

CHAPTER XXVII

INDIAN COUNCIL OF MEDICAL RESEARCH

The Indian Council of Medical Research (ICMR), New Delhi, the apex body in India for the planning, formulation, coordination, implementation and promotion of biomedical research, is one of the oldest medical research bodies in the world. It has completed 90 years of its existence.

The Government of India, as early as in 1911, set up the Indian Research Fund Association (IRFA) with the specific objective of sponsoring and coordinating medical research in the country. After independence, in 1949, the IRFA was redesignated as the Indian Council of Medical Research (ICMR) with considerably expanded scope of functions and responsibilities.

The ICMR was constituted as an autonomous organization, with the Union Health Minister as President of its Governing Body. A Scientific Advisory Board comprising eminent biomedical experts assists the ICMR in scientific and technical matters. The Council promotes biomedical research in the country through intramural research (through institutes totally funded by ICMR) and extramural research (through grants-in-aid given to projects in non-ICMR institutes).

Intramural research is carried out currently

through the Council's 21 permanent national research institutes/centres and six regional medical research centres. The permanent institutes are mission-oriented laboratories located in different parts of India and address themselves to research on specific health topics such as tuberculosis, leprosy, cholera and diarrhoeal diseases, viral diseases including AIDS, malaria, kala-azar, vector

control, nutrition, food and drug toxicology, reproduction, immunohaematology, oncology, medical statistics, etc. The regional medical research centres focus especially on the regional health problems, and also aim to strengthen or generate research capabilities in different geographic areas

of the country. In times of national emergencies there could be a coordinated attempt. Thus, many of the permanent institutes and regional medical research centres continue to take part in the serosurveillance of human immunodeficiency virus (HIV) infection, in addition to their specific fields of research. Apart from research, the permanent institutes are actively engaged in human resource development programmes by imparting training at the younger level through Masters and Doctoral programmes. In addition, many institutes/centres also organize national and international training

ICMR USES NGO'S, VILLAGE GUIDES AND EDUCATED YOUTH IN CASE FINDING AND MORE IMPORTANTLY, CASE HOLDING.

courses in specific areas in which the Council's institutes have acknowledged expertise.

Extramural research is promoted by ICMR basically to strengthen the biomedical expertise outside the Council, especially in medical colleges and the University system. This is achieved through (i) setting up Centres for Advanced Research in chosen research areas around existing expertise and infrastructure in selected departments of Medical Colleges, Universities and other non-ICMR research institutes; (ii) Task force studies which emphasize a time-bound, goal-oriented approach with clearly defined targets, specific time frames, standardized and uniform methodologies, and often a multicentric structure; and (iii) open-ended research on the basis of applications for grants-in-aid received from scientists in non-ICMR institutes located in various parts of the country.

Human resource development in biomedical research is encouraged by ICMR through various schemes such as (i) Research Fellowships i.e. Junior and Senior Fellowships and Research Associateships; (ii) Short-term Visiting Fellowships (which allow scientists to learn advanced research techniques from other well-established research institutes in India); (iii) Short-term Research Studentships (for undergraduate medical students to encourage them to familiarize themselves with research methodologies and techniques); and (iv) various Training Programmes and Workshops conducted by ICMR Institutes and Headquarters. For retired medical scientists and teachers, the Council offers the position of Emeritus Scientists to enable them to continue or take up research on specific biomedical topics. The Council also awards prizes to Indian scientists (young as well as established ones), in recognition of significant contributions to biomedical research.

In the context of the changing public health scenario, the balancing of research efforts between competing fields, especially as resources are severely limited, is a typical problem encountered in the management of medical research in developing countries. Infectious diseases, malnutrition and

excessive population growth have continued to constitute the three major priorities to be addressed in medical research throughout the past several decades. In addition to tackling these issues, research has also been intensified progressively on emerging health problems such as cardiovascular diseases, metabolic disorders (including diabetes mellitus), neurological disorders, blindness, liver diseases, cancer, mental health etc. Research on traditional medicine/herbal remedies was revived with a disease-oriented approach. Attempts have been made to strengthen and streamline medical informatics and communication to meet the growing needs and demands of the biomedical community. The Council is alert to the emerging challenges in terms of new diseases and new dimensions of existing diseases. The rapid organization of a network of Surveillance Centres for AIDS in different states of India in 1986 exemplifies this.

Two broad lines of research endeavour have been focussed in ICMR in the last two decades (1) application of available knowledge, under the prevailing socio-economic and cultural environment through Health Systems Research involving interdisciplinary efforts between biomedical, social and behavioural sciences with epidemiology acting as a bridge, and (2) application of the powerful tools of modern biology to search for the causes and also to unravel basic mechanisms and to identify risk factors leading to early diagnosis and development of new therapeutic agents including vaccines.

MAJOR CONTRIBUTIONS & ACHIEVEMENTS

During the nine decades of its existence, the ICMR has had several significant and path-breaking achievements to its credit and many of the research findings of the past have laid basis/foundation for formulating and launching several National Health programmes and Disease Control Programmes.

