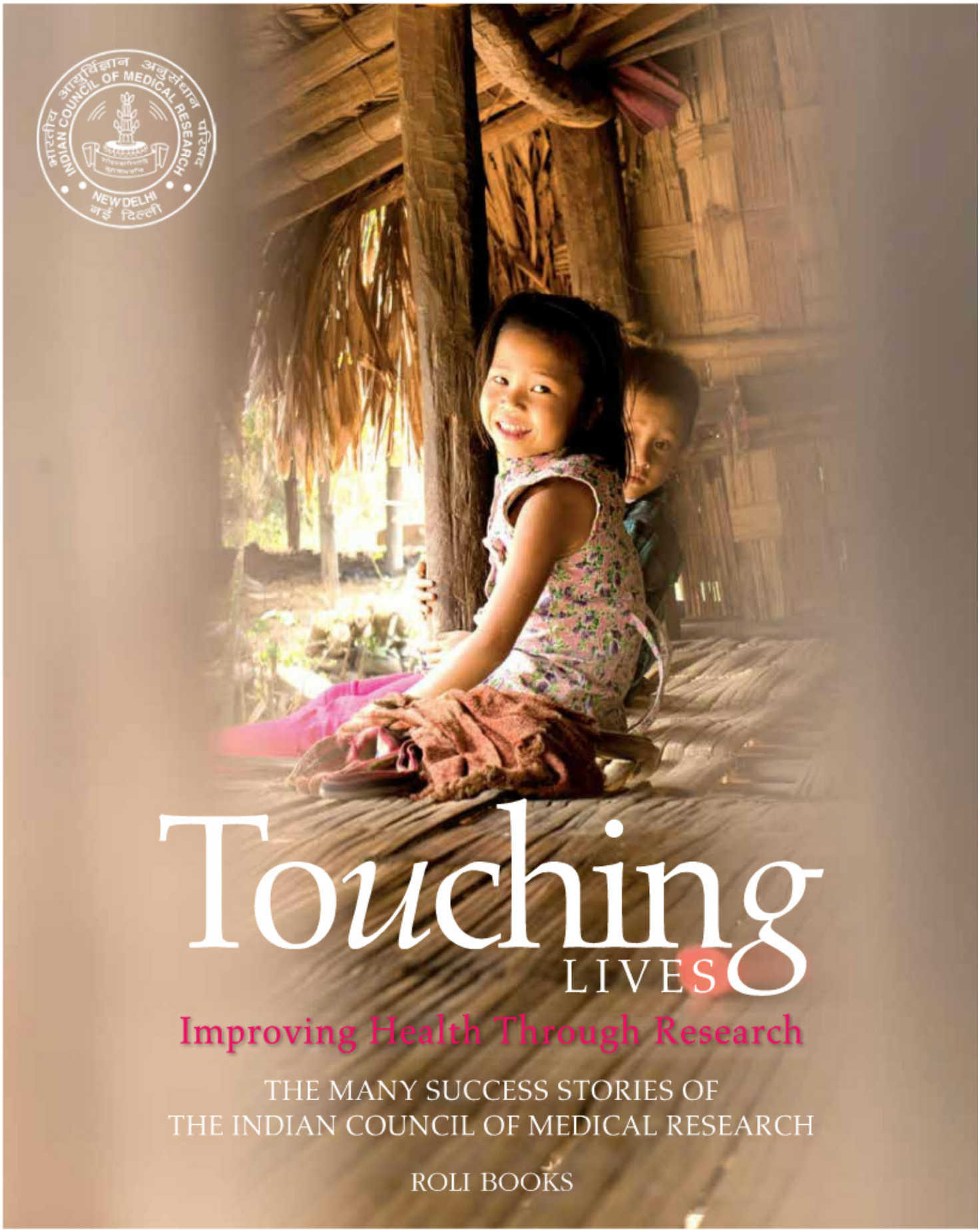

भारतीय आयुर्विज्ञान अनुसंधान परिषद
INDIAN COUNCIL OF MEDICAL RESEARCH
NEW DELHI
नई दिल्ली
Touching
LIVES
Improving Health Through Research
THE MANY SUCCESS STORIES OF
THE INDIAN COUNCIL OF MEDICAL RESEARCH
ROLI BOOKS

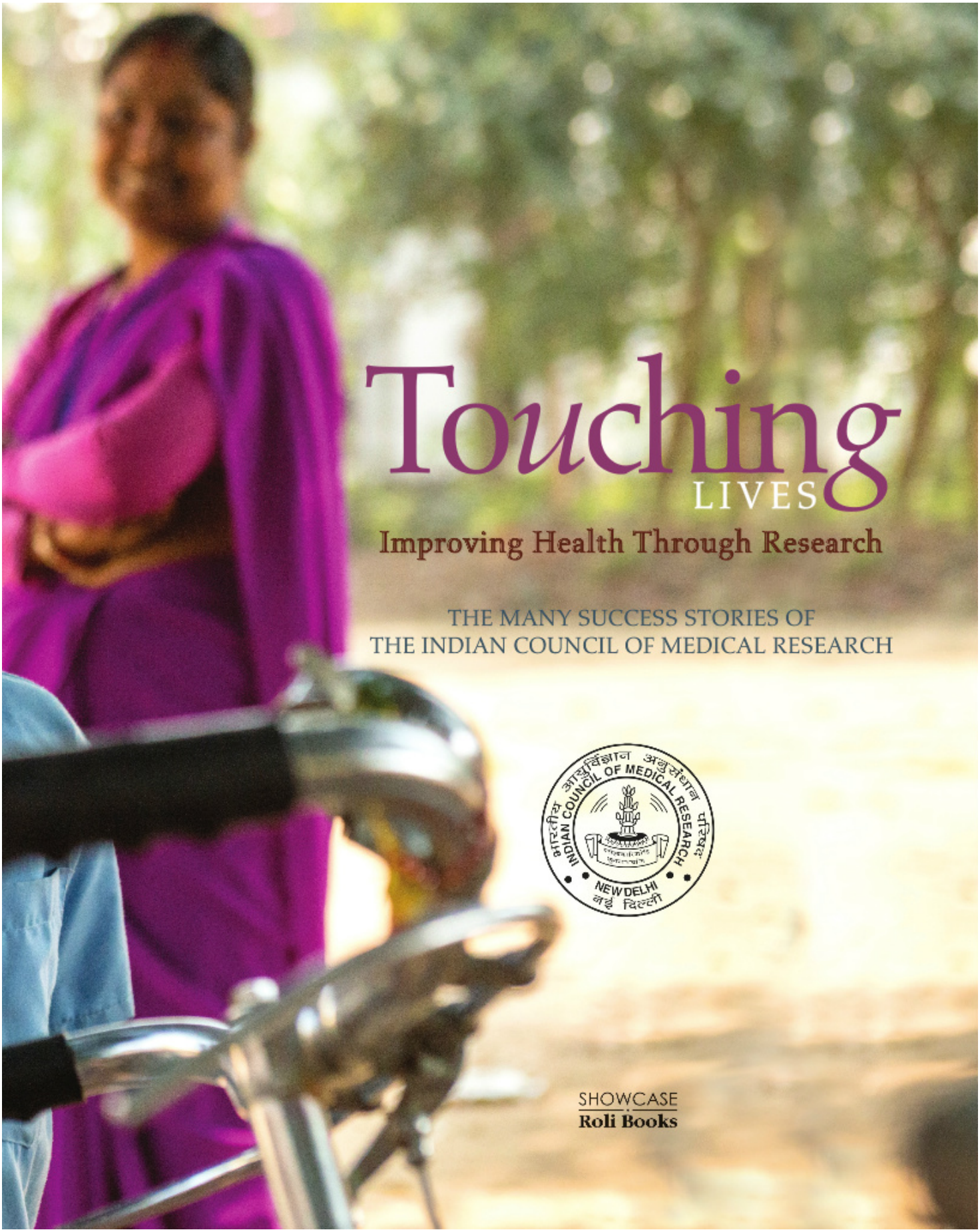
SHOWCASE
A Roli Books imprint for titles sponsored by individuals or organizations.

