Institute- Bombay, and Pasteur Institute- Coonoor. Over the past two decades production of vaccines has come to be viewed as a significant profit-making business within the pharmaceutical industry, and a large number of private companies have started production of vaccines with an eye on the huge 'market' for vaccines in India as well as in other developing countries, which have national immunization programmes. Some of the well-known private manufacturers are: Panacea Biotech, Serum Institute of India, Bharat Biotech, Shanta Biotech. The private manufacturers receive support from the government for research and development of new vaccines, in the name of applying science and technology for betterment of health of populations.

India is a major vaccine producer and supplier, with 12 major vaccine manufacturing facilities. These vaccines are used for the national and international market (150 countries), making India a major vaccine supplier across the globe. In 2012, seven vaccine manufacturers from India were producing 67 vaccines prequalified by WHO (dosage forms). Currently 16 vaccines are prequalified by WHO and exported through United Nations agencies. More than 70% of all measles vaccines used globally are produced in India.⁶ The vaccine industry is looked upon as an important constituent of the biotechnology industry in India, with vaccine sales contributing a large share to the total sales in this sector.

The Central Drugs Standards Control Organisation and the Drugs Controller of India

⁴ The Brighton Collaboration : Addressing the need for standardized case definitions for adverse events following immunization. By Bonhoeffer, J and others in Vaccine 2002, volume 21, pages 298-302.

⁵ Pharmacovigilance Programme of India (PvPI) Newsletter, 2013, April Issue, page 5.

⁶ http://www.searo.who.int/india/topics/medicines/nra_meet/en/, last accessed on 10.3.14

(DCGI), constitute the National Regulatory Authority (NRA), which regulates the manufacture, import, sale and distribution of vaccines in the country.

Introduction of New Vaccines

Over the years there has been an increase in the number of immunizations recommended for children within the first two years of age. In this time period vaccines for protection against 14 diseases are recommended in countries like the USA. There have been attempts to reduce the number of administrations and injections in order to achieve this large number of immunizations, by trying to combine vaccines. Vaccines like the one for DPT (triple antigen) were the first of the combination vaccines, to which more vaccines are being added to get quadrivalent (four-in-one) or pentavalent or even hexavalent (six-in-one) vaccines.

In the developing countries too, over the past decade there has been significant increase in activity and focus on addition of these new vaccines in the immunisation programmes. Through the WHO there have been moves to introduce vaccines for pneumococcal and rotavirus infections, hepatitis-B vaccine, human papilloma virus vaccine for protection from cervical cancer (HPV vaccine), and a pentavalent combination vaccine in all national immunization programmes. Some vaccines, such as the HPV vaccine and cholera vaccine are licensed in the country and available for use in the private sector but are not currently part of the Universal Immunization Programme.

Technically the NTAGI has been the nodal agency for giving clearance to the introduction of new vaccines. However, for most of the time, the NTAGI has been functioning in a rather ad-hoc manner, without actually having a policy document in place for introduction of new vaccines. In June 2009, a draft document for evidence based National Vaccine Policy (NVP) was put together through an interdisciplinary workshop of scientists, doctors, public health professionals, lawyers and activists, and

submitted to government for consultation. However in 2011, the Government came up with its own NVP. A vaccine policy unit was also constituted for evidence collection and compilation of underutilized and newer vaccines, which included pentavalent, hexavalent, hepatitis B, rota virus and Japanese encephalitis vaccines in endemic districts.

The need of several of these vaccines, such as for hepatitis-B and for Hib vaccine, has been a matter of intense debate, and in the past few years sections of public health professionals have raised several concerns relating to efficacy and epidemiological priorities. For instance: the introduction of Rotavirus and Pneumococcal vaccines (PCV) to reduce diarrhoea and pneumonia mortality respectively and of hepatitis-B vaccine has been questioned on grounds of epidemiological need, efficacy and safety. Unresolved issues remain regarding their efficacy and effectiveness in decreasing mortality due to childhood pneumonia and diarrhoea in developing countries. It has been repeatedly pointed out that both pneumococcal vaccine and rotavirus vaccines have low utility but high costs. For the same expenditure more lives could be saved by alternate use of the money. The concern is that introduction of these vaccines is likely to divert the meagre resources available away from more beneficial, evidence based cost-effective interventions such as supplying safe water and sanitation, promotion of early and exclusive breastfeeding, and improving health systems, which are crucial to control more sustainably morbidity and mortality due to several childhood problems such as diarrhoea, pneumonia, and others such as polio.

The Pentavalent Vaccine

As per the government, the pentavalent vaccine, in various combinations, has been used by private practitioners in India since 2004 and that lakhs of doses had been supplied to the private market since then. The cost of the vaccine was prohibitive, at Rs 6000/- for a 3-dose complete course, and hence it was not available to the poor and the neediest. The provision of the same by the government through its UIP was intended to address these equity concerns.

In 2008 the NTAGI recommended introduction of the pentavalent vaccine in the UIP and in 2009 the Ministry of Health & Family Welfare decided to go ahead with this recommendation. In August 2009 GAVI approved funding worth US\$ 165 million to the Government of India to support this measure and to continue funding support for the first two years. It needs to be mentioned that support from agencies such as GAVI or other international bodies for immunization is restricted to funds for procuring vaccine. As the programme is implemented through the public health infrastructure, all the other costs of the programme accrue to the recipient governments and hence it is not the case that the recipient countries bear no expenses. Furthermore, GAVI assistance is only for the initial two to five years. Full costs must be borne after that. As vaccination is a long term commitment, to initiate a programme simply due to the availability of a two-year grant is extremely short sighted.

The vaccine was to be introduced in a phased manner in the UIP. In the first phase, the vaccine was to have been introduced in 10 states and an estimated 18 million infants were expected to receive the vaccine.

However, the introduction of the vaccine was halted following the filing of a Public Interest Litigation (PIL) in the Delhi High Court in December 2009, raising several concerns

relating to rationale for introducing the vaccine as well as its efficacy. The petitioners, comprising medical practitioners including paediatricians submitted that the NTAGI had based its recommendation without considering data from studies which revealed that the burden of meningitis caused by Hib in Indian children is much lower than in other parts of the world. Further, evidence from countries which have used pentavalent vaccine for several years revealed that there was no real benefit to children. It also pointed out that the vaccine had been withdrawn from neighbouring Bhutan and Sri Lanka after reports of adverse effects following immunization with the vaccine. All this was in the absence of a National Immunization Policy. The petition asked for such a policy to be formulated. The Delhi High court sought a reply from the Indian Council of Medical Research (ICMR), NTAGI and Ministry of Health.

The government decided to halt the introduction of the vaccine and set up an expert committee to review all the available evidence on the Hib disease burden, to assess the need for introducing pentavalent vaccine as a part of UIP and review the possible adverse effects. This committee recommended that it should be introduced initially in just two states (of Tamil Nadu and Kerala) - to monitor the vaccine's safety. Data was to be reviewed after 1 year of introduction, before expanding the vaccine to other states. The NTAGI endorsed these recommendations.

Before the vaccine was introduced in Kerala, questions were raised from within the state. As a result, in October 2011 the Government of Kerala appointed a Committee under the chairmanship of Dr. Noel Narayanan, former Head of Paediatrics, Thiruvananthapuram Medical College to examine the controversies regarding the utility and safety of pentavalent vaccine.

According to the Committee, there were

several advantages of introducing the pentavalent vaccine. These included: (i) reduced number of injections, so instead of giving DTP, Hep B and Hib separately to an infant three times resulting in a total of 9 injections, the new combination of vaccine required only three doses to be given in all (ii) better compliance in terms of parents bringing their child for immunisation, (iii) more chances of the immunisation schedule to be successfully implemented, (iv) time and cost savings as multiple vaccinations can be given and (v) no special system or strategy needed for replacement of DPT by the pentavalent vaccine.