COMMUNICABLE DISEASES

Tuberculosis (TB): The efficacy and safety of short course chemotherapy (SCC) in pulmonary,

extra-pulmonary, and multi drug resistant (MDR) forms of affliction in adult and childhood tuberculosis have been demonstrated by the Council's Tuberculosis Research Centre (TRC), Chennai and SCC has been introduced in the National Tuberculosis Control Programme. An important breakthrough in the management of tuberculosis of spine without paraplegia has been achieved using ambulatory chemotherapy for six or nine months with daily isoniazid and rifampicin. A large scale community based double blind randomized controlled trial carried out in south India to evaluate the protective effect of BCG demonstrated that it did not offer any protection against adult forms of bacillary pulmonary tuberculosis. The Council has also achieved effective and optimal utilization of non-governmental organizations (NGOs), village health guides and students in urban areas and educated youths in tribal areas in case finding and more importantly, case holding. The TRC, Chennai has also demonstrated that supervised administration of anti-TB drugs twice weekly is as efficacious as daily self-administered treatment. The directly observed treatment short course (DOTS) is currently a globally accepted programme for control of tuberculosis.

Leprosy: The Central JALMA Institute for Leprosy (CJIL), Agra is responsible for the Council's main research activities on chemotherapy, immunology, pathology and biochemistry of leprosy. The main thrust of research in the area of leprosy now is to reduce the infection load in the community by introducing effective multi-drug therapy (MDT) and testing appropriate vaccines against leprosy.

A controlled, double blind, randomized, prophylactic leprosy vaccine trial was conducted in

south India very recently. Four vaccines, viz. BCG, BCG + killed *Mycobacterium leprae*, M.w. and ICRC were studied in comparison with a normal saline placebo. From about 3,00,000 people, 2,16,000 were found eligible for vaccination and among them, 1,71,400 volunteered to participate in the study. Intake for the study was completed in two and a half years from January 1991. There was no instance of serious toxicity or side-effect subsequent to vaccination. All the candidate vaccines were safe for human use. Decoding was done after the completion of the second resurvey in December 1998. Results for vaccine

ICMR HAS DEVELOPED GUIDELINES FOR ART TO HELP INFERTILE COUPLES WHICH INCLUDE LEGAL AND ETHICAL ASPECTS ALSO.

efficacy are based on examination of more than 70% of the original 'vaccinated' cohort population, in both the first and the second resurveys. BCG + killed *M. leprae* provided 64% protection (95% CI 50.4-73.9%), ICRC provided 65.5% protection (95% CI 48.0-77.0%), M.w. gave 25.7% protection (95% CI 1.9-43.8%) and BCG gave

34.1% protection (95% CI 13.5-49.8%). Protection observed with the ICRC vaccine and BCG + killed *M. leprae* vaccine meets the requirement of public health utility and these vaccines deserve further consideration for their ultimate applicability in leprosy prevention.

The concept of multi-drug therapy for leprosy was also field tested and evaluated. Pulsed rifampicin administration was observed to be therapeutically as good as daily or intermittent administration. A MDT regimen supplemented with one year of pyrazinamide administration has been found to have effect on persisters and subsequent faster bacteriological clearance. A MDT of longer duration for patients not responding to six months regimen has been recommended. Combined chemotherapeutic and immuno-therapeutic regimens have been designed and found to enhance killing and clearance of bacilli. These have been

found effective to reduce the duration of treatment especially in cases with high bacterial load. A new regimen comprising conventional MDT together with newer drugs like ofloxacin and minocycline has been found to be safe and well tolerated. Single dose of rifampicin, ofloxacin and minocycline (ROM) has been shown to be as effective as six months of MDT for patients with mono lesion leprosy.

Immuno-diagnostic tests (FLA-ABS, SACT-ELISA, PGL-ELISA, etc.) have been developed/tested for detection of sub-clinical infections and monitoring of chemotherapy in patients with multi-bacillary leprosy. Improved techniques for prevention and surgical correction of deformities of the hands and feet have been developed. Some probes targeting rRNA of *M. leprae* and a quantitative hybridization (microdensitometry) have been developed. These ribosomal RNA probes and rRNA-PCR techniques have been demonstrated to correlate with viability and diagnosis of active disease. This strategy shown for the first time by the ICMR is an accepted concept now.

A Mycobacterial Repository Centre has been established at the CJIL, Agra to serve as a source of reference, indigenous strains as well as for epidemiological characterization of mycobacteria.