ISBN: 978-93-5194-198-9

Published in India by Roli Books
M-75, Greater Kailash II Market
New Delhi-110 048, India.
Phone: ++91-11-40682000
Email: info@rolibooks.com
Website: www.rolibooks.com

Design: Sneha Pamneja
Text: Tanoubi Ngangom
Project Coordinator: Anisha Saigal
Editors: Priya Kapoor, Aditi Chopra
Layout: Naresh L. Mondal
Pre-press: Jyoti Dey
Production: Yuvraj Singh

Printed and bound at
Nutech Photolithographers, New Delhi


Touching
LIVES
Improving Health Through Research
THE MANY SUCCESS STORIES OF
THE INDIAN COUNCIL OF MEDICAL RESEARCH
INDIAN COUNCIL OF MEDICAL RESEARCH
NEW DELHI
SHOWCASE
Roli Books


Globe

Contents

HONOURABLE PRIME MINISTER SHRI NARENDRA MODI

सत्यमेव जयते

प्रधान मंत्री

Prime Minister

MESSAGE

I appreciate the immense contribution of ICMR to the national bio-medical and public health research in the country since Independence. The ultimate goal of "Health for All" can only be achieved through appropriate policies and effective programs which are backed by sound evidence. It is important to understand the many challenges & intricate issues related to health of the population in India and ensure better implementation of available tools. I am glad to see glimpse of ICMR's significant contributions in the form of this well-articulated coffee table book. It clearly portrays the impact of health research on people's lives and all the hard work that went into bringing the vision into reality.

I am confident that ICMR would continue its legacy as a knowledge generation agency and contribute in developing new diagnostics, medical devices, drugs, vaccines and treatment strategies to combat not only the communicable diseases of national importance such as tuberculosis, malaria, kala-azar and filiarisis but also the increasing burden of non-communicable diseases like cancer, diabetes and cardio-vascular diseases. India, as a nation, would be able to achieve the mission of health for all through consistent efforts and focused as well as directed research aimed at improving access to care for all at an affordable cost.

I wish ICMR all success in its future endeavours.

(Narendra Modi)

New Delhi
November 22, 2017

जगत प्रकाश नड्डा
Jagat Prakash Nadda

सत्यमेव जयते

स्वास्थ्य एवं परिवार कल्याण मंत्री
भारत सरकार
Minister of Health & Family Welfare
Government of India

FOREWORD

The healthcare system in an emerging economy like India faces diverse challenges. The Government is working to give an impetus to biomedical research particularly affordable innovations focused on improving access to quality of health services available to our citizens. With the changing demography and increasing burden of chronic and other emerging diseases in India, ICMR's role as the apex organization for biomedical research in India will be of tremendous importance.

ICMR's vision to provide critical support to the Government in the implementation of its national health policy and programmes is aimed at achieving the goal of universal health coverage. ICMR's expertise in capacity building, generating evidence for policy formulation, disease surveillance and mapping, designing and implementing health strategies, clinical trials and advanced technological interventions will provide significant inputs to the national efforts on attaining and sustainable development goals.

This book aptly showcases ICMR's key achievements in past few decades. It will help familiarize the people of India with key biomedical and public health successes as well as inspire young researchers to work for accessible, equitable and affordable health care for the people of India. I congratulate ICMR for its commitment towards building a cost effective healthcare milieu and for its many accomplishments in health research.

(Jagat Prakash Nadda)

सत्यमेव जयते
डा. सौम्या स्वामीनाथन
एमडी, एफएएससी, एफएनएएससी, एफएएमएस
सचिव, भारत सरकार
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
एवं
महानिदेशक, आई सी एम आर
Dr. Soumya Swaminathan
MD, FASc, FNASc, FAMS
Secretary to the Government of India
Department of Health Research
Ministry of Health & Family Welfare
&
Director-General, ICMR

भारतीय आयुर्विज्ञान अनुसंधान परिषद
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
वी. रामलिंगस्वामी भवन, अंसारी नगर
नई दिल्ली-110 029 (भारत)
Indian Council of Medical Research
Department of Health Research
Ministry of Health & Family Welfare
V. Ramalingaswami Bhawan, Ansari Nagar
New Delhi-110 029 (INDIA)

FOREWORD

Indian Council of Medical Research continues to draw its inspiration from its ability to provide solutions to the current national health challenges and to prepare the ground for those emerging in future. The Council has come a long way since its inception, with its pan-India presence. Health research initiatives of ICMR focus on field based studies, clinical research, clinical trials and basic science research in the areas of communicable and non-communicable diseases, maternal and child health, nutrition, environmental health and health systems and management. Additionally, research on health information technologies and evaluation of medical and public health interventions are given priority.

This coffee table book brings 16 success stories of ICMR as an example of brilliant and committed work conducted by ICMR researchers over several years. This publication celebrates the success of programmes of ICMR that have, in a variety of ways, impacted the quality of human lives. The stories in the book prove that innovative and consistent efforts in a targeted manner could bring significant improvements in health outcomes.

I wish to thank all the staff & scientists of ICMR for their hard work and dedication that has resulted in this publication. I am confident of a great future for ICMR in which the intellectual workforce would overpower the health challenges faced by our country.

Soumya

Dr Soumya Swaminathan
(Secretary DHR & DG, ICMR)

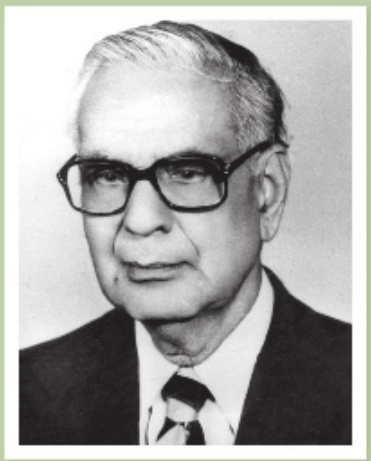
ICMR LEADERSHIP

Director-Generals

The dynamic leadership of ICMR transformed the Council into a vibrant institution and paved the way for its success. Their futuristic vision permeated the Council and led to change in health research. They recognized the strategic significance of research and discovered the vast untapped potential of the scientific workforce of India and channelized it for growth and development of public health.

DR C.G. PANDIT
Director
1948–64

COL. B.L. TANEJA
Director-General
1964–69



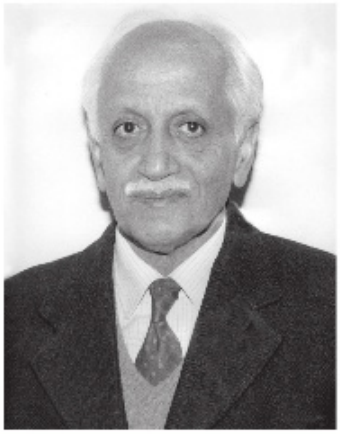
PROF. P.N. WAHI
Director-General
1969–74

DR C. GOPALAN
Director-General
1974–79

PROF. V. RAMALINGASWAMI
Director-General
1979–86

'Vision is the art of seeing the invisible'

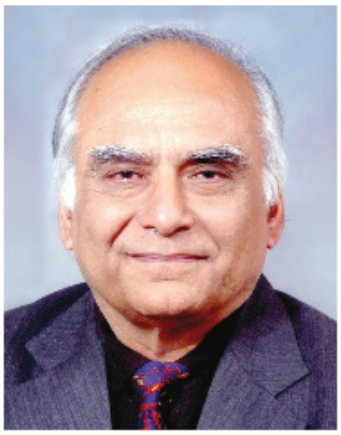
JONATHAN SWIFT



PROF. A.S. PAINTAL
Director-General
1986–91

DR S.P. TRIPATHY
Director-General
1991–94

DR G.V. SATYAVATI
Director-General
1994–97



PROF. N.K. GANGULY
Director-General
1998–2007

DR V.M. KATOCH
Director-General & Secretary, DHR
2007–15

DR SOUMYA SWAMINATHAN
Director-General & Secretary, DHR
2015–Present

Introduction

Today, we might see hardly any individuals living with polio. Thanks to better awareness among people about the importance of polio vaccine and government's efforts and initiatives to improve vaccination coverage. However, not very long ago, polio was a disease that handicapped a significant proportion of Indian children. Another great example is of Oral Rehydration Salt (ORS); most of us would now have a packet of ORS stacked away in our medicine cabinet. It would be hard to imagine that the lack of this simple solution was once the cause of extensive diarrhoea-associated deaths in the country. In fact we may take many of these critical solutions as a given, but life conditions without them would have been severely limited.