However, what is significant is that the Noel Narayanan Committee in its report acknowledged that the pentavalent vaccine

could give rise to the following adverse reactions, such as:

- (i) Fever up to 48 hours and anorexia and fretfulness,
- (ii) Local reaction in the form of tenderness, warmth, swelling, and redness upto 25 percent, at the place where the injection was administered
- (iii) Occasionally a palpable nodule and very rarely a sterile abscess,
- (iv) High Fever and inconsolable crying lasting 3 hours or more,
- (v) Rarely serious reactions like convulsions, loss of consciousness, breathing difficulties, cyanosis and anaphylactic (allergic) shock.

The Noel Committee recommended the

Legal recourse for a relook at the safety of pentavalent

Currently there are two petitions pending in the Delhi High Court (Writ Petition Civil 13698 of 2009) and the Supreme Court of India (Writ Petition Civil 697 of 2013) respectively by well known practicing paediatricians and other public health specialists of the country questioning the safety of the Pentavalent vaccine. The petitioners have laid out the problems in the manner in which the vaccine has been launched in the country and have prayed for quashing the use of the vaccine. Given below are views of two such paediatricians.

It is crucial to accept Pentavalent's role in the deaths. Government has admitted that in three cases, but all other cases should also be investigated carefully. We should accept that Pentavalent harms. We are not against Vaccines but what is most important is to ensure safety of children. If you want to give vaccines, inject them separately. This liquid Pentavalent- a combination of five vaccines is dangerous. Vaccine is important, but it should be safe & effective.

Dr Jacob Puliyl, Head of Pediatrics, St Stephen's Hospital, Delhi

My first point is, if a child dies within 24 hours of vaccination and you say it happened because of co morbidity, or there was a lack of parental care or give some other reasons for his death! This is not a satisfactory answer to an untimely death. This, according to me, is a failure of the whole immunization program & of the officials running it. My second point – has there any minimum death ratio been defined in a public health program which could tell us- that many deaths are acceptable against one lac children vaccinated?... if the answer is no, then what is the answer for the deaths caused by vaccination? Why should we use Pentavalent even after the deaths of so many children? Why are we not ready to suspend it? I am not against vaccines. I just want to say that a vaccine should save, not take lives. And if a vaccine is causing deaths, we should take immediate action.

Dr Yogesh Jain (MD), Public Health Physician, Jan Swasthya Sahyog, District Bilaspur, Chhattisgarh, Previously- Asst Professor of Pediatrics, AIIMS, Delhi

following measures to be implemented prior to introduction of pentavalent vaccine in the state. These were:

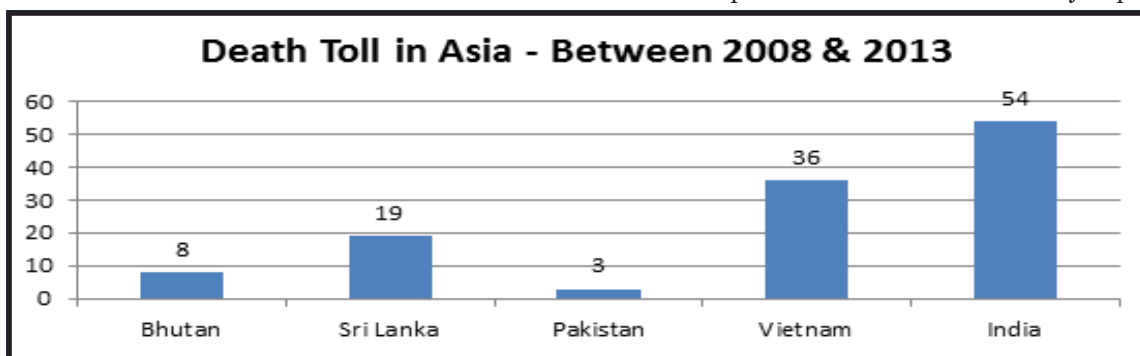
- (i) A doctor should be present when immunization is given,
- (ii) Vaccine should not be administered if there is a history of any serious reaction during previous vaccination or any serious contraindication present,
- (iii) Treatment of anaphylaxis should be available at the site of vaccination,
- (iv) Parents should be given a contact phone number and access to ambulances in case of adverse reactions,
- (v) All vaccinated children to be monitored for 48 hours after vaccination,
- (vi) ASHAs (Accredited Social Health Activists), ANMs (Auxiliary Nurse Midwife) and Anganwadi workers to monitor and record any adverse reactions,
- (vii) A post introduction evaluation should be done at least two years after to review the status of the vaccine and its impact on the incidence of meningitis and pneumonia in children,
- (viii) Steps should be taken for the local production of the vaccine to bring down the costs,
- (ix) Creation of awareness among health workers with regard to pentavalent vaccine,
- (x) Proper orientation of media, and
- (xi) Continuation of Hepatitis B at birth to

prevent vertical transmission and booster doses of DTP vaccine at 16-24 months and 5-6 years to be continued.

The pentavalent vaccine was subsequently introduced in Kerala and Tamil Nadu in December 2011. However, well before data from Kerala and Tamil Nadu had been analyzed, it was introduced between second half of 2012 and March 2013 in Karnataka, Puducherry, Goa (the state government in Goa had already introduced pentavalent in 2008, in select districts), Gujarat, Haryana, Jammu & Kashmir and Delhi. In November 2013 the NTAGI approved the national scale up of the pentavalent vaccine along with activities to monitor for potential adverse events of the vaccine, after the technical sub-committee recommended the expansion.

Adverse events following pentavalent immunisation

Serious Adverse Events Following Immunization (AEFIs) including deaths, after pentavalent vaccination have been reported in India, and several other Asian countries, since its introduction from 2008 onwards. Apart from a large number of AEFIs, 8 deaths were reported from Bhutan; 19 from Sri Lanka; 3 from Pakistan; and 36 from Vietnam⁷. There were at least 15 deaths in Kerala, 3 in Tamil Nadu, and 1 in Haryana, making a total of 19 deaths in India by the beginning of 2013. By the end of 2013 the reported death toll in India had jumped



⁷From: http://www.who.int/vaccine_safety/committee/reports/Jun_2013/en/, accessed 8.3.14; and Introducing pentavalent vaccine in the EPI in India: A counsel for caution, by Z Lone and J Puliyeel, in Indian Journal of Medical Research volume 132, July 2010, pages 1-3.

GAVI – The Global Alliance for Vaccines and Immunisation

GAVI was announced at the 2000 World Economic Forum in Davos to fund vaccines in developing countries. The founding partners of GAVI are WHO, UNICEF, World Bank, Bill & Melinda Gates Foundation, Rockefeller Foundation, the International Federation of Pharmaceutical Manufacturers' Association, and some national governments. GAVI aims to reduce under-5 mortality in the poor countries by making available new and underused vaccines, and strengthening delivery systems for immunisation. This is to be achieved by giving long-term financial support to "eligible" countries. The biggest contributors to GAVI are the Gates Foundation, US, Norway, the Netherlands and the UK. GAVI is touted as a major public-private partnership of all the "stakeholders" in immunisation. It is governed by a 16-member board, including five permanent members – the Gates Foundation, the World Bank, WHO, UNICEF, and the Vaccine Fund. The remaining 11 will include developing and developed countries and industry from each of these, NGOs, foundations, research and academia, and technical health institutes. In November 1999, the Gates Foundation pledged US\$ 750 million over five years to GAVI (www.gavialliance.org).