Diarrhoeal Diseases: The main thrust of Council's National Institute of Cholera & Enteric Diseases (NICED), Kolkata has been on continuous and in-depth study of diarrhoeal diseases and to suggest remedial measures. This institute was designated as the WHO Collaborating Centre for Research & Training in Diarrhoeal Diseases in 1980. The major achievements in the area of diarrhoeal diseases are summarized below:

The demonstration that oral rehydration therapy could prevent mortality due to diarrhoeal diseases was an important milestone. Home available fluids (HAF) such as Sherbat (salt, sugar, lemon either singly or in combination) or tender coconut water, pressed rice water has been found to be equally effective and more

NATIONAL HEALTH PROGRAMMES

- National Malaria Eradication Programme
- National Filariasis Control Programme
- National Leprosy Control Programme
- Diarrhoeal Diseases Control Programme
- National AIDS Control Programme
- Iodine Deficiency Disorders (IDD) Programme
- National Cancer Control Programme
- Universal Immunization Programme
- National Tuberculosis Programme

acceptable than oral rehydration solution (ORS). The use of hypo-osmolar oral rehydration solution (R-Hypo-ORS) reduced the total fluid requirement and loss of fluids in stools in comparison to WHO-ORS. The feasibility and effectiveness of managing cases of dehydrating diarrhoeal diseases according to their severity at various levels of health care facility was demonstrated. This has led to 3-tier approach of managing acute diarrhoea in the Diarrhoeal Disease Control Programme.

A new toxigenic strain of *Vibrio cholerae* - *V. cholerae* 0139 - was detected and characterized and its epidemiology elaborated. A new phage typing scheme for *V. cholerae* biotype Eltor strain has been developed. This could be used as an epidemiological marker for tracing the source of infection. A new recombinant cholera vaccine was developed in a collaborative effort with other sister agencies in India. This vaccine has been successfully tested in animal model and has completed Phase 1 and limited Phase 2 clinical trial.

An enteroaggregative *Escherichia coli* (E Agg EC) has been isolated as a possible etiological agent of acute diarrhoea among children in Kolkata. It was isolated more frequently from children less than 36 months of age.

The emergence of rotavirus causing diarrhoea in adults in Kolkata is a new phenomenon. The group B rotavirus resembles the Chinese adult

diarrhoea rotavirus (ADRV) strains in electrophoretic profile. An immuno-diagnostic kit was developed for diagnosis of rotavirus infection.

Vibrio parahaemolyticus strains belonging to serotype 03.IC6 emerged in Kolkata. This strain has been studied using different molecular techniques such as ribotyping-genotyping by restriction fragment length polymorphism (RFLP) and pulsed field gel electrophoresis. No RFLP in the encoding region of the thermostable direct haemolysis (TDH) was observed. These strains predominantly belonged to one clone.

Viral Diseases: Research in the area of viral diseases is being conducted at the Council's National Institute of Virology (NIV), Pune, Enterovirus Research Centre (EVRC), Mumbai, National AIDS Research Institute (NARI), Pune and Centre for Research in Medical Entomology (CRME), Madurai. The Council is supporting research in a wide range of viral diseases including HIV, hepatitis, Japanese encephalitis (JE), poliomyelitis etc.

Cell culture from mosquito (*Aedes albopictus*) tissues was established for the first time in the world at NIV, Pune. These are being used worldwide for arboviruses studies. An effective surveillance system for detection of JE virus (which incorporates monitoring of vector density and serological evidence of virus activity in sentinel animals) has been established which has been taken up by the state of Tamil Nadu. This system will help in timely action in case of impending outbreak. Effectiveness of a strategy using water and environmental management and neem coated urea for control of vector population in the rice fields has been demonstrated. Efficacy of deltamethrin impregnated poly-propylene curtains against vectors of JE at least for five months has been demonstrated.

Kyasanur forest disease (KFD) in the Sagar-Soraba area of Shimoga district in Karnataka was discovered in 1957. Vaccine against KFD was

prepared and technology has been transferred for preparation of KFD vaccine to the State Government.

Indigenous ELISA kits for the diagnosis of hepatitis A and B infection and for Group A rotaviruses from human and animals have been developed by the Council's institutes. An IgM Antibody capture (MAC) ELISA kit has also been developed for the detection of flaviviruses [JE, West Nile (WN) and Dengue]. An immuno-diagnostic kit (Dipstick test) has been developed to detect IgM antibodies against dengue virus infection in human. For some of these diagnostics, technology transfer has already been made to industry partners. For others, active efforts are being made to find suitable industry that will take up the responsibility of commercialization. A large panel of mouse monoclonal antibodies has been developed against JE, WN, Dengue (DEN), Chikungunya (CHIK) and rabies viruses, which may lead to the development of numerous commercial viral diagnostic kits. Genotyping of JE virus on the basis of partial nucleotide sequencing was done and derived amino acid sequence of some Indian JE virus strains and phylogenetic relationship have led to identifying four major groups of JE viruses. Sequencing of relevant regions of DEN genome is being done to understand the genetic basis of emergence of different biotypes of dengue virus. A novel DNA virus termed as transfusion-transmitted virus (TTV) was found to be prevalent in India, transmitted mainly by non-parenteral routes and probably not an important cause of chronic liver diseases. Several cell lines have been developed for arboviruses and hepatitis viruses to be used for basic and diagnostic purposes. Clinico-epidemiological and serological studies done by NIV, Pune indicated a new hepato-renal neuropathy syndrome associated with measles.