Apart from these more widely-known diseases, there are several others – such as the mosquito-borne Japanese encephalitis (JE), neglected tropical disease like kala-azar with high fatality and the water-borne infection leptospirosis – which affect specific pockets of the country.

The Indian Council of Medical Research (ICMR), one of the world's oldest medical research institutions, has been steering medical research and working towards providing tangible and practical solutions to the Indian people in all regions; of different income, age and gender to enable them to live fuller and healthier lives. Aligning its research priorities and focus areas with national health priorities, ICMR – through pan-India institutional network – has carried out pivotal research in a range of domains, such as nutrition, maternal and child health, infectious diseases, occupational health, and non-communicable diseases. Building on this research, the Council has led to translation of research findings into policy formation or programme implementation in collaboration with several state health departments. ICMR is also engaged in capacity-building to promote health research in medical colleges and universities spread across India. ICMR has a global recognition in many areas and many of its institutes are WHO-collaborating centres and the scientists have contributed to global disease-eradication strategies.

Each success story is, however, a product of untiring efforts of dedicated teams of scientists working at the ICMR institutes. The focus has always been on providing unique solutions especially designed to suit the local contexts. This book highlights some of ICMR's landmark contributions in ensuring a healthy India. A snapshot of these is presented as follows.

State-of-the-art infrastructure at ICMR institutes.

Better Data for Better Health

One of ICMR's seminal contributions is through its exhaustive disease-mapping exercises – ICMR's institutions have carried out multiple surveys, both national and regional for a spectrum of diseases. Through these surveys and surveillance platforms, the Council has not only been able to create awareness among the Indian people, but has also generated evidence which led to design of appropriate health interventions. Research on life-saving medications has focused on making them available to the right individuals at the right time.

For instance, ICMR's National Institute of Epidemiology (NIE), located in Chennai, carried out a two-phased rotavirus surveillance at the national scale – a major, first-of-its-kind network study in India. This exercise demonstrated the gravity of the situation and documented that rotavirus is responsible for 40 per cent of the hospitalized children with diarrhoea. Further, it highlighted disproportionate rotavirus disease burden among children below two years suffering from severe diarrhoea. It also showed that more than half of the children afflicted by the infection were suffering from a more severe form of diarrhoea. As per the current figures, 80,000 to one lakh children succumb to the disease every year. ICMR's efforts and the absolute numbers prompted the development of a national strategy to track and monitor the disease and promote development of an effective intervention and the evidence base generated has helped the policy makers to roll out the rotavirus vaccine as a part of the national vaccination programme.

A similar successful example to showcase ICMR's contribution is the elimination of poliomyelitis from the country. Given the size of India's population

Innovation, knowledge and cutting-edge skills developed at ICMR help to improve the lives of people locally, nationally and worldwide.





and highly contagious nature of polio virus, there was an urgent need for a well-informed polio elimination strategy. ICMR's Enterovirus Research Centre in Mumbai led these efforts. As a result of the centre's painstaking work and extensive studies mapping not only the polio-infected individuals but also polio-infested environments and continuously generating evidence to formulate the national vaccine strategies, India gradually eliminated polio and attained the polio-free nation status in 2012. The last reported case of polio was from Howrah district in West Bengal in January 2011.

ICMR's surveillance programmes have also led to identification of what were earlier considered as mysterious provincial diseases. In the remote Andaman Islands, several individuals were detected with similar symptoms – haemorrhages, fever and respiratory problems leading to deaths. The disease was so prevalent that it earned its own colloquial term – the Andaman Haemorrhagic Fever. Owing to detailed investigations conducted by ICMR's Regional Medical Research Centre (RMRC) at Port Blair, it was finally diagnosed to be leptospirosis and RMRC today employs a multi-layered strategy to safely tackle the highly infectious disease. The Port Blair Centre has also developed post-disaster outbreak detection technologies and essential medical supplies management which were employed following the super-cyclone of 1999 in Odisha and the Mumbai floods in 2000 and 2005.

In case of Japanese encephalitis (JE), ICMR's Regional Medical Research Centre for the northeast in Dibrugarh, Assam, in collaboration with the North East Space Applications Centre, Shillong, developed an Early Warning System (EWS). The EWS has helped to identify villages-at-risk almost

Fruits of labour: Intense research of ICMR scientists resulted in the introduction of Nylon gloves for protection and prevention from green tobacco sickness among tobacco cultivation workforce.

two to three months prior to the actual outbreak season on an annual basis.

Working with the Community

The sustainability and effectiveness of health interventions are contingent on the acceptability of such solutions by the potential beneficiaries universally. The National Institute of Occupational Health (NIOH), Ahmedabad's efforts towards combating silicosis among Gujarat's agate industry workers is a case in point. The town of Khambat in Gujarat is known for its booming export-oriented agate industry. However, grinding of the agate stone produces a substantial amount of silica – making the agate workers extremely vulnerable to silicosis. Augmented stone-grinding machines with minimum silica emission were introduced. However, the new machines achieved limited success. Workers refused to use them, stating that they consumed more power. Thus, in close consultation with the affected workers, NIOH came up with a modified dust control device, consisting of blowers and bag filters, which could be attached to the traditional machines. Scientists at NIOH went a step further and took the lead in establishing the *Akik Kamdar Kalyan Trust* – for advocacy and safe environment. Modified machines have been made available at subsidized rates and 500 such machines have now been installed at several units.

The National Institute for Research in Tribal Health (NIRTH), a permanent ICMR institute, was also able to make crucial headway in the fight against fluorosis by partnering with the local affected populations in Madhya Pradesh. When taken in significant amounts, fluoride leads to a disabling disease that may cause weak teeth, or

Research efforts of ICMR led to finding home-based solutions for various health problems.



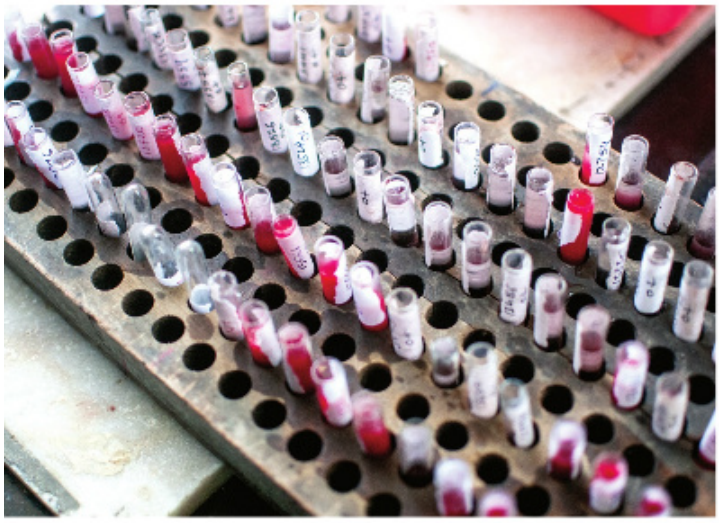

stiffness of the muscles and joints, and ultimately leading to crippling fluorosis. A primary measure to address this disease is ensuring adequate consumption of certain micronutrients essential to checking fluorosis, including Calcium, Vitamin D_3, Vitamin C, and Iron. In order to ensure greater acceptability of the treatment among the native people, the Institute recommended intake of a locally available shrub called *Chakoda Bhaji* rich in these nutrients.