GAVI conditions for support include a guarantee for "reasonable prices", support for a credible and sustainable market, advanced market commitments for vaccines, safeguards against re-export of products from developing countries to higher-priced markets, and prohibition on compulsory licensing. GAVI did not support provision of the six basic EPI vaccines, DTP, polio, measles, and BCG, unless DTP was combined with hepatitis-B and/or *Haemophilus influenzae* type b (Hib) vaccines. India has so far taken GAVI support for introduction of the hepatitis-B vaccine in the routine immunisation in several states, and now for the pentavalent vaccine. In January 2013 GAVI organised a meeting of health economists and other experts to discuss the value of investing in vaccines.

A close ally of GAVI is the International Finance Facility for Immunisation (IFFI), a new "international development institution" designed to make funds available for GAVI projects. In October 2006 the IFFI launched a supranational bond to raise funds from potential investors, with the World Bank as its treasury manager. This is being projected as a new way of funding international development, and addressing "*the seemingly intractable problems of poor nations with a tried and true model from the world of business*" (see www.iffim.org). The International Finance Facility for Immunisation (IFFIm) uses long-term pledges from donor governments to sell 'vaccine bonds' in the capital markets, making large volumes of funds immediately available for GAVI programmes.

IFFIm was the first aid-financing entity in history to attract legally-binding commitments of up to 20 years from donors and offers the "predictability" that developing countries need to make long-term budget and planning decisions about immunisation programmes. IFFIm has got US\$ 6.3 billion in donor contributions over 23 years from the governments of the United Kingdom, France, Italy, Norway, Australia, Spain, The Netherlands, Sweden and South Africa. These long-term pledges are used to issue vaccine bonds, which have been issued in various markets - from London 2006 to Tokyo in 2010, - and are reported to be remarkably popular with institutional and individual investors who want a market-based return and an ethical investment opportunity. The World Bank is its treasury manager.

No matter what is said about the noble intentions to ensure vaccine reach to the poor millions in developing countries, one finds that a large number of vested interests (politely referred to as stakeholders) in the form of first world governments, sections of scientists, vaccine manufacturers, UN institutions such as WHO and UNICEF, and the World Bank have seamlessly aligned with the paternalism of multilateral aid, development, and philanthropic agencies, to form this supranational corporation in the name of using science and technology to address the poverty and health problems of developing countries.

to 54. These deaths, in different countries using vaccine from different manufacturers, ruled out defects in some specific batch of the vaccine, and also indicate that they are unlikely to be because of incorrect administration of the vaccine.

The WHO considers two deaths due to vaccination as a cluster that mandates rapid evaluation of the risk to public safety. The investigations and expert reviews by WHO Global Advisory Committee on Vaccine Safety, of deaths following introduction of pentavalent vaccine in the four countries (Sri Lanka, Vietnam, Bhutan, and India) could not attribute an alternate cause for the death; although in some cases causality could not be ascertained due to incomplete data. Yet, WHO continues to propagate that the deaths are not related to the immunization. In Sri Lanka and Bhutan, where vaccine was suspended due to reports of infant death, the programs have been reinstated following these investigations. Vietnam has taken precautionary steps to suspend individual lots of vaccine pending testing by an independent laboratory, but continues the program.

Studies from low-income countries indicate that co-administration of inactivated diphtheria–tetanus–pertussis (DTP) vaccine and live attenuated measles vaccine (MV) is associated with increased mortality compared with receiving MV only. A study from Guinea-Bissau, in West Africa, to examine the impact of co-administration of pentavalent with MV or yellow fever (YF) vaccine conducted between 2007-11 showed that pentavalent vaccine co-administered with MV and YF was also associated with increased mortality⁸.

In Kerala, the autopsy reports of two infant deaths following immunization with pentavalent vaccine said that ‘death as a result of post vaccination sequelae could not be ruled out’, and suggested that the vaccine was the

most likely cause for the deaths but stopped short of saying the vaccine definitely caused the deaths. Four out of five deaths occurred with the first dose of the vaccine and on the day of vaccination or the following day⁹.

Pentavalent vaccine is given to healthy babies. Each baby is examined by healthcare personnel before vaccination. Mothers in Kerala do not ordinarily bring very sick babies for immunisation. So it is unlikely that sick babies would have received vaccination. Babies who die are usually severely ill. The deaths in these vaccinated babies were deaths in apparently healthy babies who no one anticipated would die over the next few hours. Another possibility could be the rare SIDS (Sudden Infant Death Syndrome), the death of an apparently healthy baby without explanation. SIDS may be the explanation for a very small number of deaths. Here the ‘unexplained deaths’ following immunisation, are four times the number that usually die after the first month of life. SIDS is very unlikely to be the explanation for these deaths following Pentavalent vaccination. Furthermore, the SIDS rate in the third month of life is higher than that in the second month, and if these deaths were merely coincidental with the Pentavalent vaccine there should be more deaths after the second dose rather than the first.

The Noel Narayanan Committee had recommended that the Government collect data on each child immunised for 48 hours after immunisation. A government affidavit to the Delhi High Court suggests this was not done in a systematic way but reporting of adverse events was left to voluntary ASHA workers. These workers are given incentives depending on the number of children receiving pentavalent vaccine in their area. This could be a disincentive for reporting adverse events as such reports could reduce vaccine uptake and her earnings.

⁸Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau. Fisker, A.B. and others, in *Vaccine*, Volume 32, Issue 5, 23 January 2014, Pages 598–605.

⁹Pentavalent vaccine: Doing more harm than good?. Puliyeil, Jacob. 1 April, 2013. <http://pharma.financialexpress.com/sections/res/1971-pentavalent-vaccine-doing-more-harm-than-good>

-III-

Pentavalent Use in Jammu and Kashmir

The pentavalent vaccine was introduced in Jammu & Kashmir in February 2013, as part of the Universal Immunization Programme (UIP). In Srinagar six infant deaths were reported in October in the press following immunization with this vaccine.

The PUDR team visited the families of those infants who had developed serious adverse events after the immunization and had been admitted in the children's hospital in Srinagar. It was found that the FIR (First Information Report) filed by a doctor or health worker for reporting AEFI within 24 hours of recording (AE) had been recorded largely in cases of death and not in cases of those infants who had survived; in other words FIR was found to be prepared not in all cases, which is a gross violation of the AEFI Guidelines. Most of the infants had received the vaccine in a dispensary or health centre near their homes during the regular immunization day (Wednesdays), without a doctor in attendance in most cases. However, some of the children developed serious reaction later in the day or the following day, but could not be taken to the nearby dispensary as there was no doctor there. The parents rushed them to the G.B. Pant Hospital in Srinagar, the tertiary level children's hospital attached to the Government Medical College. In at least one case this travel took up to two hours, and by the time the baby reached the hospital, the case was reported as 'brought dead'. The team was told of about at least 9 deaths following immunization and could meet with some such families.

Baby A (born on 7.8.13) died on 10th October 2013. The date of death was wrongly recorded in the hospital records as 1.10.13. Baby A was vaccinated on the 9th of October at around 11.30 am at the local dispensary. She developed mild fever soon afterwards. Her parents administered paracetamol as advised by the

doctor. Next day around 1.00 pm., A started crying inconsolably with very high fever. As the local clinic did not deal with such emergencies, her parents braved a two hour journey to G.B. Pant hospital. She died within half an hour of reaching the hospital. However, hospital records accessed by PUDR recorded her as 'brought dead.' Representatives of the Central team who met A's parents told them that her death was not related to the vaccine as 25 other children had also received vaccination at the same centre the very same day, without any adverse effects being recorded.

