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# CLOSING GAPS TO ACHIEVE THE MILLENNIUM DEVELOPMENT GOALS : ROLES A MEDICAL RESEARCH COUNCIL CAN PLAY - THE INDIAN EXPERIENCE

The Indian Council of Medical Research (ICMR) is an autonomous organization within the Ministry of Health and Family Welfare. Established in 1911, it has grown into a vibrant apex health research organization with the mandate to undertake and support basic, epidemiological, applied and operational research in areas of national public health importance. It directs its resources towards developing an indigenous research capacity to find practical, long-term sustainable solutions to the health problems the people of India face.

The Council supports two broad categories of research: upstream *i.e.* basic and strategic research aimed at generation of knowledge; and downstream, the applied and operational research leading to the development of tools for prevention, diagnosis and management, and translation of research findings into policy and action. It conducts research in its 26 permanent institutes and supports research in universities, medical colleges, research institutions, *etc.* in the form of grants-in-aid.

India is among the 189 member states of the United Nations that have committed themselves in September 2000 to an expanded vision of development – the Millennium Development Goals (MDGs); a vision that has human development at its core to sustain social and economic progress. Eight goals, eighteen targets, and forty-eight indicators (see Box) have been accepted as a framework for measuring development progress. These were adopted by a consensus of experts from the United Nations Secretariat, IMF, OECD and the World Bank. The goals are to be achieved not later than 2015. The importance of health to development is now well recognized and this is also reflected in the MDGs by giving prominence to health objectives. It is the result of health research that the people enjoy a longer life expectancy through use of products of research like vaccines, drugs, better management of diseases and life-threatening conditions, *etc.* Meeting targets related to income, poverty and education will not be possible until there is improvement in health of the communities.

It is believed that, if global progress continues at the same pace as in the 1990s, only the Millennium Development Goals of halving poverty and halving the proportion of people without access to safe water stand a realistic chance of being met, because of progress made by China and India. Regionally, at the current pace sub-Saharan Africa would not reach the Goals for poverty until 2147 and for child mortality until 2165. And for HIV/AIDS and hunger, trends in the region are heading up, not down. It is thus being increasingly realized that for many countries several of the goals seem out of reach. Though impressive strides have been made in biomedicine, their benefits are not reaching the poor people, and the communities who need it most.

There is an urgent need, therefore, to identify approaches and means to translate knowledge into effective interventions. This means better utilization of the existing tools, development of new tools for diagnosis, treatment, and prevention of diseases as well as working out strategies that would result in their reaching the populations in greatest need.

#### Millennnium Development Goals, Targets and Indicators

MDG	Goals and Targets
Goal 1	Eradicate extreme poverty and hunger
Target 1	Halve, between 1990 and 2015, the proportion of people whose income is less than \$1 a day
Target 2	Halve, between 1990 and 2015, the proportion of people who suffer from hunger
Goal 2	Achieve universal primary education
Target 3	Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling
Goal 3	Promote gender equality and empower women
Target 4	Eliminate gender disparity in primary and secondary education preferably by 2005 and in all levels of education no later than 2015
Goal 4	Reduce child mortality
Target 5	Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate
<b>Goal 5</b> Target 6	Improve maternal health Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio
Goal 6	Combat HIV/AIDS, malaria and other
Target 7	diseases Have halted by 2015 and begun to reverse the spread of HIV/AIDS
Target 8	Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases
Goal 7	Ensure environmental sustainability
Target 9	Integrate the principles of sustainable development into country policies and programmes and reverse the loss of environmental resources