There are several other examples as well. FILCO movement in Cherthala region of Kerala was initiated by the Vector Control Research Centre in Puducherry. This people's movement led to introduction of a mass drug administration programme in the filariasis endemic areas, thereby successfully reducing the parasite load in the community. In the malaria endemic Kheda district of Gujarat too, National Institute of Malaria Research's efforts prompted *Shramdaan* – community members voluntarily filled numerous unused ditches, pools, and drains, and converted these into playgrounds – thus effectively controlling the breeding of mosquitoes and arresting the spread of malaria.

Indigenous Solutions for Local Problems

ICMR has also been responsible for introducing a number of indigenously developed health solutions, especially designed keeping the Indian needs in mind. For one, as a result of the persistent efforts of the National Institute of Epidemiology, today we are able to witness a watershed moment in child health when India has recently introduced an India-made, affordable and high quality rotavirus vaccine, *Rotavac*, as part of the national vaccination

Customizing interventions at ICMR institute.



programme – thus contributing to a healthy childhood for every Indian.

ICMR's oral rehydration solution (ORS) intervention is another example of a cost-effective and practical intervention for treatment of dehydration resulting from severe diarrhoea. Scientists at the National Institute of Cholera and Enteric Diseases, located in Kolkata, realized that there was a distinct imbalance between commercial ORS production and requirement. To overcome the shortage of ORS production, the scientists recommended implementation of a 3-tier strategy of oral rehydration therapy (ORT) at the community level, where ORS was supplemented by home-available fluids to effectively treat mild cases of diarrhoea at home.

Through extensive bio-medical research on the various strains of the Japanese encephalitis virus at the National Institute of Virology, India got its first-ever indigenously developed JE vaccine – JENVAC – through a public–private partnership with Bharat Biotech Ltd. Prior to this, India had to depend on Chinese-manufactured live attenuated vaccines in the national programmes to address the domestic JE epidemics. JENVAC possesses a distinct superiority over other vaccines. Live attenuated vaccines are created using live pathogens with reduced virulence. As opposed to these, JENVAC comprises 'killed' pathogens – thus, they have very little virulence and are safe to be administered even during epidemic situations, where the target individuals are likely to be less healthy. With the launch of JENVAC, the Indian government can now use a safe and effective Indian product to protect its young population from the crippling JE infection.

Similarly, ICMR's Rajendra Memorial Research Institute of Medical Sciences demonstrated the efficacy of the first-ever oral drug, Miltefosine, which revolutionized the treatment of kala-azar – one of the most dangerous and neglected tropical diseases.

Another example is in the field of nutrition. Recommendations of the National Institute of Nutrition's study led to the introduction of a superior food supplement aimed at addressing the nutrition challenge among children in India. As per the new recipe, Telangana Foods is now producing and supplying the milk-based Ready-to-Eat supplements from 6 to 35 months old children in the state of Telangana under the product name *Balamrutham*.

Leaving no one Behind

As the apex body tasked with promoting and supporting medical research in India, ICMR's contributions have enriched the lives of people living in the remotest parts of the country. Further, it has equally invested in tackling health issues that affect the masses and those that tend to inflict only a fraction of the nation's citizens.

Take the example of the Bombay Blood Group – the Bombay phenotype is a rare blood type found predominantly in the Konkan and Goa regions of India. This rare blood group was discovered for the first time in 1952 in a blood bank of a general hospital in Bombay (now Mumbai) by the scientists of ICMR's National Institute of Immunohematology. The Institute is proud to maintain a directory of individuals with this and other rare blood types and provides a crucial link between the limited blood donors and the needy recipients.

Monitoring the health of the community

ICMR has also engaged extensively in promoting the well-being of individuals in the tribal hinterlands of the country. Every year, during the lean agricultural period, thousands of tribal people from Madhya Pradesh travel to the towns of Godhra and Balasinore in Gujarat to fill up crushed quartz stone in bags – working 8 to 12 hours a day. Quartz-grinding is one of the deadliest occupations, which causes exposure to almost 100 per cent free silica, leading to silicosis in a matter of few months. Thus, silicosis has emerged as a major cause of death in Alirajpur of Madhya Pradesh, which is home to many migrant workers. Scientists at the National Institute of Occupational Health have been able to identify specific sources of dust generation in the quartz-crushing units and their recommendations, such as the enclosure of dust sources and the use of powerful exhausts, have been incorporated by the industry. NIOH's industrial hygiene survey conducted thereafter in six factories showed that respirable air-borne dust levels had been reduced by 80 to 96 per cent.

Paragonimiasis is a food-borne illness caused by the infection of the flatworm. In India, paragonimiasis was known to occur only in the state of Manipur. ICMR's RMRC, Dibrugarh carried out protracted studies. Their efforts revealed that paragonimiasis has emerged as a much wider problem with detection of several cases in the state of Arunachal Pradesh and other states of the Northeast.

Translating Research into Action

Apart from its primary mandate of research and surveillance for diseases, ICMR has, in many instances, partnered with state governments and local bodies to build the critical bridge between research and programme implementation. Owing to its seminal work, the Supreme Court has identified the National Institute of Occupational Health as the final authority for diagnosis of asbestosis for compensation purpose.

To effectively check leptospirosis in the Andamans, RMRC, in collaboration with the

Directorate of Health Services, the Department of Animal Husbandry and the Department of Agriculture, has been carrying out regular awareness programmes among farmers, medical and paramedical professionals, and veterinarians. Further, the animals in the Andamans are regularly monitored for infection.

Thanks to the leadership of the National Institute for Research in Tuberculosis in demonstrating the efficacy of Directly Observed Treatment Short course (DOTS), that has played a crucial role in shaping India's TB policy framework – the Revised National Tuberculosis Control Program.

With increasing globalization, and the consequently increasing mobility of individuals across the national jurisdiction, Indians are now vulnerable to a wide range of global ailments. Diseases such as Ebola and Zika – originating elsewhere – have today become real threats for the citizens of India. Further, Indians continue to bear the dual disease burden of lifestyle diseases such as diabetes, cancers and chronic heart problems as well as infectious diseases such as malaria and tuberculosis. In this context, ICMR's role in ensuring the well-being of the Indian population in the future would be of paramount importance.

GENESIS OF TEST TUBE BABY

India's First Scientifically Documented Test Tube Baby

NATIONAL INSTITUTE FOR RESEARCH
IN REPRODUCTIVE HEALTH, MUMBAI

Most ground-breaking scientific developments are fruits of relentless and protracted labour. So was the genesis of the technology that gave India its first scientifically documented test tube baby: Harsha who was born on 6 August 1986, almost three decades ago. ICMR's National Institute for Research in Reproductive Health (NIRRH), situated amidst a myriad of general hospitals in Parel locality of Mumbai, has come a long way since then. Tracing the footprints of events that led to this wonderful achievement, one realizes that the journey was truly revolutionary, especially given the norms of the time.

This was at a time when the general environment towards assisted reproduction was not very favourable. Issues of morality were raised. Several questions were asked: Does India need test tube babies? Is it justifiable to 'treat' infertility with hundreds of babies already available? Our country is over-populated – we do not need test tube babies!

Now, looking at the number of In Vitro Fertilization (IVF) cases and infertility clinics across the country – an outcome of that initial achievement – it is difficult to even imagine the initial dismissal. Infertility, today, is on the rise and Assisted Reproductive Technologies (ART) such as IVF, Intracytoplasmic Sperm Injection (ICSI) and Intrauterine Insemination (IUI) have emerged as a boon to millions – particularly in a country where not having a biological child still has a stigma attached to it.

The IVF-ET technology has brought hope and smiles on the faces of millions of childless couples. It opened avenues for technologies such as ICSI, TESA, ROSI adjunct to IVF for less severe infertility issues.