Another family that the PUDR team met was that of Baby B, who had died on 3rd October 2013. Born by caesarean section on 5th July 2013, she was a perfectly healthy baby. After the 1st dose of pentavalent, B had slight fever for 24 hours and a lump for a few days on her thigh. After the 2nd dose on 25.9.2013 at a clinic, she developed high fever within half an hour and after having a feed within that first half hour, she refused to have any more feed or open her eyes crying inconsolably. Her mother took her to the local doctor, who prescribed paracetamol for the fever. Next day, however, when things did not improve, the family took her to G.B. Pant hospital. The FIR records of the hospital wrongly recorded the first symptoms of adverse effects as having occurred after 24 hours and not within half an hour of vaccination. At G.B. Pant hospital Baby B suffered repeated convulsions and finally died on 3.10.13. The family said that during their stay at the hospital they saw 5 other children also die after receiving the pentavalent vaccine.

Interestingly, B's cousin, C, who was born 12 days after her on 17.7.13, also developed fever and had repeated convulsions after receiving the vaccine. Fortunately, C recovered after hospitalization for four days in G.B. Pant hospital. However, the records at GB Pant do not record this case under those having adverse reactions. In fact, the hospital doctors told C's mother that there was no co-relation between

the convulsions and the pentavalent vaccine. At the time that the PUDR team met him, his mother confirmed that he was still on anti-convulsants.

PUDR also met up with the family of Baby D who also survived an adverse reaction following pentavalent vaccination. Baby D had been vaccinated on 21st October 2013 at around 10.00 am at the local dispensary. Within two and a half hours, by 12.30 pm he developed fever and started vomiting. By 6.30 pm he also had diarrhoea. After two days on the 23rd, his father took him to a private doctor who asked them to go to G.B. Pant hospital. Following this, D was admitted at the G.B. Pant for three days, till he recovered. Unlike C's case, D's admission in G.B. Pant had been recorded as a case of adverse event.

The PUDR team also visited the G.B. Pant hospital, where they met some junior doctors. The team was told that around 100-150 FIRs were recorded post pentavalent vaccine and kept with the State Nodal Immunization Officer. Subsequently, PUDR along with Jammu Kashmir Coalition of Civil Society (JKCCS) filed an application seeking further information under the Right to Information Act.

The reply to this RTI states that in 2013, 22 First Information Reports (FIRs) were filed regarding serious events following immunization. There were 14 deaths following immunization: 1 in June 2013; 1 in September 2013; 11 in October 2013; and 1 in December 2013.

All the 22 districts of the state are reported to have district level AEFI committee, while 7 have a District Immunization Officer: Anantnag, Budgam, Baramulla, Kathua, Leh, Samba and Rajouri. Health Workers are reported to be trained in reporting of AEFI at the Block and District level.

The RTI reply suggests the cause of death was sepsis, based on raised markers of Systemic Inflammatory Response Syndrome (SIRS), such as a raised blood neutrophil count. However, this need not be due to sepsis, but could be due

to any systemic insult. It is fallacious to attribute all SIRS like responses to sepsis.

Death in Haryana

On 5th February 2014, PUDR met the parents of Baby E in Jhajhar district, Haryana. E had died on 9th January 2013, shortly after receiving pentavalent vaccine.

Baby E was born on 22nd October 2012 after a full cycle of nine months and was a healthy child. Breastfed frequently and adequately, he gained weight in following weeks. On the fateful day of 9th January 2013, his mother took him to a nearby Aanganwadi Kendra, where he was administered the liquid Pentavalent injection, a vaccine that had been inaugurated in the village that very month.

E became unconscious within seconds of receiving the vaccine injection. His family thought he had slept due to vaccine effect, and took him home. But when he did not wake up till late that night, they rushed him to a private clinic in Rohtak where the doctor declared him brain dead.

E's grandmother still breaks down while narrating how the child was healthy and well the day they took him for vaccination. He did not have any symptoms of cough, fits or pneumonia, as was told by an Aanganwadi worker who tried to convince them that E had died due to the reaction as he had already been suffering with some disease. His family knew that was not true, E was perfectly well that day. The family is so frightened by the experience that they do not want to take E's brother for vaccination despite repeated requests by Aanganwadi workers.

As in Srinagar, in this case too we see that there was no monitoring of the child following immunization by a doctor; despite the fact that the child seems to have become unconscious very soon after. There was no follow-up or support to the parents and they had to go on their own to a private doctor for treatment.

AEFI from other States

(Refer to table under Section IV for statewise breakup)

At the second meeting of the Global Vaccine Safety Initiative in November 2013, held in India, it was reported that since the introduction of the liquid pentavalent vaccine here in December 2011, 176 serious AEFI including 54 deaths and 122 hospitalizations after 1,14,28,907 doses had been reported¹⁰.

As per information received under the Right to Information Act, the total number of AEFI following administration of pentavalent and oral polio vaccine (OPV) was 189; reported deaths following pentavalent immunisation in India stood at 54 as of December 2013. The state-wise figures are: 3 children in Delhi, 2 in Goa, 2 in Gujarat, 5 in Haryana, 12 in Jammu & Kashmir, 6 in Karnataka, 16 in Kerala and 8 in Tamil Nadu, while 135 children had been hospitalized. The data also shows that maximum babies died after receiving their first dose while others died after second dose and the third dose. A pattern may be deciphered here, if majority of deaths occur after the first dose, this indicates that the events are not random or happening by chance on the day of immunization. A random event happening coincidentally on the day of vaccination would happen equally regardless of the doses received previously. If a child was to be prone to reactions then also, the majority of those who are sensitive would be prone to reaction on administration of the first dose.

Why no reports of adverse events from the private practitioners?

It has been argued that no adverse events, including deaths, have been reported by medical practitioners from the private sector, where the pentavalent vaccine has been used prior to its

introduction in the UIP in 2011. This could be due to the fact that there is no systematic reporting or recording of such events by the private sector; it is not mandatory for them to report. For example, in February 2012 there was a death in North Kerala in a private hospital that did not figure in the list of AEFI from Kerala obtained under RTI. On inquiring about this from the designated Public Information Officer, the PIO replied that they had information on the death but had not included it as it was in private practice, because the vaccine had not been given through government sources.

In fact the NTAGI meeting in May 2012 gives a clear indication of this fact and suggests that “private sector deaths following immunization should also be communicated to the GoI”, and post-marketing surveillance reports must be closely monitored following introduction of the new vaccines¹¹. Hence, *the claim of no reported adverse events does not necessarily mean that they are not occurring; nobody has been looking for them systematically*. The fact that the doctor administering the vaccine in his private clinic for personal profit has reason to misrepresent the adverse events as unrelated to vaccination could be an important reason for non-reporting of the adverse events, for turning a blind eye. Secondly, anaphylaxis – the most serious of the adverse events and potentially fatal – is treatable without leaving long-term effects. It is possible that the availability of prompt follow-up and immediate treatment for adverse events to families that can afford to go to private practitioners and avail of immediate treatment, howsoever expensive, could be preventing deaths of children. Further, vaccines are given in the private sector to a miniscule proportion of the Indian population. Reactions will be seen more frequently when the vaccine is given to a larger number of children, as under the government UIP.

¹⁰ WHO Report of the Second Meeting of the Global Vaccine Safety Initiative, 19-20th November 2013, New Delhi, India. Available on: http://cdrwww.who.int/vaccine_safety/GlobalVaccineSafetyInitiative-Meeting-report.pdf.

¹¹Minutes, dated 11th June 2012, of the meeting of the National Technical Advisory Group on Immunization (NTAGI) held on 18th May 2012, under the chairpersonship of Secretary (Health & Family Welfare), Agenda No. 3.