The ICMR demonstrated the presence of HIV infection in India and initiated country-wide serosurveillance. The information so obtained on the magnitude of HIV infection and major modes of its transmission has become the basis, first for drawing up the national medium-term plan for AIDS control in

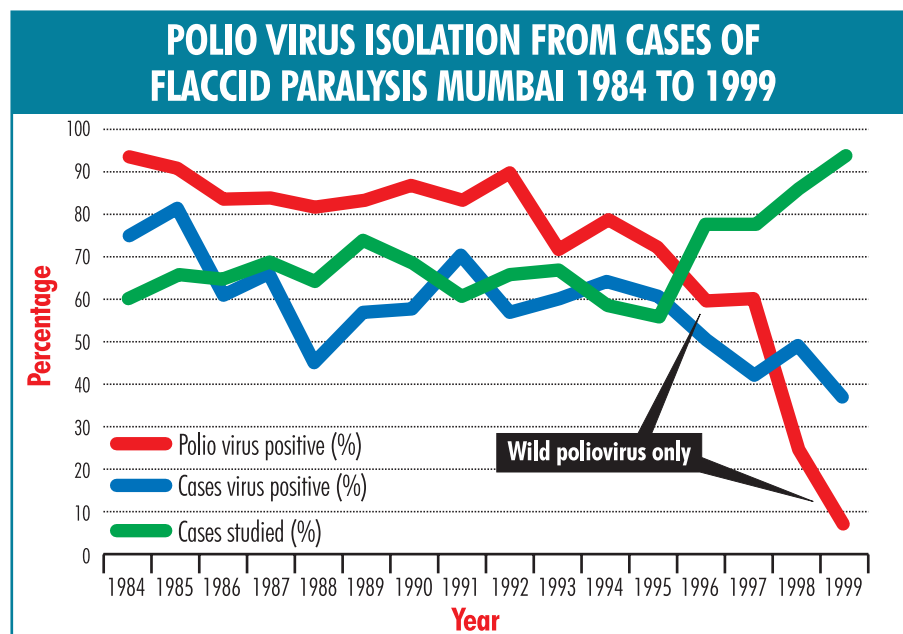
India and later for setting up the National AIDS Control Programme (NACP). Studies carried out by the Council led to the detection of HIV epidemic in injecting drug users in north-east (NE) India and initiation of intervention programmes. The presence of HIV-2 has been detected in India, which led to the incorporation of HIV-1, and HIV-2 screening tests in the NACP. Studies carried out in Manipur showed that in HIV infected individuals, herpes zoster had a high positive predictive value and could serve as a surrogate marker for HIV in areas where injecting practices are very common. HIV-1 subtype analysis was carried out for the first time in India by Heteroduplex Mapping Analysis (HMA) and the studies revealed that 96% samples were of subtype C. The other subtypes prevalent in India are B and A.

Poliomyelitis: Absence of paralytic poliomyelitis due to wild poliovirus infections and absence of wild poliovirus from the environment are essential components of polio eradication. An environmental surveillance study has been initiated using transgenic mouse cell line (L20 B) for virus detection. Poliovirus types 1 and 3 wild viruses were detected indicating the sensitivity and applicability of environmental surveillance.

Nucleotide sequence comparison has helped to determine genomic relationship among virus isolates. Sequence data of 72 wild poliovirus type 1 strains circulating in 13 states of India during 1997-98 have been generated. Sequences of wild poliovirus type 1 isolates from India and Bangladesh were also compared. As per the definition of genotypes, isolates from both countries are independent of a single major genotype. Wild poliovirus type 2 transmission has been eliminated from most parts of India and two distinct groups of wild poliovirus type 3 have been found in India.

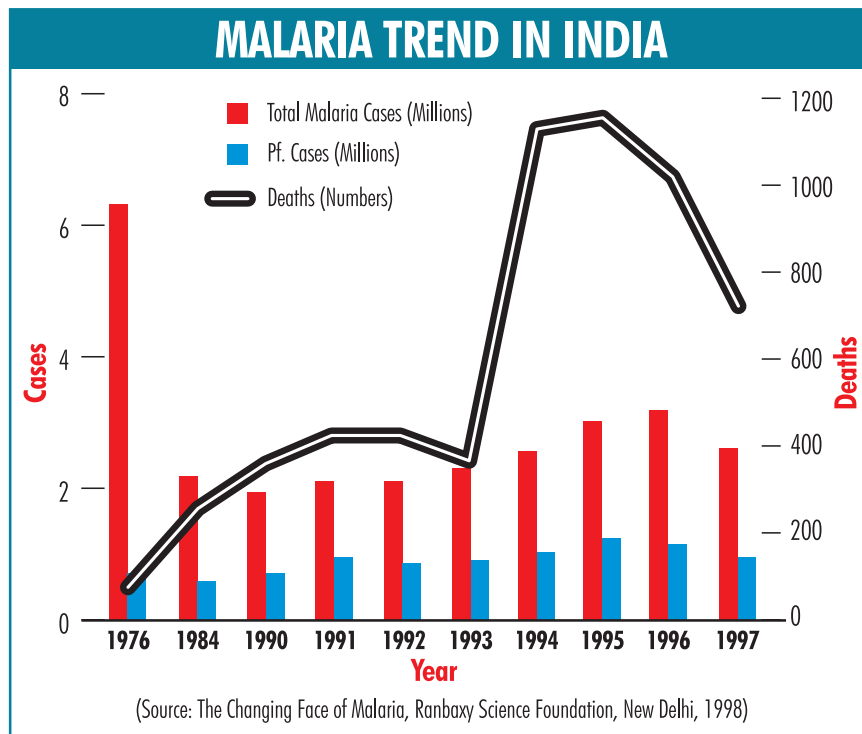
Malaria: Extensive field, basic and applied research has resulted in recognition of malaria paradigms in the country. New epidemiological paradigms have been formulated and are being used for the national malaria control strategy to review drug policy, insecticide policy and re-organization of the National Anti Malaria Programme (NAMP). A rapid, simple manual immuno-chromatographic technique (ICT) has been validated for detection of *Plasmodium falciparum* histidine rich protein (HRP) for on the spot diagnosis of this malaria in the field. Remote sensing and geographical information systems were