DR SMITA MAHALE
Director, NIRRH

Dr T. C. Anand Kumar, Director, IRR (now NIRRH), and Dr Indira Hinduja, Gynaecologist, KEM Hospital with India's first scientifically documented test tube baby Harsha, born on 6 August 1986.

The NIRRH, which was at that time referred to as the Institute for Research in Reproduction (IRR), was established on 21 February 1970. It was, and continues to be, the World Health Organization (WHO) Collaborating Centre for Research and Training in Reproductive Health. Located right across the King Edward Memorial (KEM) Hospital, one of the largest municipal hospitals in Mumbai, this technology was the product of a perfect collaboration between a hospital, which had the infrastructure for the bedside procedures, and a research institute that had the necessary settings for all the laboratory procedures.

During the initial years, the mandate of IRR was to explore and provide contraceptive options to men and women in the reproductive age group. Several trials were also conducted during that time to test the safety and efficacy of the available contraceptives. Along the way, scientists at NIRRH realized that there was an unmet need among infertile men and women for methods that could help them conceive a child. This, then, led to research efforts towards seeking treatment for infertility.

The world's first test tube baby was born in UK on 25 July 1978 through the collaborative efforts of British physiologist Sir Robert Geoffrey Edwards, and obstetrician and gynaecologist Dr Patrick Christopher Steptoe. Around the same time, our country's very own gynaecologist and scientist Dr Subhas Mukherjee from Kolkata succeeded in his efforts to, what could have been, India's first test tube baby: baby Durga (Kanupriya Agarwal) was born on 3 October 1978. Unfortunately, documentation of this experience could not be established at the time. It was only after his demise that his work got recognition and acceptance through the initiative and efforts of ICMR.

The failure to document any of Dr Mukherjee's experiences meant that ICMR's efforts towards assisted reproduction had to be made from scratch. Thus, studies were first initiated to evaluate the probable causes for unexplained infertility in order to identify the sources of the problem.

The creation of the test tube baby was a systematic bench to bedside effort, which was a result of the hard work put in by multiple

Babies born subsequently using the Assisted Reproductive Technology (ART) Facility at the Institute.

NIRRH, under the leadership of Dr T.C. Anand Kumar, established the Scanning Electron Microscopy, used to assess sperm structures.

AT A GLANCE

The National Institute for Research in Reproductive Health (NIRRH), earlier called Institute for Research in Reproduction (IRR), was established on 21 February 1970. It is the WHO Collaborating Centre for Research and Training in Reproductive Health.

The world's first test tube baby was born in UK in July 1978. Around the same time, India's first test tube baby was born in October 1978 due to the efforts of gynaecologist and scientist Dr Subhas Mukherjee. Unfortunately, it was only after his demise that his work got recognition through the initiatives of ICMR.

Infertility, today, is on the rise and Assisted Reproductive Technologies (ART) such as In Vitro Fertilization (IVF), Intracytoplasmic Sperm Injection (ICSI) and Intrauterine insemination (IUI) have emerged as a boon to millions.

Scientists at NIRRH have established infrastructure and technologies for the creation of a test tube baby, such as standardizing steroid radioimmunoassays technique to monitor ovarian response; and optimizing the zona free hamster egg penetration assay to check male sperm fertility.

NIRRH scientists have mastered egg cell collection, fertilization, embryo replacement or transfer and implantation – critical steps for success of IVF Pre-Embryo Transfer (IVF-ET) programme. In order to maximize chances of pregnancies, the IVF-ET Team uses a combination of ovulation-inducing agents.

After various breakthroughs, the IVF-ET technique was finally performed as a collaborative project between the King Edward Memorial Hospital, Mumbai, and IRR (now NIRRH). India's first ever, scientifically documented, test tube baby was born in August 1986.

Through ovulation-inducing therapy, IRR improved the success rate of obtaining eggs by about five times.

scientists at NIRRH. They established the required infrastructure and the entire spectrum of technologies needed at every step of this creation. Dr Kamala Gopalakrishnan set up the tests required for semen analysis. The institute, under the leadership of Prof. T.C. Anand Kumar, established the Scanning Electron Microscopy which was used to assess sperm structures. Before application of these procedures on humans, NIRRH scientists established the necessary protocols through several animal experimentations. The steroid radioimmunoassays technique for the hormones – estradiol and progesterone – was standardized by Dr Chander Puri and others to monitor the ovarian response. Dr Judith Menezes, Dr Joshua Peter and Prof T.C. Anand Kumar, along with Dr Indira Hinduja from the KEM Hospital, optimized the zona free hamster egg penetration assay – a test to check male sperm fertility, where human sperms are mixed with hamster eggs to determine the number of sperms that penetrate the eggs. They also mastered egg cell collection,

LEFT TO RIGHT, FROM FACING PAGE: Dr Chander Puri, ex-Director, NIRRH, Dr Kamala Gopalakrishnan and present Director, Dr Smita Mahale; Harsha with her husband, their baby and Dr Indira Hinduja; Dr Hinduja with Harsha.

fertilization, embryo replacement or transfer and implantation – critical steps mandatory for success of IVF Pre-Embryo Transfer (IVF-ET) programme. None of these steps have a 100 per cent success rate. Therefore, in order to maximize chances of pregnancies in humans, the IVF-ET Team at NIRRH used a combination of ovulation-inducing agents to fulfil the three major aims: obtaining as many egg cells as possible for fertilization, achieving synchronization in egg cell maturity, and decreasing incidences of degenerated or atretic eggs.

All patients undergoing ovulation-inducing therapy were monitored closely so as to ensure that the maximum number of eggs could be retrieved. This monitoring was done by ultrasonography and through the estimation of the estradiol hormone excreted in urine. Drs Usha Joshi and Ikram Khatkhatey developed indigenous tests to quantitate the estradiol hormone. With this monitoring, the success rate of obtaining the eggs improved by about five times and also reduced recovery of degenerative eggs.

Through the various breakthroughs, the IVF-ET technique was finally perfected and performed as a collaborative project between the KEM Hospital and the then IRR. This resulted in the birth of the country's first ever, scientifically documented, test tube baby. The occurrence of this pregnancy was announced in January 1986 at the International Meeting on 'Biological Basis of Medicine' in Mumbai.

The quest towards an answer for infertility and the final culmination to the constitution of the IVF-ET programme demonstrated that the curiosity to solve a problem given the right nudge – in this case in the form of an ICMR Institution – could successfully realize a scientific feat. The manifestation of this achievement is Baby Harsha, who is now married, has conceived naturally and delivered a healthy baby boy in March 2016.

ENSURING A POLIO-FREE INDIA

Landmark Achievements in Eliminating Polio

ENTEROVIRUS RESEARCH CENTRE, MUMBAI

Polio is a disease familiar to all of us – It has one of the most widespread vaccination programmes, with regular outreach on television and radio, promoted by many prominent figures. It is an extremely infectious disease transmitted through the faecal-oral route. It attacks an individual's nervous system – 1 in every 200 – causing irreversible paralysis. About 5 to 10 per cent of the paralysed succumb to the disease due to immobilization of breathing muscles.

Given the highly infectious nature of polio, India continued to struggle with disease for a prolonged period of time. The enormous population, coupled with significant development challenges, such as the lack of access to safe drinking water and the common practice of open defecation, meant that tackling polio was especially difficult for India. The World Health Organization (WHO) describes the country as 'arguably the most technically-challenging place'. Even as recent as 2009, India was home to half the polio-infected population of the world. However, India managed to eliminate polio in a matter of mere two years – in what may be called an incredible feat. The last reported case was from Howrah district in West Bengal in January 2011. According to WHO, in 2014 – three years after the last detected case – the South-East Asia region was certified as polio-free.

