

# INDIAN COUNCIL OF MEDICAL RESEARCH (ICMR): INITIATIVES IN NEUROLOGICAL DISORDER RESEARCH

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## Introduction

Since its inception as Indian Research Fund Association (IRFA) in 1911 and re-designation to its present name in 1949, the Indian Council of Medical Research (ICMR) has been a major stakeholder in formulation, coordination and promotion of biomedical research in areas of national priority. In the year 2007, the Council was brought under the purview of Department of Health Research (DHR) under Government of India's Ministry of Health and Family Welfare. DHR is envisaged to play a major role in health research and guide the government in coming up with new health policies.

The health status of the country has improved since independence as is reflected by an increase in life expectancy at birth, decrease in maternal and infant mortality rates. However, the interactive, additive and synergistic effects of increased longevity, socio-economic development, growing urbanization, overindulgence in unhealthy life styles has led to emergence of a huge burden of non-communicable diseases in a background of as yet unfinished agenda of infectious diseases (Reddy et al., 2005).

Though infectious diseases and excessive population growth have continued to be a major priority for the past several decades, the Council also keeps a vigil on emerging and re-emerging diseases. A study on "Cause of Death by Verbal autopsy" by ICMR in parts of five states, viz. Assam, Maharashtra, Bihar, Rajasthan and Tamilnadu also reflected that the country is passing through a phase of epidemiological transition. In states like Bihar and Rajasthan with lower index of socioeconomic (SE) development, deaths due to infectious diseases (pulmonary tuberculosis and diarrhea) continued to be high where as in other states with higher SE index, noncommunicable diseases (NCD) emerged as leading cause of mortality. Assam had highest number of deaths due to stroke. In another effort to assess the burden due to chronic disease related mortalities, YLL and DALYs, few selected diseases including stroke and two of its associated risk factors, hypertension and tobacco were examined (Assessment of Burden of Disease, ICMR 2006). The study estimated that the number of cases due to stroke would have increased from 7.9 lakhs in 1998 to 9.31 lakhs in 2004. An increase in mortalities, total number of YLL and DALYs due to stroke was also projected (5.9 vs. 6.4 lakhs; 48.2 vs. 52.9 lakhs; 58.0 vs. 63.7 lakhs respectively). Other neurological disorders like epilepsy, cerebrovascular disorders, migraine, dementia, Parkinson's disease, motor neuron disorder, traumatic injuries, brain damage due to birth trauma, neuromuscular disorders, demyelinating disorders and neurological disorders consequent to nutritional deficiency and exposure to neurotoxic

substances have also been identified as major causes of mortality, morbidity and socioeconomic loss in several cross-sectional epidemiological studies. Also, neurological deficit arising due to infections of nervous system such as tuberculosis, malaria, cysticercosis and viral infections, particularly Japanese encephalitis and HIV are of great concern to India and therefore are vital component of research programs at the Council.

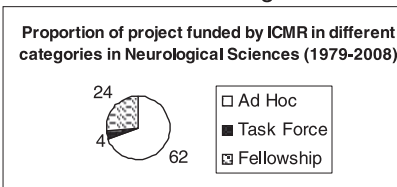
The focus of epidemiological research at Council is not only to collect morbidity and mortality data on neurological disorders but also formulate strategies for prevention through research. Though there are other agencies like Department of Science and Technology, Department of Biotechnology and Council of Scientific and Industrial Research, which supports basic research in Neurosciences, the clinical research in this area is almost solely undertaken by the Council.

### Mode of Research Funding at ICMR

The Council promotes research through intramural and extramural funding. Intramural research is carried through ICMR's 23 permanent research institutes/centres and 6 Regional Medical Research Centres. Extramural research is promoted by ICMR through Centres for Advanced Research in particular area, task force projects and open-ended research/ adhoc projects (applications for grants-in-aid received from scientists).

### ICMR's initiative to build a foundation for research in neurological disorders

ICMR, with a goal to reduce the burden of neurological diseases, conducts and supports research on neurological disorders. To accomplish this goal, financial support is provided to conduct epidemiological research as well as both basic and clinical research. Through the translation of knowledge provided by basic and clinical research activities, better diagnostics, treatments and prevention tools of tomorrow are hoped to be generated. Most of the ICMR-funded research in Neurosciences is conducted by extramural researchers in public and private institutions, such as medical colleges, universities, hospitals and institutions, as there is no permanent intramural research institution dedicated to Neurosciences under the Council.



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During the last three decades, ICMR funded one hundred and thirty one projects in the area of neurological sciences. Though a major proportion (62%) of these projects were funded in open ended research scheme (see figure 1), around 24% of these projects led to development of human resource (32 fellowships), i.e. young researchers in the area of neurological sciences. Facilities for undertaking cutting edge research in Neurosciences were created, with Human Brain Tissue Repository, and National Neuroscience Information Centre (NNIC) at NIMHANS, Bangalore being the outstanding examples.

A Core Group of eminent neurologists and experts with research experience in neuroepidemiology, clinical and basic research at ICMR identifies key areas in neurosciences where research can be initiated and funded by the Council. The framework used by Core Group for scientific discussions and deliberations focuses on four guiding principles for undertaking research over next five years:

1. What are the most important neurological disorders which will require epidemiological research during the next five years?
2. In which areas tools for diagnosis and treatment need to be developed?
3. What important tools for prevention, diagnosis and treatment are emerging globally and need to be validated in the country?
4. What are the important challenges arising for future research in neurosciences and what strategies can be used to tackle these?

Once the areas for research and researchers for undertaking these activities have been identified by the Core Committee, the Council invites applications from scientists with relevant expertise.