Quality of the vaccines

Several irregularities/malpractices by vaccine manufacturers have been reported in the press that raised serious concerns regarding the quality of vaccines. In August 2011 WHO removed Easy Five of Panacea Biotech from its list of pre-qualified vaccines, due to quality concerns following a routine site audit by a WHO team. It was brought back into the list by WHO in early 2013. Similarly Shan 5 made by Shantha Biotechnics was also removed from the WHO list of pre-qualified vaccines in July 2010 following reports of a white sediment in the glass vial. It was to be back in the list at the end of 2013.

An investigation in Chandigarh in April 2013 into the death of a six-week old infant following administration of pentavalent vaccine found that Easy Five had been administered to the baby. As per a press note issued by the government, on 24.4.13 a telephonic complaint was received regarding the death of an infant who had received pentavalent vaccine the previous day, 23.4.13. Investigations revealed that the vaccine used was Easy Five of Panacea Biotech, whose manufacturing date was April 2011 and expiry date was March 2014¹². In May 2013 a former director of a public sector vaccine manufacturing unit sought a CBI inquiry into the recall by Panacea of a batch of its vaccine after the Tamil Nadu government seized some of its relabelled vials. According to media reports the company had re-labelled its vaccine vials manufactured in 2011 with an extended expiry date of 2014. While the expiry given by most manufacturers was 24 months, Panacea gave an expiry period of 36 months, which was said to be false.

The reports in the newspapers suggested that the deaths in Srinagar followed use of Easy five vaccine (manufactured by Panacea Biotec). Subsequently the vaccine was changed. Easy Five had been used in Bhutan, from where serious adverse events were reported. The

newspaper reports of use of Easy Five and the excess deaths in October may be a pointer that this brand of the vaccine is particularly likely to cause deaths. This fact does not appear to have been considered, or has not been highlighted by any of the investigating teams looking into the deaths.

For new vaccines, manufacturers have to furnish periodic safety update reports (PSUR) to CDSCO every six months for first two years and then annually for next two years. In response to a petition filed in the Supreme Court of India in 2013, Serum Institute of India, Pune (SII) being one of the respondents, had submitted three PSURs and two post-marketing surveillance (PMS) reports, but its sample size was very small. According to SII, no neurological, hypersensitivity reaction or any vaccine related adverse events were seen, indicating excellent safety and tolerability profile of vaccine. They were advised to continue the study for another two years. However, once again SII completed the study based on data of 1927 doses with similar findings. What is unexplained in their study is that from the period that the license was given up to 31st March 2013, there were a total of 66 AEFIs. These include 31 expected vaccine reactions, 19 program errors, 10 coincidental events and 6 unknown causes.

¹² <http://admser.chd.nic.in/uploadfiles/press/pressnote/pr7815.pdf>

-IV-

Discussion

In response to the questions in our RTI we have been told that all the districts in J&K have district level AEFI committees, and that all health workers have been trained in reporting of AEFI.

However, from the visit we gather that several precautions that should have been observed, several recommendations that had been made regarding pentavalent vaccination have not been observed. Such as: monitoring of children for 48 hours after, provisions for treatment of anaphylaxis at site of vaccination, a contact number and access to ambulances in case of adverse reactions, monitoring and recording of adverse reactions by local health workers. We found that after immunization the family was left to its own resources to access treatment for conditions such as fever and diarrhoea. The families had to take their children all the way to the Government Hospital in the capital city, by which time one child had already died. Could the deaths have been averted if timely treatment had been available at the peripheral health institutions (at block level – Community Health Centre or Primary Health Centre)? Why was no such information and treatment available to the parents? Should not these issues be addressed and the system strengthened before administering such vaccines that are known to be causing adverse effects?

A year after pentavalent was introduced in Kerala & Tamil Nadu, Kerala registered 14 deaths & Tamil Nadu registered 4 deaths, although the number of vaccine doses administered in the latter were much higher than that of Kerala. Similarly as the vaccine was scaled up in another seven states, this difference in figures showed up more starkly. On the face of it, it seems that Kerala which otherwise tops the human development rankings amongst States, actually has the largest number of deaths reported, while a state

like Gujarat actually has just 2 reported deaths.

State	Children fully vaccinated	Deaths
Goa	7,658	2
J&K	87,416	12
Haryana	1,91,361	5
Kerala	1,96,038	16
Tamil Nadu	4,14,591	8
Karnataka	4,50,903	6
Gujarat	4,58,492	2

State	Deaths per 1 lakh vaccinated	IMR
Goa	26.1	10
J&K	13.7	49
Haryana	2.6	54
Kerala	8.2	12
Tamil Nadu	1.9	31
Karnataka	1.3	45
Gujarat	0.4	50

(Source for both tables: PubMed Commons http://www.ncbi.nlm.nih.gov/pubmed/24021304#cm24021304_3394)

The difference in rates of deaths is shown up as evidence that the deaths are not due to vaccine but to unrelated events. However a look at the Infant Mortality Rate (IMR) data of these states provides some answers to this question. Goa, Kerala & Tamil Nadu are states with good surveillance system & low IMR, while in states like Gujarat the surveillance system is poor and IMR is higher (See Tables on the last page). Figures regarding children fully vaccinated for Tamil Nadu and Kerala is from December 2011 onwards, for Goa and Haryana it is from December 2012 onwards, for Puducherry and Gujarat from January 2013 onwards and for J&K and Karnataka is from February and March 2013 onwards. All the figures are upto October 2013.

Whereas in Goa one death is recorded per 3829 children vaccinated, in Gujarat, one death is recorded per 2.3 lakh children vaccinated. The difference here is because of differences in the IMR of both states. This is clear that states like Goa and Kerala with 10 & 12 IMR respectively, recorded higher IMR after introduction of pentavalent while in Gujarat where surveillance system is poor & IMR is already high, it can be linked to poor reporting of cases in the state.

However, the point here is the overall number of untimely, sudden deaths of infants, all adverse events following immunization with pentavalent vaccine. Why is it that the NTAGI and the government continue to ignore these events and have decided to not only continue the vaccination, but extend it to all other states?

If we use the data from the best case scenario for reporting (Goa), there is one death for every 4000 babies vaccinated with pentavalent vaccine and if the birth cohort in India of 25 million is vaccinated, the fatality statistics would probably be approximately 6250 each year. The Minz study on incidence of Hib meningitis shows an incidence of 7 cases per

100,000 children under 5¹³. With a 10% mortality rate from Hib meningitis only 175 children would die of Hib meningitis in the year's birth cohort of 25 million. 6250 vaccine deaths to prevent 175 deaths from the Hib meningitis seems unreasonable and unscientific! (Death from Hib pneumonia is even lower).

The investigations by the government team appear to be focussing solely on the clinical cause of death, they do not seem to be looking at the systems failure issues such as lack of follow-up and lack of treatment locally for adverse effects. The entire effort appears to be to only deny that they are in any way caused by the vaccine, rather than be concerned about the large number of deaths and look for insights into possible causes or pool all the data to generate and investigate hypotheses, as rational and ethical public health practice demands. The investigations into the deaths are not even considering other possibilities - such as: possible consequences of co-administration of pentavalent with OPV or measles vaccine, as the study from Africa cited above indicates; or the large number and frequency of deaths and serious AEFI being a signal or indicator of some as yet unknown adverse event.

Vaccine experts opine that safety of vaccine cannot be measured directly; it can only be inferred indirectly by absence or infrequency of measured adverse events. A scientific approach therefore would be to accept that more information and knowledge is needed and therefore halt the use; on the contrary we find that the concerned experts are only expanding the use of the vaccine. There is also attempt to modify the available classification of AEFI to deny any causality, as revealed by discussions among sections of doctors and public health experts on the web site PubMed Commons, of the US National Library of Medicine National Institutes of Health¹⁴.