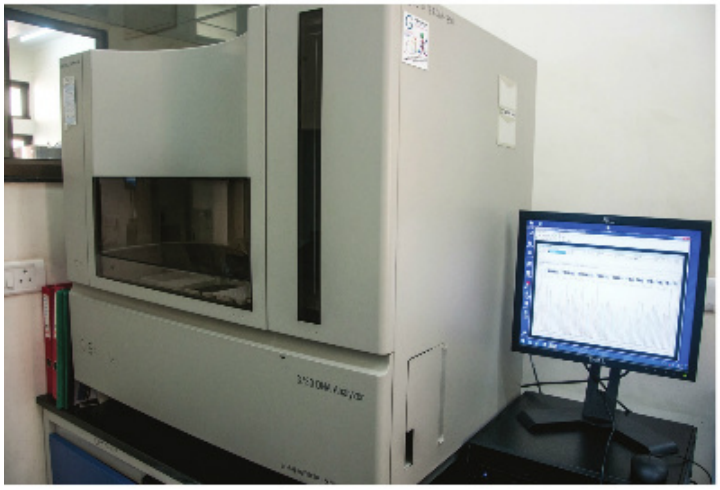
Polio eradication ensures health equity for children. It eliminates lifelong agony of paralysis. In its legacy, polio eradication has given to the country a strong surveillance system for vaccine preventable diseases, improved routine immunization, efficient diagnostic and research laboratory networks and boosted confidence for achieving measles elimination.

DR JAGADISH DESHPANDE
Technical Coordinator, National Task Force on Poliovirus Containment, ICMR, Former Director, Enterovirus Research Centre, Mumbai

Isolation of polioviruses from stool samples of Acute Flaccid Paralysis (AFP) cases. As recommended by WHO, ERC carried out laboratory diagnosis and was able to detect the prevalence of polio in high-endemic states as well as monitor the overall progress of polio eradication in the country.
FACING PAGE: Instruments used for studying poliovirus. ERC also developed a new testing algorithm that reduced the time for reporting poliovirus detection in AFP cases from 28 days to merely 14 days.

ICMR's Enterovirus Research Centre (ERC) – a WHO Global Specialized Laboratory (GSL) for polio located in Mumbai – has played a leading role in elimination of polio from India. India's unusually high vulnerability to polio meant that checking the spread of the disease required targeted timely action based on effective surveillance. ERC's mapping studies of infected population and high-risk sites have made a major contribution to the national polio elimination effort by providing crucial information regarding high-endemic zones, the type of polio infection and primary modes of transmission.

For instance, the Centre conducted large-scale mapping exercises to determine the prevalence of polio in India by carrying out surveillance of Acute Flaccid Paralysis (AFP). AFP is a clinical syndrome where children under the age of 15 suffer from a sudden onset of muscle weakness or paralysis – the most common effect of a polio viral infection. As recommended by WHO, ERC carried out laboratory diagnosis to investigate the presence of poliovirus in stool samples of individuals with AFP. By doing so, it was not only able to detect the prevalence of polio in the states of Maharashtra, Madhya Pradesh, Chhattisgarh and Goa, but also monitor the overall progress of polio eradication in the country. In 2009, out of the total surveyed AFP cases, 741 were found to be polio-positive; in 2010, the figure fell dramatically to only 42; and in 2011 only a single case was tested positive.



Complementing the AFP surveillance, ERC also developed a new testing algorithm that reduced the time for reporting poliovirus detection in AFP cases from 28 days to merely 14 days. Thus, the national polio elimination programme could be shaped more efficiently owing to the availability of prompt data. Following the demonstrated superiority of the test algorithm, it was implemented globally.

In addition to conducting AFP surveillance, ERC has also put in place an environment surveillance system since 2001 to determine the circulation of poliovirus in the community. Sewage samples from various locations were tested – starting with three high-risk areas in Mumbai, and expanding to additional locations in Mumbai, Delhi, Patna, Kolkata,

AT A GLANCE

ICMR's Enterovirus Research Centre (ERC) – a WHO Global Specialized Laboratory (GSL) for polio in Mumbai – has played a leading role in eliminating polio from India. The last reported case was from Howrah, West Bengal in January 2011.

ERC carried out laboratory diagnosis to investigate the presence of poliovirus in individuals with AFP – a clinical syndrome where children under the age of 15 suffer from sudden onset of muscle weakness or paralysis.

In 2009, out of the total surveyed cases, 741 were found to be polio-positive; in 2010, it was only 42; and in 2011, only a single case was tested positive. ERC also developed a new testing algorithm that reduced the time for reporting poliovirus detection in AFP cases from 28 days to 14 days – it has now been implemented globally.

ERC has also put in place an environment surveillance system since 2001, by testing sewage samples from various locations to determine the circulation of poliovirus.

In 1963, ERC introduced Oral Polio Vaccine (OPV) in India by conducting the very first OPV Clinical trial in the country in the three states of Andhra Pradesh, Rajasthan and Maharashtra.

ERC has been responsible for switchover from trivalent OPVs to bivalent OPV and testing its efficacy. Owing to these tests, India is now introducing the bivalent polio vaccine in all hospitals.

To mitigate risks associated with immunity gaps post the transition to bivalent OPVs, one dose of inactivated polio vaccine (IPV) was introduced in the routine immunization programme at the end of 2015.

Till 2009, India was home to half the polio-infected population of the world. According to WHO, in 2014 the South-East Asia region was certified as polio-free.

Ahmedabad, Punjab and recently in Hyderabad as well. Findings from environmental surveillance have supplemented the AFP surveillance and in planning vaccination campaigns at the county level.

In 1963, ERC introduced the Oral Polio Vaccine (OPV) in India by conducting the very first OPV clinical trial in the county in the three states of Andhra Pradesh, Rajasthan and Maharashtra. This was carried out within just 2 years of licensure of the trivalent OPV in the United States.

ERC has also helped insure the effectiveness of polio vaccines used under the national polio vaccination programme. A recent example was the switchover from trivalent OPV to bivalent OPV. Trivalent vaccines (tOPV), containing live and weakened versions of all the three types of poliovirus (1, 2 and 3) was most commonly used. However, the type 2 virus has been globally eliminated, making the incorporation of type 2 vaccine redundant. Further, the type 2 vaccine increases the chances of contracting vaccine-associated paralytic polio – that is, polio caused when the vaccine mutates and starts attacking the body, causing polio.

LEFT TO RIGHT, FROM FACING PAGE: Environmental surveillance involving testing of sewage samples for the circulation of wild poliovirus and VDPV. The sewage samples are collected from open drainage in highly populated slum areas in Mumbai. They are processed at Enterovirus Research Centre for virological testing to detect the presence of poliovirus.

ERC was involved in testing the efficacy of bivalent vaccine (bOPV) containing Sabin 1 and Sabin 3. Since 2007, population immunity surveys have been carried out to determine the capacity of bivalent vaccine-immunized individuals in overcoming the polio infection. Serological surveys were conducted in Moradabad, Uttar Pradesh in 2007; in 25 districts of western UP in 2008-09; and in high-risk blocks in UP and Bihar in 2010, 2011, 2012. Owing to the tests conducted by ERC, bOPV was licensed in India in December 2009 and used in supplementary immunization activities (SIA) since January 2010.

To mitigate risks associated with immunity gaps post transition to bivalent OPV, one dose of Inactivated Polio Vaccine (IPV) was introduced in routine immunization programmes at the end of 2015. ERC, being the leading polio laboratory in India, has conducted additional studies to evaluate the efficacy of IPV Immunization. In, 2013–2014 and 2015–2016 ERC participated in WHO collaborative projects to evaluate the immunogenicity against poliovirus type 1 and 3 by bOPV and tOPV with IPV.

The effectiveness of the polio vaccine is also affected by the distribution system employed. Polio vaccine storage and distribution is carried out through the cold chain system in order to retain potency. ERC studies have helped ensure that vaccines in India are stored and transported according to the appropriate cold chain system. The Centre also conducts a range of studies of the poliovirus itself through genome sequencing techniques.