During 2002-07, a focused approach to augment research in neurosciences was made by Core Group, covering epidemiological and basic research through a task force mode. The Core Group in Neurosciences at ICMR identified Parkinson's disease, Stroke, Neurocysticercosis, Epilepsy, Gullian Barre Syndrome, Dementia, Muscular dystrophy and Movement Disorders as areas for research. Some of the key studies undertaken and their salient findings are given below:

### **Major studies in Neurosciences conducted by ICMR during 2002-07**

**Neuroepidemiology:** An epidemiological study on major neurological disorders conducted in Kolkatta in 2002-2005 covering a population of 52,377 showed that age adjusted prevalence rates for stroke, epilepsy, primary dystonia, parkinsons, dementia and cerebral palsy were 765.6, 516.5, 55, 74, 87.8 and 127 per hundred thousand. Age specific prevalence rates of parkinsonism showed higher rate with advancement of age, increasing up to 544/100,000 in the age group 70-79 years. Similarly prevalence rates of dementia increased to 480/100,000 in persons aged e" 50years. A higher proportion of dementia cases were of Alzheimer type. Prevalence rate of Mild Cognitive Impairment (MCI) could be documented and was observed to be 6.04% in population aged e" 50 years.

**Stroke:** Four studies were undertaken to understand the etiology of stroke in Indian subjects. Prevalence of stenosis in internal carotid arteries in asymptomatic individuals (> 40 years of age) was observed to be higher in cases with risk factors like hypertension, diabetes, smoking, alcoholism. A strong correlation was observed with the number of associated risk factors, highest being in those with three risk factors. Prothrombotic factors including Protein C deficiency,

Protein S deficiency, antithrombin deficiency, Lupus anticoagulant, anticardiolipin antibodies and TAFI were significantly elevated in young stroke patients (<45 years) indicating a need for surveillance of factors responsible for prothrombotic state for prevention of young stroke.

**Registry of epilepsy in pregnant women:** Major malformations were found in about 3% children born to the women with epilepsy as compared to about 1.4% in controlled group. Polytherapy was observed to be associated with higher percentage (10%) of malformation. Use of single anti epileptic drug did not have significant association with occurrence of malformations in children

**Community based study on Neurocysticercosis (NCC):** A high prevalence of NCC (27.7%) was observed in patients with active epilepsy. The sero-prevalence of cysticercosis in patients with active epilepsy than in community was four times higher (12.48% vs. 51.6%).

**Hospital-based study on Neurocysticercosis:** Focal seizure semiologies such as focal-clonic, focal-tonic, aphasic and visual seizures were predictive of NCC among persons with one or two seizures. However, occurrence of myoclonic seizures alone or in combination with tonic clonic seizures practically ruled out a diagnosis of NCC.

**Parkin gene analysis in Parkinson disease:** Study on Parkin gene mutations in Indian patients with young onset Parkin disease (YOPD) and Autosomal Recessive Juvenile Parkinsonism (ARJP) was carried out. The Parkin gene mutations were studied using PCR, SSCP and Parkin antibody title using ELISA/FACS. It was found that Exons Ex-1, Ex-3, Ex-6, Ex-9 are the mutational hot spots for homozygous exon deletions in juvenile/YOPD cases. Exonic deletions in Ex-1 and Ex-12 were the leading cause of pathogenesis in sporadic PD cases.

## **International Collaboration**

ICMR has signed a Memorandum of Understanding with INSERM, France whereby it supports and conducts research in major areas of neurosciences. Under this Indo-French (ICMR-INSERM) collaboration, the initial focus was primarily on basic research in neurological diseases, which led to the development of experimental models for studying the effects of malnutrition on developing brain. Research was focused so as to unravel the process of neural development at molecular level and to develop markers for early detection of acute non-embolic stroke. An Indo-French (ICMR-INSERM) Workshop on “Neuroprotection in Early Life” held at NIMHANS, Bangalore in 2003 recommended undertaking collaborative research in following areas:

- Basic research in normal neural development and experimental models of developmental lesions in brain.

- Molecular genetics and pharmacogenetics (epilepsy and psychiatric disorders)
- Microcephaly (Clinical and linkage studies to identify genes and mutations)
- Fragile X and other mental retardations (Genetic and experimental studies)
- Metabolic disorders associated with development
- Neuroprotection through preventive measures – Public health
- Genetic network and clinical collaboration through telemedicine and video conferencing to exchange information about diagnosis and therapeutic approaches
- Exchange programmes for students, post doctoral fellows and senior researchers
- Think tank on specific issues and
- Joint research publications.

In order to widen the scope of research in neurosciences at ICMR, the areas for this Indo French joint collaboration has been recently expanded to epidemiological, clinical and translation research.

### **Neurosciences Research: Future Strategies**

The Council's endeavors, during the next five years, are a combination of vision for the future with practical strategies for effectively pursuing research to reduce the burden of neurological disorders. Efforts are made to keep an optimal balance across basic, clinical and epidemiological research in neurosciences. The challenge is to encourage research in targeted areas with simultaneous efforts to allow scientific growth for novel and unexpected discoveries. This is planned to be met through following activities:

1. Initiation of a network of registries including those for stroke, epilepsy and dementia, etc.
2. Evaluation of efficacy of treatment modalities for neurological disorders , e.g. neuromuscular diseases and neurotuberculosis through multicentre studies.
3. Developing preventive strategies to reduce burden of neurological diseases.
4. Development of biomarkers for early detection, treatment and prognosis of neurological disorders.

ICMR is also committed to build a foundation for neurosciences research in the country. In its efforts to build a pool of next generation of neuroscientists, ICMR funds research training at national (fellowships) and international level (e.g. through ICMR INSERM collaborative projects). For more details about funding mechanisms, please visit our ICMR website [www.icmr.org.in](http://www.icmr.org.in).

## **References**

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