The Investigations by the national team

¹³ Incidence of Haemophilus influenzae type b meningitis in India. By Minz, S. and others, in *Indian Journal of Medical Research*, 2008, volume 128, pages 57-64. Available on: <http://icmr.nic.in/ijmr/2008/july/0711.pdf>

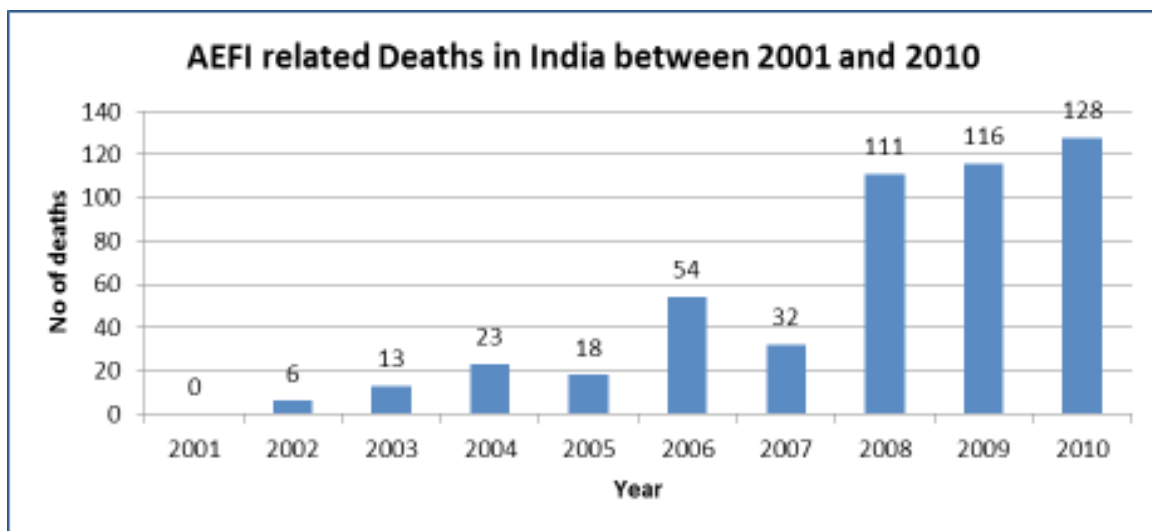
¹⁴ http://www.ncbi.nlm.nih.gov/pubmed/23452584#cm23452584_3553 and http://www.ncbi.nlm.nih.gov/pubmed/24021304#cm24021304_3490

rely only on hospital/clinical records to arrive at their conclusions on cause of death. Given that the infants were not monitored and observed for 24-48 hours, or till they were brought to the hospital, is it not possible that critical signs could have been completely missed? Is it not possible that the junior doctors attending to the infants may not have been experienced or trained enough to pick up or look for unusual or potential danger signs?

This is not the first time that AEFI and deaths following immunization are being reported. The monitoring of severe adverse events following immunization was started in India in 1985. In 1990, 29 incidents of severe adverse events following immunization were recorded, including ones where the cause of death was temporally related to immunization, or could not be determined, but was 'most likely to be coincidental to immunization'. Deaths varying from one to six were reported in 25 of these 29 cluster of incidents, amounting to nearly 30 deaths. Majority of the incidents were following DPT immunization¹⁵; a finding similar to the analysis of the PvPI findings mentioned above.

It is a matter of concern that, as per

information given by the Union Minister for Health & Family Welfare in the Rajya Sabha in September 2012, total number of deaths following immunization in the country (AEFI) during the previous decade (2002-12) was 644¹⁶. Data provided in response to a RTI application indicate an increase in the country in vaccine-related deaths since 2008. The total number of deaths reported due to adverse effects from immunisation (AEFI) from 2001 to 2007 was only 146, whereas it went up to 355 in the following three years. As per the Ministry of Health and Family Welfare, there were no AEFI deaths in 2001. There were 6 deaths reportedly after immunisation in 2002, which went up to 13 in 2003. As many as 23 children died following immunisation in 2004, 18 in 2005, 54 in 2006 and 32 in 2007. In 2008 alone, 111 AEFI deaths were reported. There was a marginal increase to 116 in the following year, and in 2010 there were 128 deaths. The government's response to the number of AEFI deaths in 2010 said there were 48 'coincidental' deaths with Maharashtra topping with eight such deaths; two children (one each in Maharashtra and Delhi) died on injection reaction; two died of program error (one each in Chhattisgarh and Maharashtra) and four had



¹⁵Adverse Events following Immunization: 1990. By J. Sokhey in *Indian Pediatrics*, June 1991, volume 28, number 6, pages 593-607

¹⁶ <http://pib.nic.in/newsite/erelease.aspx?relid=87561>, last accessed on 1.11.2013

died of vaccine reaction. As many as 72 deaths have been attributed to 'unknown' cause. Again Maharashtra topped with 18, followed by Uttar Pradesh and seven in Andhra Pradesh¹⁷.

All data that is being collected regarding AEFI is being used to deny any causal link with vaccination, and does not seem to be used to avert deaths or mitigate the seriousness. The increase in AEFI cases is always explained away by attributing it to better monitoring and surveillance, as an indicator of a robust surveillance system. However, government officials themselves say that India lacks a strong system of AEFI surveillance and investigation¹⁸, that there is lack of information on background rates of several AEFI¹⁹. Even if there was a good surveillance system in place, is it not important to study the individual cases, to compare this with base-line information, to make use of findings becoming available from other studies on immunization, to lay down what is acceptable and what is not?

Lastly, attempts to draw attention to the large number of adverse events and deaths are being dismissed and the concerned clinicians and public health professionals speaking of these events are being labelled as 'anti-vaccine lobby'. Indeed it has been reported at the meeting of the Global Vaccine Safety Initiative that the AEFI system is now "better equipped to handle media issues and voices raised by anti-vaccine groups through a coordinated mechanism and involvement of communication experts at ITSU."²⁰

Concluding Remarks

We find that there are problems, unresolved issues with pentavalent vaccines at several levels: relating to the very need, regarding its safety, about quality of vaccines, about preparedness of the healthcare system to handle, to manage and prevent adverse events.

Yet the policy makers persist on underplaying or even denying serious adverse effects and going ahead. What is the reason for this urgency to extend to all states, in disregard of so many problems, of the government's own recommendations to review all information from TN, Kerala, Haryana? Such an attitude points more towards callousness than concern for health of the children. It is not that there are no other ways of preventing morbidity and mortality even from meningitis. Timely medical attention can prevent minor illnesses from developing into serious ones; even serious ones can be treated with appropriate medical care. A Core committee on Vaccines, constituted by the ICMR to examine the recommendations of the Expert Committee on hepatitis and Hib vaccines, noted: "Pyogenic meningitis cases constitute 2-4% of all paediatric admissions and most of the children affected are less than 2 years of age. That of all the children with pyogenic meningitis a third each of the cases die, or recover with sequelae, or recover fully. That it is a medical emergency to be diagnosed and treated within 8 hours. That the healthcare system is unable to provide prompt, equitable healthcare and rehabilitation of assured quality to rural, peri-urban and urban poor. Hence prevention is ethical."²¹

Instead of improving the abysmal healthcare system, especially in rural and peri-urban areas, which would go a long way in

¹⁷ <http://www.thehindu.com/news/national/vaccinerelated-deaths-show-an-increase/article2057501.ece?ref=relatedNews>

¹⁸ Malik, 2014, in http://www.ncbi.nlm.nih.gov/pubmed/24021304#cm24021304_3490

¹⁹ See footnote no. 5

²⁰ See footnote no. 5

²¹ Minutes, dated 16.7.2010, of the meetings of the ICMR Core Committee on Vaccines held on 27th January and 26th April 2010, Agenda 5

addressing many health problems, minor and major, the policy makers choose to focus only on few measures and programmes, such as immunization and pose it as a matter of ethics. *That the healthcare system is not providing timely care for treatable illnesses is, however, not considered unethical.*

Immunization is a useful measure and we need to improve the healthcare system to carry it out safely and effectively. The issue is how does one go about it? Vaccines are generally introduced into the national programme of countries based on the burden and seriousness of disease to be prevented, the safety and efficacy of the vaccine and its economic affordability in the context of the national economy. Feasibility for inclusion in the routine immunization schedule and acceptance of the people at large also needs to be considered. Resolution 45.17 of the World Health Assembly mandates that member countries integrate cost effective 'newer vaccines' into the national immunization programs.