The successful elimination of polio, in a populous country like India, has meant that the country has become a role model for the remaining endemic countries in polio-eradication efforts. However, the resurgence of polio, in the form of vaccine-derived poliovirus, and the risk of importation from endemic countries, like the neighbouring Pakistan and Afghanistan, means that the threat of polio is still very real. ERC's continuing endeavour – through its various programmes, from surveillance to scientific research – will play a big role in keeping India polio-free.

TREATING TUBERCULOSIS

Research towards Shaping India's TB Policy

NATIONAL INSTITUTE FOR RESEARCH
IN TUBERCULOSIS, CHENNAI

While there have been significant reductions in prevalence and mortality rates of TB over the past 25 years, new challenges like Multi-drug Resistant (MDR) TB have emerged. As per current WHO estimates, India's Tuberculosis (TB) burden is the highest in the world, with an estimated 2.8 million new cases and 500,000 deaths each year.

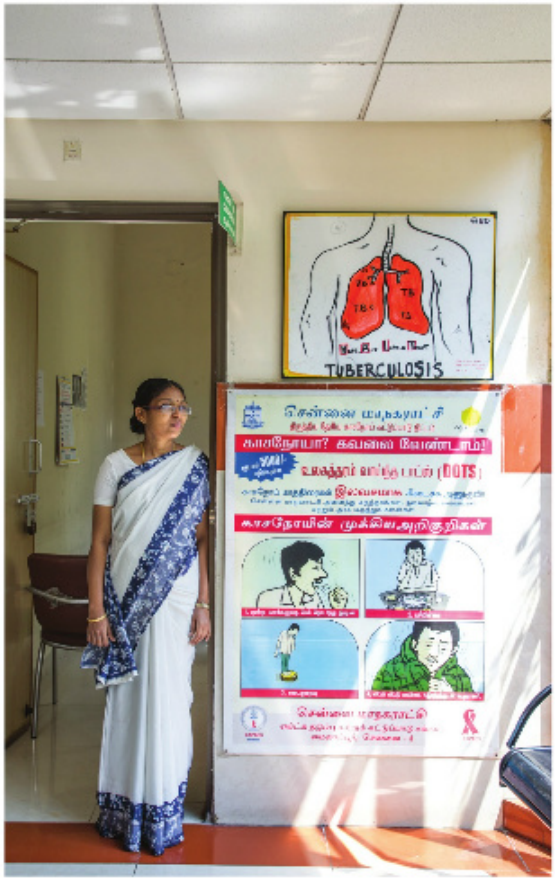
The National Institute for Research in Tuberculosis (NIRT), previously the Tuberculosis Research Centre (TRC), is internationally recognized as one of the pioneers of the globally accepted Directly Observed Treatment Short-course (DOTS) strategy for TB control. NIRT clinical trials have also played a crucial role in shaping India's TB policy framework – the Revised National Tuberculosis Control Program (RNTCP).

Till the 1960s, TB treatment was restricted to specialized hospital units and sanitoria under the supervision of TB specialist doctors. This was because specialist physicians

When I was diagnosed with TB my husband refused to come near me fearing he would get infected. My children were kept away too. My mother-in-law started looking for another girl for my husband fearing I wouldn't be able to fulfil my responsibilities as a wife. I am grateful to the NIRT counsellor who explained to my family that TB was curable. She told me how I needed to come regularly for treatment and have everyone tested in the family. Things changed at home and I am doing very well and I am so happy.

FEMALE, 27 YEARS, A TREATED TB PATIENT

CLOCKWISE FROM LEFT: Posters related to tuberculosis on display at the NIRT clinic; Chest x-ray examination of a patient at NIRT Clinic; Oxygen saturation being measured with pulse oxymeter.



were unsure about the feasibility and efficacy of outpatient care as they thought it would adversely impact treatment adherence, and to compound the problem, that patients would also infect other members of the household. However, providing hospitalized treatment to all TB patients was beyond the capacity of a country like India where resources are scarce and burden of disease high. Moreover, most of these sanatoria were privately run, which meant only the affluent sections of society had access to their facilities.

Things changed when TRC's so called 'HomeSan' study conclusively showed that domiciliary treatment for TB patients was as effective as sanatorium treatment, with no additional risk to household contacts. This was a critical milestone in TB control as it meant that patients no longer needed to be admitted into TB sanatoria, which was at that time the only method of treatment. Thus, it reduced treatment costs and enabled patients to access treatment from home where they could enjoy family and social support. The study further demonstrated the role of extra nutrition in weight gain and recovery among these patients. Another landmark trial, the 'Chingleput BCG Trial' was the largest ever vaccine trial to be done anywhere in the world and showed that BCG did not protect adults against pulmonary TB.

However, drug therapy alone was insufficient for TB control as non-adherence to TB treatment

became a huge challenge to TB control. NIRT then focused on trying to understand these challenges and study findings brought the need for patient oriented treatment keeping their interests in mind. These findings paved way for the DOTS strategy which has become the international strategy for TB treatment and control.

In addition to transforming TB treatment, NIRT identified social and behavioural issues including stigma especially among women which need to be addressed to promote treatment adherence.

The other area where NIRT has made a significant impact is paediatric TB. Given the dearth of information on management of paediatric TB, an NIRT study showed that children with pulmonary TB can be successfully treated with 6 months' intermittent therapy that incorporated a combination of three drugs in the initial 2 months. NIRT clinical trials also endorsed that extra-pulmonary forms of TB – such as TB impacting lymph nodes, the central nervous system, skin, abdomen, and spine – could be successfully treated within 6–9 months.

The risk of developing TB is estimated to be about 20 times more in people living with HIV than among those without HIV infection. In India, about 5-6 per cent of TB patients have HIV infection though this varies widely between states and districts. Therefore, NIRT expanded its research activities to include HIV – a disease that influences the clinical presentation and outcome of TB.

NIRT demonstrated that among HIV-infected TB patients, a 6-month thrice-weekly regimen was as effective as a 9-month regimen even in patients without Antiretroviral Therapy (ART). However, there was a reduction in recurrence with the 9-month regimen. NIRT's study on daily versus intermittent Anti-TB Therapy (ATT) in HIV positive patients also showed greater efficacy and lesser emergence of drug resistance with daily regimen.

The need to integrate HIV and TB services was recommended through studies from this centre along with the National Tuberculosis Institute, Bangalore and this has allowed policymakers to come up with targeted approaches based on specificities of each

AT A GLANCE

From 1990 to 2015, there was a 58 per cent reduction in TB mortality rate, a 55 per cent reduction in TB prevalence rate. Despite this decline, TB continues to be a major public health concern in India, with 2.8 million new cases occurring each year.

The National Institute for Research in Tuberculosis (NIRT) is internationally recognized as one of the pioneers of Directly Observed Treatment Short-course (DOTS) strategy for TB control. Research has also played a crucial role in shaping India's TB policy framework – the Revised National Tuberculosis Control Program (RNTCP).

NIRT's study showed that domiciliary treatment for TB patients was as good as sanatorium treatment, thus reducing treatment costs and enabling patients to access treatment from home.

The risk of developing TB is estimated to be between 26 and 31 times more in people living with HIV. In 2016, there were 2.8 million new cases of TB, among which 5 per cent were people with HIV. In the year 2000, NIRT expanded its research activities to include HIV.

Researchers at NIRT found that being over 45 years of age, being male, smoking and alcoholism were independent risk factors for the development of pulmonary TB.

NIRT estimated excess general mortality among TB patients to be 4.2 times in rural and 6.1 times in urban areas.

Studying already 'cured' patients, NIRT found that 12 per cent of these patients relapsed over 18 months follow-up and the predictors of relapse include irregular treatment, smoking and resistance to isoniazid/rifampicin.

Sputum collection and anti-TB drug administration using DOTS at NIRT clinic. NIRT is internationally recognized as one of the pioneers of DOTS strategy for TB control. DOTS has also played a crucial role in shaping India's TB policy framework – RNTCP.

of these groups. The approach has worked towards early diagnosis and treatment of both TB and HIV.