#### Indicators

- 1. Proportion of population below \$1 a day
- 2. Poverty gap ratio (incidence X depth of poverty)
- 3. Share of poorest quintile in national consumption
- 4. Prevalence of underweight children (under 5 years of age)
- 5. Proportion of population below minimum level of dietary energy consumption
- 6. Net enrolment ratio in primary education
- 7. Proportion of pupils starting grade 1 who reach grade 5
- 8. Literacy rate of 15 to 24 year olds
- 9. Ratio of girls to boys in primary, secondary and tertiary education
- 10. Ratio of literate females to males among 15 to 24 year olds
- 11. Share of women in wage employment in the non-agricultural sector
- 12. Proportion of seats held by women in national parliament
- 13. Under-five mortality rate
- 14. Infant mortality rate
- 15. Proportion of one-year-old children immunized against measles
- 16. Maternal mortality ratio
- 17. Proportion of births attended by skilled health personnel
- 18. HIV prevalence among 15-to-24 year old pregnant women
- 19. Condom use rate of the contraceptive prevalence rate
- 20. Ratio of school attendance of orphans to school attendance of non-orphans aged 10-14
- 21. Prevalence and death rates associated with malaria
- 22. Proportion of population in malaria-risk areas using effective malaria prevention and treatment measures
- 23. Prevalence and death rates associated with tuberculosis
- 24. proportion of tuberculosis cases detected and cured under directly observed treatment short course (DOTS)
- 25. Proportion of land area covered by forest
- 26. Ratio of area protected to maintain biological diversity to surface area
- 27. Energy use per unit of GDP
- 28. Carbon dioxide emissions (per capita) and consumption of ozone-depleting chlorofluorocarbons

MDG	Goals and Targets	Indicators
Target 10	Halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation	<ol> <li>Proportion of population using solid fuels (proposed as an additional MDG indicator: not yet adopted)</li> <li>Proportion of population with sustainable access to an improved water source, urban and rural</li> <li>Proportion of population with access to improved sanitation</li> </ol>
Target 11	Have achieved, by 2020, a significant improvement in the lives of at least 100 million slum dwellers	32. Proportion of households with access to secure tenure
Goal 8	Develop a global partnership for development	Some of the indicators listed below will be monitored separately for the least developed countries, Africa, landlocked countries,
Target 12	Develop further an open, rule-based, predictable, non-discriminatory trading and financial system (includes a commitment to good governance, development, and poverty reduction – both nationally and internationally).	<ul> <li>and small island developing states.</li> <li>Official development assistance</li> <li>33. Net ODA total and to least developed countries, as a percentage of OECD/DAC donors' gross income</li> <li>34. Proportion of bilateral, sector-allocable ODA of OECD/DAC donors for basic social services (basic education, primary health care, nutrition, safe water, and sanitation)</li> <li>35. Proportion of bilateral ODA of OECD/DAC donors that is untied</li> <li>36. ODA received in landlocked countries as proportion of their GNI</li> <li>37. ODA received in small island developing states as proportion of their GNI</li> </ul>
Target 13	Address the special needs of the least developed countries (includes tariff-and quota free access for exports, enhanced programme of debt relief for HIPC and cancellation of official bilateral, debt, and more generous ODA for countries committed to poverty reduction)	<ul> <li>Market access</li> <li>38. Proportion of total developed country imports (excluding arms) from developing countries and least developed countries admitted free of duties</li> <li>39. Average tariffs imposed by developed countries on agricultural products and clothing from developing countries</li> </ul>
Target 14	Address the special needs of landlocked countries and small Island developing states (through the Programme of Action for the Sustainable Development of Small Island Developing States and 22nd General Assembly provisions).	<ol> <li>Agricultural support estimate for OECD countries as a percentage of their GDP</li> <li>Proportion of ODA provided to help build trade capacity</li> </ol>
Target 15	Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term	<ul> <li>Debt sustainability</li> <li>42. Total number of countries that have reached their HIPC decision points and completion points (cumulative)</li> <li>43. Debt relief committed under HIPC initiative, US\$</li> <li>44. Debt service as a percentage of exports of goods and services</li> </ul>
Target 16	In cooperation with developing countries, develop and implement strategies for decent and productive work for youth	45. Unemployment rate of 15-to-24 year olds, male and female and total
Target 17	In cooperation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries	46. Proportion of population with access to affordable, essential drugs on a sustainable basis
Target 18	In cooperation with the private sector, make available the benefits of new technologies, especially information and communications.	<ul><li>47. Telephone lines and cellular subscribers per 100 population</li><li>48. (a)Personal computers in use and (b) internet users, each per 100 population</li></ul>

The areas of ICMR's focus are the communicable diseases, maternal and child health, nutrition, and non-communicable diseases. As the few examples below illustrate, these broad avenues of health research support the Millennium Development Goals both directly and indirectly.