It is difficult to ignore the current context of health policy formulation and of vaccine manufacture that began in the 1980s with the selective primary health care model. It is difficult to ignore the developments that have occurred in the name of 'globalisation of health', the compulsions of structural adjustment policies and health sector reforms, and the accompanying involvement of international agencies such as the World Bank, multi-lateral donors such as USAID and DFID, large foundations such as Bill & Melinda Gates Foundation (BMGF), and public-private institutions such as the GAVI, in health policy making in developing countries.

One finds that over the past few years advisory groups, such as the NTAGI, have been set up to promote advocacy for vaccines, especially for the introduction of new vaccines in the national immunization programmes. The push to form such advisory committees came from the World Bank and other international agencies. Secondly, WHO has been making

A case of different standards for developed countries and developing countries

Rotavirus infection is a common cause of severe diarrhoea in infants and children. The first vaccine for rotavirus, RotaShield manufactured by Wyeth Pharmaceuticals, was licensed and recommended for routine childhood immunization in the USA 1998. Wyeth withdrew the vaccine in 1999 due to safety concerns. The vaccine was associated with a rare intestinal problem called intussusception, a potentially fatal telescoping of part of the bowel, at an estimated excess risk of 1-2 cases in 10,000 cases of vaccine receivers. No rotavirus vaccine was available until RotaTaq vaccine (by Merck) was licensed in 2006 and Rotarix (by GlaxoSmithKline) in 2008 for use in US. Before being licensed, RotaTaq and Rotarix were each tested in about 60,000 to 70,000 infants, half of whom got the vaccine and half got a placebo.

Since licensure, the Centers for Disease Control (CDC) and the Food and Drug Administration (FDA) have been closely checking the safety of rotavirus vaccines as pre-licensure trials are often too small to detect rare events, and special populations may not be adequately represented. This post-licensure monitoring is being done through three different monitoring systems; to not only monitor adverse events already known to be caused by vaccines, but to also detect rare adverse events that were not identified during pre-licensure clinical trials.

The question that is raised is about why expert committees like NTAGI, institutions like WHO and other international agencies like USAID, Gates Foundation that are supposed to be offering technical advice, not recommend and follow such procedures in developing countries, even after so many deaths have been reported following use of the pentavalent vaccine? It is being only pushed further instead of being stopped and more studies being conducted. Why such a differential approach to safety with the same strategy of immunization?

recommendations for universal inclusion of vaccines like the rotavirus vaccine without regard to local needs and cost effectiveness. The WHO has been shown to be considerably influenced by business interests of the pharmaceutical industry, as well as by large non-governmental organisations like the Gates Foundation. In the name of technical assistance agencies like WHO exert considerable influence on governments to adopt certain programmes, irrespective of their desirability, need and costs to the public health needs of concerned countries. Funding mechanisms like GAVI and bilateral donors have been persuading developing countries to use new vaccines by providing donor grants. Along with these grants, they also impose strategies such as 'advance market commitments' for purchase of vaccines;

in this WHO again provides its name by 'pre-qualifying' certain manufacturers. Through these arrangements the vaccine manufacturers are assured of a ready-steady market.

Until recently, when a vaccine was proposed to be introduced, a subcommittee of the NTAGI would review the available literature and consult prominent experts to make an informed decision about introduction of the vaccine into the UIP. To promote transparency and to facilitate access to everyone, the minutes and recommendations (<http://mohfw.nic.in/dofwpercent20website/june.pdf>) were published on the website of the Ministry of Health & Family Welfare. As a consequence of this openness, NTAGI decisions could be subjected to scrutiny. For example, while the Minz et al study, based on meticulous surveillance of Hib

Health Ministry official and vocal advocate of pentavalent vaccine becomes Deputy CEO, GAVI

In early April 2014 an Additional Secretary and Mission Director, National Health Mission, Ministry of Health & Family Welfare, Ms Anuradha Gupta was appointed as Deputy CEO of the GAVI Alliance. Ms Gupta has been a very vocal proponent of the pentavalent vaccine. At a time when GAVI is talking of moving into massive expansion of GAVI-supported immunisation programmes, is it a mere coincidence that an influential government official in India will also occupy an important position in an international network of commercial interests supported large private foundations and other multilateral donor agencies from developed countries? If this is not using governments to promote private commercial interests at the expense of public health, then what else is? Given below are excerpts from a national print news item about the same.

"Gupta is currently responsible for managing the world's largest public health program, with an annual budget equivalent to US\$ 3.5 billion...", stated GAVI's announcement of her appointment. "It is not really appropriate when you have to deal with the same organisation in the future. From an ethical point of view it is wrong. But the bureaucracy is already full of conflict of interest, so hers is not an isolated case," said a retired bureaucrat about the appointment.

Gupta's impending move to GAVI is being seen as a classic example of the revolving door phenomenon - a term used to describe the movement of officials between the public and private sectors. It's a phenomenon that has raised eyebrows among many. According to a Transparency International working paper on 'Regulating the Revolving Door', for example, the main concern is how it compromises the integrity and impartiality of public office. "The use of insider information, including personal and professional contacts, obtained in one's prior employment in the government may be exploited to create an unfair advantage for the industry or company when it comes to policy negotiations, public contracting and other interactions with public sector entities," stated the paper.

Source: <http://timesofindia.indiatimes.com/india/GAVI-hiring-senior-health-ministry-official-raises-concern-over-conflict-of-interest/articleshow/33661542.cms>, April 12 2014

meningitis in a population of 6.5 lac persons, over a two year period (1997 to 1999), found the incidence of Hib meningitis of 7 per 100,000 children under 5, the NTAGI recorded that there are 52,000 new cases of Hib meningitis in the country each year based on a small survey of cases of 'presumed meningitis' in one district in Kerala.

A very significant development in June 2013 has been the reconstitution of the NTAGI and the setting up of Immunization Technical Support Unit (ITSU) to assist the NTAGI. The ITSU is funded by Bill & Melinda Gates Foundation specifically to provide technical and managerial support to accelerate coverage and to ensure system preparedness for new vaccines. A new confidentiality clause has now been inserted, ostensibly to protect the 'proprietary' interests of commercial, academic and other research institutions. However, the confidentiality clause extends beyond proprietary matters and no member is allowed to disclose the discussions, opinions or decisions of the NTAGI on a public or private forum for 10 years after leaving the committee. With this new confidentiality clause, the public will have less access to the rationale for decisions regarding immunizations.

Thus, in the name of technical advice and support, in reality there are several pressures on national governments to introduce new vaccines into their UIP without evaluating the local burden of disease or cost-benefits, in effect perverting the intention of the World Health Assembly.