used to reveal malaria transmission dynamics at the local level. Cytogenetic studies in sibling species and combination of malariogenic indices and entomological parameters have helped in the malariogenic stratification of the country, which has provided vital information for the NAMP. A Malaria Parasite Bank has been established at the Malaria Research Centre as a centralized facility supported by DBT to cater to the needs of scientists and researchers.



Bioenvironmental methods of malaria control and other technologies in vector control were developed and applied in different geo-ecological sites in the country which are sustainable, free from ecological hazards and are also economical. This has provided a feasible alternative to the insecticide-based approach to control malaria. The indigenous, economic and environmentally compatible neem products were found to be effective for their larvicidal impact against *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti*. Mats containing neem oil were found to be effective repellents similar to allethrin mats which are ready for commercialization. The malaria situation is deteriorating in terms of morbidity and mortality due to increase in *P. falciparum* incidence and drug resistance in *P. falciparum* and *P. vivax*. The broad approach to fulfill the objectives of roll back malaria is prevention.

Filariasis: A community based integrated vector management programme achieved significant reduction in vector density in Cherthala, Kerala. No new infection of brugian filariasis in age group 1 to 7 has been reported in this area since 1990. This community oriented control programme is a unique example of inter-sectoral coordination where government and non-government agencies have worked together for success of the programme. Biological control of mosquitoes with a biocide *Bacillus sphaericus*, has shown specific larvicidal action especially against *Culex quinquefasciatus* in polluted breeding habitats. Extracts of *Anacardium* sps. have been tested for anti larval and anti pupal activity to control mosquito breeding. A slow release microgel formulation of *B. thuringiensis* var. *israelensis* has been validated for reducing the larval



density of *C. quinquefasciatus* in cess pits, cess pools and disused wells. A Cell has been set up at Vector Control Research Centre, Pondicherry for studies linked to elimination of lymphatic filariasis from India using Community Based Mass Control (CBMC) programme and comparing effects of DEC alone and DEC + albendazole.

Leishmaniasis: Simple, cost effective, easy to prepare culture media were developed for *in vitro* maintenance of *Leishmania promastigotes*, based on hemin or haemoglobin powder / clotted and dried rabbit blood on filter paper or fresh blood. It is completely autoclavable and can be used in an ordinary laboratory. Direct Agglutination Test (DAT) was established as early diagnostic tool for Kala-azar.

Clinical trials with combination of pentamidine and SAG (sodium antimony gluconate) in reduced dosage showed effective results similar to therapy with pentamidine alone but without any serious side-effects. Double drug combinations using pentamidine and allopurinol in reduced dosage were found to be better tolerated and showed good results when compared to pentamidine and SAG and pentamidine alone.

Leptospirosis: The Council's RMRC, Port Blair has done a sero-prevalence study of leptospirosis among the tribal population of Andaman and Nicobar Islands. A LEPTO dipstick assay was evaluated at RMRC and compared with IgM ELISA. This test has good sensitivity (78.7%) and specificity (88.3%) and was simple to use with stable shelf life of reagents. Various risk factors associated with acquiring leptospiral infection were also studied. RMRC, Port Blair has been providing referral services for the diagnosis of leptospirosis to other states of the country.

Tribal Health: Studies on the health, morbidity and mortality pattern and the nutrition profile of all the seven tribal groups (*Abujhmarias, Balgas, Birhor, Bharias, Kamars* and *Hill Korwaas* and *Saharlyas*) of Madhya Pradesh have been carried out. The prevalence of yaws was found to be 7% in *Abhujmarias* and goitre was a major public health problem in *Balgas* specially in children below 15 years. A drug delivery strategy has been developed and tested involving traditional healers of tribal communities as link workers in the state of Orissa.