#### Halving Extreme Poverty and Hunger

In India as in most developing countries, the bulk of cost of treatment for ill health is met by out-of-pocket expenses, estimated to amount to 84.6% of the total health expenditure. This has serious consequences for the poor. A World Bank analysis has shown that direct out-of-pocket medical costs may push 2.2% of Indians to poverty in one year<sup>1</sup>.

ICMR believes that reduction of poverty through income generating schemes catalyses community participation in disease control programmes. Except during an epidemic, poor villagers cannot be expected to devote time to participation in a disease control programme at the cost of other tasks related to their livelihood. Innovative strategies are being applied to engage these populations in income generating profitable activities in which health interventions are a by-product<sup>2</sup>.

In a project on integrated bio-environmental control of malaria, schemes such as social forestry in areas with a high water table, production of edible fish along side larvivorous ones, and conversion of lagoons with mosquitogenic conditions into prawn culture ponds have been used. In some areas algae grow profusely in ponds and protect the mosquito larvae and the eggs from being devoured by larvivorous fishes. Algae removed from such ponds has been used to prepare paper and cardboard. These schemes appealed to the community as they helped in generating income (by selling of wood, fish, prawns, paper, *etc.*) and mosquito control is a spin-off<sup>3-5</sup>.

ICMR is facilitating schemes aimed at eradicating extreme poverty indirectly by decreasing loss of wages involved in the days lost due to illness, through developing more effective treatments (*e.g.* introduction of  $\alpha$ , $\beta$  -arteether, and drug combination treatment of malaria using drugs like artesunate and sulfadoxipyrimethamine) and regimens of shorter duration (especially for chronic diseases like tuberculosis using fluoroquinolones, adding ofloxacin and minocycline to WHO's multi-drug therapy for leprosy and kala-azar).

One of the targets of the Goal is to also reduce the percentage of underweight children by one-half between 1990 and 2015. For India, this would mean a reduction in child underweight rate from 54.8% in 1990 to 27.4% in 2015.

The major causes of child malnutrition in India include:-

 Infant feeding practices: National Family Health Survey-2 (NFHS-2) data indicate that nearly half of Indian babies have to wait to be breastfed for more than a day after they have been born. Another common feeding practice is the early termination of exclusive breastfeeding and introduction of supplementary feeding<sup>6</sup>.

- Infections: Illnesses and infections, especially diarrhoeal diseases, are strongly associated with child malnutrition. NFHS-2 data suggest infants suffer from diarrhoea by the age of six months, having experienced an average of 2.2 diarrhoeal episodes and by age of 12 months 5.2 illness episodes. NFHS-2 data also show that children who have suffered a diarrhoeal episode are 15% more likely to be underweight compared to children who have not experienced diarrhoea<sup>6</sup>.
- Maternal weight and low birth weight: Malnutrition begins early in life when children are born with low birth weight. Nationally, 20-25% of births are at low birth weights. Low birth weight of offspring is not only an evidence of poor maternal nutritional status but also an indication, of course, of future developments.
- ICMR is supporting studies on counseling for exclusive breast feeding, safe weaning practices for prevention of diarrhoea, community-based interventions for prevention of neonatal sepsis, and national nutrition monitoring.

#### Promoting Gender Equality and Empowering Women

Gender equality is central to many research studies being undertaken under the aegis of the ICMR. In India there has been a more than 200% increase in employment of women in industry. The Council is supporting studies focusing on environmental health problems of women and determinants of outcome.

Fertility regulation is an important element of reproductive health. In order to help women in fertility regulation, research is being directed towards increasing contraceptive choices for women (implants like Norplant-6, Norplant-2 and implanoa; injectables like two monthly NET-enanthate, monthly Cyclofem, vaginal sponge, triphasic pills) and promoting emergency contraception (levonorgestril, Cu-T200B). Development and evaluation of women-controlled interventions like the microbicides (Praneam polyherbal tablet for management of abnormal vaginal discharge, development of microbicides using peptides like maganin, nicin and cellular sulphate), and research on female condoms is also being undertaken.