It is difficult to understand why the proceedings and decisions of agencies ostensibly set up for technical support for activities that affect the public at large should be "confidential", should be hidden from public scrutiny? Are

propriety interests of commercial organisations more important than the health of children? It is difficult to understand why an agency such as ITSU should be "equipped to handle anti-vaccine voices", rather than have an open scientific discussion among the different views on immunization before arriving at decisions?

It also needs to be pointed out that concerns regarding vaccine safety and efficacy are not new, nor is it restricted to India. It is not widely known that there has been opposition to vaccination almost since its inception, such as to small-pox vaccination in England, United States and in India in mid-late 1800s. Over the last two-three decades in developed countries there has been either questioning of or opposition on grounds of safety and efficacy of certain vaccines. It is looked upon as an issue where mandatory vaccination measures to promote public health are in conflict with basic human rights and liberties, and has given rise to ethical problems, and questions of informed consent, etc²². It has also raised questions such as: who decides what is in the best interests of the community? There is a growing view on the need to move from the current situation, "which largely assumes the passive compliance of the population, to a policy where people are actively involved and their views respected", towards concordance rather than compliance²³ to include the views of dissenting health professionals, parents and others²⁴.

The question of immunisation is intrinsically linked with questions of public health services and priorities. Considering the critical and sustainable role breastfeeding, water-supply and sanitation can play, and their ability to reduce overall disease-burden, it seems more logical to invest in these interventions. It is also clear that presence of strong and well

²² Anti-vaccination movements and their interpretations. by Blume, S. In: Social Science and Medicine 2006, volume 62, pages 628-642

²³ Immunisation Policy: From Compliance to Concordance. by J Gervase Vernon. In: British Journal of General Practice, 2003, volume 53, pages 399-404

¹⁴ Mass childhood immunization: some ethical doubts for primary health care workers. By: Pilgrim D and Rogers A. In: Nursing Ethics 1995, volume 2, issue 1, pages 63-70

functioning health system is required without which it would not be possible to achieve meaningful coverage of any vaccine and monitoring and treatment of adverse effects. Both these aspects have been raised and recognised by both policymakers and medical practitioners. In the second meeting of the Global Vaccine Safety Initiative, held in 19-20 November 2013 in Delhi, for example, it was stated: ‘active surveillance studies in developing countries are important with increased vaccine uptake. Vaccines are being introduced earlier or exclusively in developing countries with incomplete safety profiles.’²⁵

Should there not be at least a moratorium on the use and a re-evaluation of the safety of this vaccine? The crucial question is - how many infant deaths following vaccination would we ignore or consider as acceptable, as the price, the collateral damage, to be paid in the name of science and for the cause of public health?

One finds that no lessons are being learnt from earlier tragedies (with use of thalidomide, of stilbesterol, of indiscriminate use of x-rays) for need for caution in medicine and health, and the need to remember always the dictum – first do no harm.

After all, “The aim of science is not to open the door to infinite wisdom, but to set a limit to infinite error”.²⁶

¹ See footnote no. 5

² Life of Galileo by Bertolt Brecht, 1939.

List of recent PUDR Reports		
S No.	Year	Name of Report
1	2011	Of Hum an Bondage :An Account of Hostage Taking in Bastar
2	2011	खेल खत्म पैसा हज़म : राष्ट्रमंडल खेल के निर्माण कार्य में मज़दूरों के शोषण की कहानी पर एक रिपोर्ट
3	2011	Shocking Calbusness and Neglect:A report on industrial accident and its aftermath
4	2011	Loot of the Land, Livelihood and Life:A joint fact finding in to incidents of crime against people in Odisha
5	2011	Beyond the Prison Gates:A Report on Living Conditions in Thar Jail
6	2011	बेमानी ज़िदगियों : एक औद्योगिक दुर्घटना और उसके बाद के घटनाक्रम
7	2011	A STORY OF SUICIDE 'AND SURVIVAL:Death in the custody of Vijay Vihar Police Station
8	2012	The Terror of Law :UAPA And The Myth of National Security
9	2012	Anything goes...In the name of National Security: Story of Soni Sori
10	2012	Travesty of Justice in the Seema Azad and the Vishwa Vijay case
11	2012	Bitter Affertaste :Exploitation of Workers in Almond Enterprises in Dehi
12	2012	कड़वे बादाम : दिल्ली की बादाम इकाइयों में मज़दूरों का शोषण
13	2012	Who is the state hunting? Incidents of Massacre by Security Forces and Salwa Judum under Operation Green Hunt, in Bhopur and Dantewada districts of Chhattisgarh
14	2012	Working Against Odds:Condition of Workers in the Cement Industry in Chhattisgarh
15	2012	आतंक के साये में आम झारखंडी : झारखंड के सुदूर गांवों में जनसंघर्ष और सैन्य दमन
16	2012	THIS VILLAGE IS MINE TOO :Dalit Assertion, Land Rights and Social Boycott in Bhagana
17	2013	यह गाँव मेरा भी है: भगाना में दलित दावेदारी, भूमि अधिकार और सामाजिक बहिष्कार
18	2013	A Death Most Foul:The Unnatural Death of Naim Ahmad in Thar Jail
19	2013	DAMS , DEVELOPMENT AND THE NORTH EAST:A Report on the Peoples' Resistance to Mega Dam s in the Brahmaputra and Barak Valley
20	2013	DRIVING FORCE :Labour Struggles and Violation of Rights in Maruti Suzuki India Limited
21	2013	Fake Encounters in Odisha:How the State Picks, Arrests and Kills Its Maoists'
22	2013	शोषण का पहिया : मारुति सुजुकि इंडिया लिमिटेड में मज़दूर संघर्ष और अधिकारों का हनन

About PUDR

Over the last 20-30 years, the civil rights movement in India has emerged as an independent one in defense of civil liberties and democratic rights of our people. The People's Union for Democratic Rights (PUDR), Delhi, is part of this movement. In 1976-77, it was part of a larger national forum of PUCL and DR and became PUDR on 1 February 1981.

In the last two and a half decades of its existence the organisation has taken up hundreds of instances of violations of democratic rights, covering most parts of the country and involving the rights of many sections of society. The right to life, liberty and equality, the freedom of expression, the right to struggle against oppression and the right to association are essential for the functioning of a just democratic state and society.

Some of the issues taken up by PUDR over the years include workers' rights, agrarian movements, forest policy, displacement, communal riots, caste massacres and repression on *dalits*, encounter killings, deaths and rapes in custody, anti-democratic laws, death penalty etc. PUDR conducts investigations, publishes reports, issues statements, distributes leaflets, organizes public meetings, demonstrations and *dharnas*, and fights legal cases to highlight the violation of people's rights, and to help towards their redressal.

PUDR is a non-funded democratic rights organization. It is not affiliated to any political party. Activists give their time on a voluntary basis and the organization meets its expenditures entirely through the sale of its literature and small donations by individuals with a cap of Rs. 3000 per year. PUDR does not accept foreign funds, or funds from any institutional funding agencies, foreign or national. Anyone can come for the weekly activist meetings, where ideas, issues and suggestions are discussed and debated in an informal and non-hierarchical atmosphere. To date, not a single weekly meeting has been missed. Members include people from all walks of life: academics, journalists, students, workers, people between jobs or even unemployed, lawyers, private sector employees, bank officials etc. If you wish to know more about us or become associated with PUDR, please contact us at the addresses given below or visit our website.

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For Copies: Dr. Moushumi Basu, A-6/1, Aditi Apartments, Block D, Janakpuri, New Delhi
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