REPRODUCTIVE HEALTH

The Council's research efforts in the field of reproductive health are mainly conducted by the Institute for Research in Reproduction (IRR), Mumbai, which is now renowned for its contributions in both basic and applied research. The Institute's work on inhibin and its potential application for male contraception are now widely recognized and cited extensively. The IRR's major focus is on three important leads in the area of male fertility regulation, viz. Human seminal plasma inhibin (HSPi), 80 kDa and 26 kDa proteins. The other activities include basic aspects of male and female fertility regulation, immuno-contraception, infertility, reproductive tract infection, diagnostics and operational researches on the fertility attitudes of men. Human sperm antigen, 80 kDa, has been identified from human sperm extract and efforts are ongoing to develop this peptide as an immunogen for develop-

ing anti-fertility vaccine. Efforts are being continued to develop intigrin as a clinical marker to assess the fertility potential in men. Resazurin Reduction Test (RRT) for evaluation of semen quality has been developed and validated. RRT is a simple, rapid, cheap and sensitive test, which is useful in diagnosis of infertility in men.

Based on the results of the clinical trials on several intrauterine contraceptive devices (IUCDs) CuT 200 was recommended in 1975 for use in the National Family Welfare Programme (NFWP). Multicentric clinical trials and pre-programme introduction studies were carried out through the network of human reproduction research centres (HRRCs) to evaluate newer contraceptives for their possible use in the programme; newer methods included improved intrauterine devices (CuT220C, CuT380A, CuT380Ag, LNG IUD), injectable contraceptives (200 mg NET OEN (2-monthly) and combined monthly injectable), subdermal implants (Norplant II 2 rods) and Norplant (6 capsules), triphasic oral pills, non-steroidal weekly oral pill (Centchroman), non-surgical methods for female sterilization, barrier methods (diaphragm, vaginal pessary), Billing ovulation method of natural family planning. Study on Sequelae of Female Sterilization carried out on 32,000 women indicated that Minilap may be recommended for National Family Welfare Programme as it is more efficacious and safer than laparoscopic sterilization under field conditions. The ICMR has prepared national guidelines for tubal sterilization by laparoscopy and minilap methods after studying the sequelae of female sterilization. Collaborative research efforts done for *in vitro* fertilization and embryo transfer among infertile couples has been of significant benefit.

Immunodiagnostic kits for urinary esterone glucuronide, pregnanediol glucuronide, luteinising hormone and follicle stimulating hormones have been prepared and evaluated. Some of these kits have been commercialized. A low cost, high sensitivity test for pregnancy detection has also been developed and is in the process of being commercialized.

Two new diagnostic techniques viz. ELISA for Hb

A2 for beta thalassaemia and FISH technique for detection of specific DNA sequence in morphologically preserved cells and tissues have been standardised. These techniques are being converted into user-friendly kits so that these could be used at peripheral hospitals.

Optimal time and safe procedures for medical termination of pregnancy (MTP) were recommended and non-surgical methods for MTP were evaluated. RU-486 in combination with PGE vaginal gel was found to be successful in 90% of women who sought termination of early pregnancy. Use of slow cervical dilator prior to vacuum suction during first trimester MTP was evaluated. Information on the extent of illegal abortions in India was generated.

MATERNAL & CHILD HEALTH

Studies were conducted in rural and urban-slum communities in various parts of India for the identification of high-risk mothers and fate of their offsprings. The risk factors identified were – maternal age (< 18 or more than 35 years), parity (primi para), bad obstetric history (1 or more abortion/still birth), preterm birth (less than 37 weeks), maternal anaemia, previous pre-term or low birth weight baby, birth interval (less than 2 years), previous foetal and neonatal mortality, low birth weight (less than 2000 g). Based on the results of these studies suitable intervention strategies were worked out to improve coverage and quality of MCH and FP services at PHC level using comprehensive health care package and high-risk approach. This approach has demonstrated significant improvement in antenatal coverage, referral of high-risk pregnancies and quality of care.

Maternal mortality and reproductive morbidity of women were studied both in the hospital based and community based settings. The studies showed that about two-third of these deaths occurred before reaching health care facility. Major causes of death were haemorrhage, sepsis, pregnancy induced hypertension and anaemia.

Clinical and ultrasonographic foetal growth parameters were developed. Feasibility of providing genetic counselling and identification of

referral has been successfully established in the peripheral hospitals in the country. The Council has also evaluated the quality of family welfare services at the PHC level.

The ICMR has prepared guidelines for Assisted Reproductive Technology (ART). These Guidelines have addressed several issues such as screening of infertile couple, selection criteria for candidates for ART, selection of donor, informed consent, procedures used, legal and ethical aspects. Infrastructure and training required, accrediting and registry, establishment of protocol and maintenance of records were also addressed in this study.

Scientists at IRR, Mumbai were the first ones in the country to report scientifically documented delivery of a baby using *in vitro* fertilization procedure. The institute continues to offer infertility services and train the doctors from other institutes in ART techniques.