#### Reducing by Two-thilrds Deaths Among the Under Fives

It is considered that reduction in infant and child mortality is in many ways the most important MDG, as children are the most important assets of a nation. In India, approximately 1.72 million children die each year before reaching their first birthday. The MDG target is to reduce infant and child mortality by two-thirds between 1990 and 2015. For India, this would imply a reduction of infant mortality ratio (IMR) to 27 and of the under five mortality rate (U5MR) to 32 by 2015.

Results of previous surveys and multi-variate analysis of NFHS-2 data, as well as a simulation model, indicate that a package consisting of expanded child and maternal immunization, antenatal coverage, nutritional supplements and home-based neonatal services is likely to be a high impact intervention strategy.

The ICMR is supporting a study for the use of bug-busters (probiotics) for prevention of sepsis in neonates. While probiotics have been described for many decades, their scientific basis for use in human medicine has arisen only recently. The strain Lactobacillus planatarum has been found to block Escherichia coli adherence to caco-2 cells and passage of E. coli in a transwell cluster system. Several studies have reported immunomodulatory, specific anti-infective and antiinflammatory action of normal gut flora and probiotics. A Indo-US collaborative study is ongoing in the state of Orissa with the objective to develop an appropriate infrastructure to monitor occurrence of neonatal sepsis in community and hospital born infants. The study also emphasizes developing and implementing interventions to reduce risk of neonatal sepsis by use of probiotics and alcohol-based products for hand washing in hospitals and community based health care setups to reduce pathogen transmission.

Another study that merits attention is aimed at promoting home-based new born and infant care. Although the infant mortality rate in the country has declined over the years, it is observed that most of this reduction is due to a decline in the post neonatal component. Neonatal mortality constitutes about two thirds of infant mortality. In India, most deliveries take place at home and the community has limited means of reaching health facilities during emergencies. In addition, their inability to recognize danger signs in the newborn results in delayed care-seeking and hence most neonatal deaths occur at home. This scenario is unlikely to change in the near future. Thus, it has become essential to find ways to provide neonatal care to normal, 'at risk' and sick neonates in the home setting to reduce neonatal mortality. A recent study on home-based newborn care, including treatment of sepsis by village level workers, has shown more than 50% reduction in neonatal mortality in a district in Maharashtra. The feasibility of extending this experiment through existing health systems in rural sites of five states is being tested. If found successful, this will be a model for reduction of neonatal mortality in the country, given the fact that in India only 25% of all births take place in institutions like hospitals and primary health centres and the rest take place at home; moreover, skilled attendants at the time of delivery are available only for 43% of births. In addition, nutrition monitoring for identification of malnutrition is being continued on an ongoing basis.

As indicated above, a large number of children die because of severe infections. Effective vaccines are available against some of these, but it has not been possible to introduce them in the national immunization programme because of lack of evidence on the magnitude of the problem in India, and the cost. One such infection is that of *H. influenzae* b (Hib). A vaccine-probe study is being planned to begin shortly using Hib conjugate vaccine/DTP/Hep combination vaccines (study vaccine) and DTP/Hep B (control vaccine). Alternative methods of delivery of existing vaccines is also being explored. It is planned that measles vaccine, which is presently administered subcutaneously, will be tried as an aerosol. Phase I clinical trials are scheduled for later this year. Administration of measles vaccine as an aerosol would help achieve higher coverage, and should be devoid of problems associated with unsafe injection practices. The trials will also enable assessment of a technology which could be used for mass administration of vaccine should a measles eradication programme arise in future.