NUTRITION

The Council's research efforts in the field of nutrition are in consonance with National Nutrition Policy and have been directed to combat malnutrition and promote nutritional well being. This is achieved through continuous research, monitoring, extension education and training carried out by the National Institute of Nutrition (NIN), Hyderabad and the network of National Nutrition Monitoring Bureau (NNMB).

NNMB has been continuously providing national data on dietary intake and nutritional status of population groups from different parts of the country. The studies indicate that about 30% of the households consume less than 70% of energy requirement. Dietary micronutrient deficiency particularly vitamin A and iron is widespread. About 80% of the individuals consume less than half their requirements. The studies revealed that half of the children are underweight and half of the adults and elder suffer from chronic energy malnutrition. Nutritional status of tribals is worse than their rural counterpart.

More than 650 types of different categories of

foods – cereals, millets, pulses, oils and fats, vegetables, milk and its products, fruits etc. have been analysed for the content of their energy, protein, fat, vitamins and minerals. Information generated by this activity is compiled in the well acclaimed publication - Nutritive value of Indian foods.

The indigenous sandwich ELISA method, developed at NIN, for the assay of serum transferrin receptor (STfR) was found to be a good indicator of iron status.

The Council's National Centre for Laboratory Animal Sciences (NICLAS) located at the NIN, Hyderabad is one of the major centers of its kind in India disseminating knowledge on the care, breeding and management of laboratory animals and their use in biomedical research. The NICLAS scientists have identified several natural mutants in mouse which are good models for drug development and chronic diseases such as – diabetes, tumours, cancers, infertility and obesity.

NON - COMMUNICABLE DISEASES

Oncology/Cancer: The National Cancer Registry Programme (NCRP) set up in 1982 has provided long term community based data on the occurrence of various types of cancers in India. The NCRP continues to generate data on the national cancer status in India. The operational feasibility of early detection of cervical cancer by para-medical workers through Pap smear screening and visual inspection of the cervix was established.

Cardiovascular Diseases: Secondary prophylaxis for rheumatic heart disease (RHD) with three-weekly penicillin injections has been demonstrated and a module for detection and management of sore throat, rheumatic fever (RF) and RHD utilizing the PHC infrastructure has been developed. A *Jai Vigyan* Mission mode project on RF/RHD control has been initiated.

The prevalence of coronary artery disease (CAD) and distribution of risk factors for CAD were established. Prevalence of CAD and population distribution of known risk factors was low in rural

as compared to urban areas. A multicentric case-control study has been initiated at four centres to identify the factors and quantify the association of risk factors with acute myocardial infarction.

Ophthalmology: The magnitude of blindness problem in various parts of the country has been determined. These data formed the basis for National Programme for Control of Blindness (NPCB). Prevalence of cataract has been determined in various parts of the country and data are being used in promoting eye camp approach in NPCB. Risk factors (use of cow dung and wood fuels and systolic blood pressure towards higher side within normal range) for cataract have also been identified.

Environmental & Occupational Health: Cardiac toxicity in humans as well as in experimental animals due to methomyl in pesticide spray has been described which has resulted in active consideration of banning of this pesticide by Government of India. Prevalence of occupation pneumoconiosis in high proportion has been described in Ladakh region of Western Himalayas. A multi-method ergonomics review technique for work systems analysis and design has been developed. Commissioning and standardization of acoustic, illumination and climatic chambers were done and data provided to set safe limits of exposure to noise, illumination and heat respectively.

Mental Health: Data have been generated on the magnitude of psychiatric problems in the country through community-based surveys. The Council's research on the integration of mental health care with general health care facilitated the formulation and implementation of the National Mental Health Programme.

ICMR has also generated data on prognostic outcomes of psychiatric disorders in India through longitudinal studies. The study of acute psychosis led to inclusion of a new diagnostic category in ICD-10. The Council has developed measurement tools for health such as for assessment of quality of life at

the individual, family and community levels, and also developed measures of psychosocial stress.

A community based epidemiological study of child and adolescent psychiatric disorders in rural and urban areas found the prevalence and type of psychiatric disorders and generated data on psychosocial correlates of childhood psychiatric disorders and on felt treatment need of the community. The Centre for Advanced Research on Health Consequences of Earthquake Disaster with special reference to Mental Health found that there was excess psychiatric morbidity in earthquake affected Marathwada region as compared to control areas.

Neurophysiology: The Neurophysiology Research Unit established in 1950s carried out several path-breaking studies on the intricate mechanisms for coordinating the physiological activities of the central nervous system. The mechanisms regulating hunger involving the two centres, one regulating food intake and the other inducing satiety were rigorously investigated.

Further studies on the role of hypothalamus on cardio-vascular and respiratory activities showed its wide influence on the various bodily activities including hormonal activity relating to reproductive function. Further, with collaboration from neurologists, pioneering studies were initiated on Yoga. This group provided for the first time unequivocal scientific basis for the positive influence of Yoga on human health. Some of these studies are being followed up even today. This group expanded their attention on the high altitude physiology. Their findings on the hypoxia, acclimation strategies and the physiological adaptation to high altitude and cold temperature were utilized by defense medical officers attending to the soldiers in these areas.

Neurological sciences: Multicentric, clinical and epidemiological studies were undertaken on epilepsy, head injury, peripheral neuropathy, subarachnoid haemorrhage and Landry's Guillian Barre (LGB) syndrome. The clinical presentations and associated etiological factors in these disorders were studied. The study on subarachnoid haemorrhage

disproved the widely held contention that aneurysms were extremely rare in India as compared to Western countries. Over one-fourth of all patients studied had aneurysm. There was also a preponderance of men to women in the ratio of 3:2. In addition, people from the North and Western India showed more atherosclerotic lesions in the Circle of Willis, as compared to the people based in the South.

A multicentric collaborative study was also taken up on stroke and ischaemic heart disease in the young and old populations of India. It was shown that, in contrast to the condition in the Western countries, nearly 30% of all strokes in India occurred in young subjects below forty years and ischaemic heart disease in the young constitutes about 15 to 20 per cent.

Haematology: A new blood group, the Mumbai group was discovered by the Council's Institute of Immunohaematology, Mumbai. A globin chain synthesis technique and chorionic villus sample biopsies have been developed for the prenatal diagnosis of thalassaemia and other haemoglobinopathies. Prevalence of thalassaemia trait and also of haemophilia has been determined. The findings of biochemical and molecular studies on red cell glucose-6-phosphate dehydrogenase (G-6-PD) deficiency in India brings out the fact that the deficiency is heterogeneous in nature as opposed to the common belief that it is only the Mediterranean type which is prevalent in India. The Council's studies also led to the discovery of two new G-6-PD variants namely G-6-PD Rohini and G-6-PD Jamnagar. The ICMR carried out detailed survey in tribal populations in different parts of India particularly in Madhya Pradesh and based on the information collected a *Genetic Atlas of Indian Tribes* has been prepared. The Council's Centre for Advanced Research for Bone Marrow Transplantation for Thalassaemia at Vellore completed bone marrow transplantation in 51 cases of thalassaemia major with a success rate of 72.5% comparable to anywhere else in the world. This is now the only Centre in the country, which is able to

offer services from antenatal diagnosis to bone marrow transplantation for thalassaemia major.

Pathology: Thrust areas of research consist of tumour biology (breast cancer, genitourinary malignancies, lymphoma), infectious diseases (chlamydia, leishmaniasis, tuberculosis), reproductive biology, Indian childhood cirrhosis, and environmental biology. Teaching material in the form of microscopic slides, colour transparencies in different branches of pathology has been prepared and distributed.

Traditional Medicine: Through multicentric clinical trials, the ICMR has demonstrated that *Kshaarasootra* (a medicated Ayurvedic thread) technique is a safe, acceptable, cost-effective, non-surgical and ambulatory alternative to surgery for the management of fistula-in-ano. Studies on the use of wood of the Vijayasara (*Pterocarpus marsupium*) in the control of diabetes mellitus has provided highly encouraging results.

PUBLICATION, INFORMATION & COMMUNICATION

The Indian Journal of Medical Research (IJMR), one of the oldest biomedical Journals of the country has completed 88 years of its publication. A large number of special issues/supplements on important biomedical topics have been published. The Integrated Research Information System (IRIS) was set up in early 1980s to provide information on inventories of scientists, information on extramural projects funded by the ICMR publications. The IRIS has been upgraded into a Bioinformatics Centre in New Delhi with strong communication links between ICMR Institutes and ICMR headquarters. A website has been created for the ICMR (<http://icmr.nic.in>). The ICMR-NIC Centre for Biomedical information has been identified as the Indian MEDLARS Centre. The Centre has developed IndMED, a database on the

Internet, of Indian biomedical publications not included in major international databases.

ETHICAL GUIDELINES

The need for uniform ethical guidelines for research on human subjects is universally recognized and the Council has prepared national guidelines on this. In the year 2000, the Council released a comprehensive document entitled Ethical Guidelines for Biomedical Research on Human Subjects.

INTERNATIONAL COLLABORATION

The ICMR coordinates the processing, implementing and monitoring of biomedical research programmes carried out under the auspices of either bilateral agreements between India and countries such as USA, UK, Russia and other CIS countries (formerly the USSR), France, Germany or as assistance from international agencies such as the WHO, Ford Foundation, Rockefeller Foundation, NIH, World AIDS Foundation (WAF), UNDP, IDRC, etc. Proposals received from various national laboratories in India are subjected to a rigorous peer review process followed by appropriate clearances from the Government of India. These programmes are intended to facilitate and promote biomedical research in areas of mutual interest to India and other countries/international agencies, with transfer of technology being one of the prime objectives. The facilities available and the modalities of operation vary according to the country or agency concerned. Other Departments/Agencies of the Government of India also deal with similar programmes, foremost among them being the DST, DBT, CSIR, etc. The ICMR offers consultation to other organizations and interacts with agencies for the approval of proposals dealing with biomedical research for implementation. Information on specific procedures for international collaboration/assistance in biomedical research is available with the Indo-Foreign Cell of the ICMR.