# Reducing by Three-quarters the Number of Women Dying in Child Birth

India has a high maternal mortality ratio (4-5 per 1000 live births). It is estimated that 25,000 women die annually due to haemorrhages. Post partum haemorrhage (PPH) and underlying anaemia are the primary causes of maternal mortality in India and account for approximately 25-30% of maternal deaths. A multi-site study is being carried out to examine the feasibility of the proplylactic use of misoprostol in the prevention of PPH, to be applied at the peripheral level by paramedical workers at the time of conducting delivery. This project would serve as a model applicable to rural settings throughtout the country and possibly have implications as well for improving delivery practices in other developing countries. The study is being carried out in a sample of Primary Health Centres in five states in the country. Active management of the third stage of labour, a known evidence-based intervention that includes administration of a uterotonic, can prevent PPH due to uterine atony. Misoprostol (oral prostaglandin) has a tremendous advantage over other currently available uterotonics, as it is inexpensive, stable at room temperature and is given orally. It has minor side effects that are selflimiting and usually do no require any medication.

Anaemia is the commonest medical cause of maternal death. Encouraged by the success of universal iodisation of salt in the control of micronutrient deficiency due to iodine, studies are being undertaken on double fortification of common salt with iodine and iron as a means of combating nutritional anaemia.

Approximately 20,000 women die each year due to unsafe abortions, usually as a result of termination of pregnancy by unqualified and untrained providers performed under unsafe conditions. Evaluation of simple kits for early detection of pregnancy and studies on medical methods of pregnancy termination for unwanted pregnancies, such as RU486 with prostaglandins, are being carried out.

# Halting and Beginning to Reverse Spread of HIV/AIDS, and Incidence of Malaria and Other Major Diseases

Each year there are about 5.1 million reported cases of HIV; 1.6 million cases and 500 deaths due to malaria and 14 million cases with 1.8 million new cases and 0.4 million deaths due to tuberculosis.

Research on HIV/AIDS, tuberculosis, and malaria are high on the priority list of the ICMR. It has initiated several studies directed at combating HIV/AIDS (e.g. development and evaluation of an effective and affordable vaccine; cost-effective anti-retroviral therapy, large scale prevention trials using female condoms; newer regimens for prevention of mother to child transmission; paediatric AIDS; behavioural interventions to prevent HIV); malaria (eco-friendly integrated methods for control of malaria; development and evaluation of new drugs including combination therapy, development and evaluation of new insecticides and bio-control methods; preparation of sites for malaria vaccine(s) evaluation, development and identification of tools for stratification of malariogenic area for developing situation-specific control strategies to improve the efficacy of implementation of control programmes); tuberculosis (e.g.development of new-generation vaccines, development and evaluation of new drugs and drug regimens which are more effective and are of shorter duration for pulmonary and extra-pulmonary tuberculosis, chemotherapy trials and epidemiological studies in HIV-TB, development of rapid and reliable diagnostics); and other infectious diseases through development of preventive and therapeutic approaches.

#### **Ensuring Environmental Sustainability**

ICMR's initiatives include conducting studies related to environmental stability (like occupational exposures, indoor air-pollution, arsenic levels in water, pesticides in environment and foods, develop biomarkers of exposures to environmental toxicants, *etc*); study extent of occupational exposures, indoor air pollution to develop interventions; monitoring pesticides in environment and foods; environmental genetics (development of biomarkers of exposure to environmental toxicants); and development of hazard communication procedures.

#### Forging Partnerships for Development

Some examples of ICMR's initiatives in establishing partnerships for improving the availability and access and decreasing the cost of drugs needed for diseases of poverty include: TDR-Asta Medical, Germany for miltefosine; Panacea Biotec for praneem (a microbicide); WHO-SmithKline Beecham for albendazole in filariasis elimination strategy; aerosol measles vaccine – Serum Institute of India; typhoid vaccine – International Vaccine Institute, Seoul, Korea; hepatitis A vaccine – BBIL; Interferon – Shantha Biotech; rota virus vaccine – Bharat Biotech. The Council is also one of the founding partners in setting up a new initiative for development and evaluation of drugs for neglected diseases (DNDi).

India today is better placed in terms of knowledge to tackle the challenges of poverty, malnutrition, maternal and child health, infectious diseases, gender equality, unclean environments, *etc.* The issue is how best to apply the knowledge to benefit the poorest people. ICMR is contributing towards reduction of the gap in achieving the MDGs through health research. Many of the Council's research findings have found a place in national programmes, while efficacy of others is being demonstrated. This account illustrates how a medical research council can contribute to achieving the MDGs<sup>7</sup>.

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