In addition to transforming TB treatment, NIRT has undertaken substantial work in identifying populations most susceptible to TB and devising ways to encourage patients to complete treatment. Researchers at NIRT found that being over 45 years of age, being male, smoking and alcoholism were independent risk factors for the development of pulmonary TB. Moreover, NIRT estimated excess general mortality among TB patients to be 4.2 times in rural and 6.1 times in urban areas.

NIRT also showed how despite facing more stigma, women approach health facilities, get diagnosed and are more compliant with TB treatment compared to men. Studying already 'cured' patients, NIRT found that 12 per cent of these patients relapsed over 18 months follow-up and the predictors of relapse include irregular treatment, smoking and resistance to isoniazid/rifampicin.

Conducting a series of state level drug resistance surveys in Tamil Nadu, NIRT researchers showed that the rate of drug resistance to rifampicin had not changed much, but to newer drugs like fluoroquinolines, had increased over the past 10 years. Participating in many global clinical trials of new TB drug molecules, NIRT scientists have also discovered a novel compound from marine bacteria, which may one day become a new drug for TB.

Community outreach programmes are an integral part of the activities of NIRT. The activities include TB sensitization programmes among various target groups which include corporation school students, bonded labourers, conservancy

TB Survey being conducted in the community. NIRT's study showed the effects of domiciliary treatment for TB patients, in comparison to sanitorium treatment in reducing treatment costs and enabling patients to access treatment from home.

An estimated 300,000 children drop out of school every year due to parental TB. NIRT estimates annual cost of TB as Rs 13,000 crore.

workers, tribal population, women Self Help Groups (SHGs) and youth. The awareness programmes are tailor made to address gaps in knowledge and the misconceptions existing in the community through an IEC (Information, Education, and Communication) package. The activities cover various areas including issues related to sanitation, health and hygiene, and nutrition.

The economic cost of TB, as estimated by NIRT, is Rs 13,000 crore annually. Moreover, due to parental TB, 300,000 children are estimated to drop out of school every year. Diseases such as TB are major impediments to India's growth. The efforts undertaken by NIRT are ground-breaking and contribute immensely towards India's developmental needs. Recently, ICMR has established the India TB Research Consortium which aims to develop new tools (diagnostics, drug regimens and vaccines) in mission mode in order to help achieve India's goal of eliminating TB by 2025.

SAVING LIVES WITH ORS

Preventing Diarrhoeal Deaths among Children

NATIONAL INSTITUTE OF CHOLERA AND
ENTERIC DISEASES, KOLKATA

Diarrhoea is one of the major causes of death in children below five years in India. As estimated by the Ministry of Health and Family Welfare (MoHFW), Government of India, 1.2 lakh under-five children die due to diarrhoea every year, which indicated that about 328 children succumb to diarrhoea per day and 13 per hour. The primary reason for this is the lack of access to basic public services in major parts of the country. Even today, several households, particularly in the villages, still lack access to clean piped water. Open defecation is still widely practised. Further, malnourished children are more vulnerable to diarrhoeal deaths.

The Oral Rehydration Solution (ORS) – a simple mixture of sodium chloride, potassium chloride, sodium bicarbonate (or tri sodium citrate dehydrate) and glucose – is perhaps one of the most notable medical inventions of the 20th century. The introduction of ORS has markedly changed the treatment of diarrhoea-induced dehydration, offering a safe, easy and effective alternative to intravenous fluid infusion therapy. Thus, the inexpensive and easy-to-administer ORS has become the backbone of Diarrheal Diseases Control Program (CDD) of World Health Organization (WHO) – a global effort to reduce mortality from diarrhoeal diseases. In India, the National Institute of Cholera and Enteric Diseases (NICED), located in Kolkata, is at the forefront in the development and dissemination of knowledge and the use of Oral Rehydration Therapy (ORT)

NICED, a leader in the enteric disease research in India, has played pivotal role in translating research into action like – Oral Rehydration Solution, enteric vaccines, and diagnostics for use in real life situation. Training health workers, informing policy makers, support programs has always remained Institute's prime endeavour.

DR SHANTA DUTTA
Director, NICED

Scientists of NICED who worked on ORT during 1970s and 1980s – (Left to Right) Dr S.K. Mondal, Dr P. Dutta and Dr D. N. Gupta
FACING PAGE: A bacteriology lab at NICED. Beyond bio-medical research on ORS, scientists at NICED have also undertaken various community-level interventions to address the issue of diarrhoeal deaths.

According to MoHFW 1.2 lakh children in the under-5 population die due to diarrhoea every year in India.

throughout the country. As WHO reference centre for Diarrhoeal Diseases Research and Training, NICED imparted hands-on training on ORT to health service providers including doctors of several low- and middle-income countries.

In 1964, Captain Phillips of the US Army and his group for the first time scientifically demonstrated that addition of glucose in sodium chloride solution helped increase the absorption of sodium and water in cholera patients; this in turn helped maintain fluid balance in the body. Inspired by this observation, scientists developed a universal formula of ORS containing sodium (90 mmol/l), potassium (20 mmol/l), chloride (80 mmol/l), bicarbonate (30 mmol/l) or citrate (10 mmol/l) and glucose (111 mmol/l). This standard ORS was considered to provide optimum salt and water absorption in the human intestine, and was thus recommended to correct dehydration associated with diarrhoea and to maintain positive fluid balance even during continuation of diarrhoea. This fluid can also be used for prevention of dehydration in diarrhoea. The single ORS formula could be used globally for all age groups and for all types of diarrhoea.

NICED took the lead in establishing this new treatment in India as well as in many other low- and middle-income countries. After the formulation of standard ORS, several hospital-based clinical

AT A GLANCE

According to MoHFW, 328 children per day and 13 children per hour succumb to diarrhoea.

The Oral Rehydration Solution (ORS) – a simple mixture of sodium chloride, potassium chloride, sodium bicarbonate and glucose – is perhaps one of the most notable medical inventions of the 20th century.

National Institute of Cholera and Enteric Diseases (NICED), located in Kolkata, is at the forefront in the development and dissemination of the Oral Rehydration Therapy (ORT).

Studies on 'improved ORS' formula were launched by WHO in 1980s to overcome the shortcomings of the existing ORS. NICED conducted several studies on 'improved ORS' and also documented the superiority of this formula by carrying out a study on dehydrating persistent diarrhoea.

WHO/UNICEF introduced the new ORS formula containing 75 mmol/l of sodium and 75 mmol/l of glucose in children and adults suffering from cholera as well as non-cholera diarrhoea.

The new ORS formula was launched by WHO and its partners during the United Nations General Assembly, Special Session of Children in May 2002.

In early 1980s, scientists at NICED identified a distinct imbalance between ORS production and requirement. To overcome the shortage of ORS, the NICED scientists carried out bio-medical research and implemented 3-tier strategies of ORT at the community level.

NICED found that home available fluids (HAFs) – like sharbat, lassi, and rice water – were equally effective for mild diarrhoea without any dehydration, and recommended mothers to give adequate amounts of HAFs to children at the beginning of diarrhoea.

CLOCKWISE FROM LEFT:: Mother feeding ORS to her child suffering from diarrhoea with dehydration; A mother preparing ORS at home; ORS packets in a doctor's chamber.

'ORS is so popular and useful; I always keep some packets at home to start initial treatment of diarrhoea for my children and also for ourselves.'

A MOTHER

studies were conducted throughout the country after getting scientific and technical support from NICED. NICED was also able to demonstrate that most patients including neonates, young infants and severely malnourished (marasmic) children with dehydration could be rehydrated safely and their hydration status could be maintained effectively with the administration of the standard ORS, in addition to extra plain water and continuation of breast feeding. NICED also documented that some proportion of severely dehydrated diarrhoea patients without shock could also be managed with standard ORS alone with special supervision.

In the monsoon of 1978, the central district of the north-eastern state of Manipur experienced an extensive cholera outbreak. Affecting individuals of all age groups, almost 4,500 individuals in the nearby villages were infected by the cholera bacteria. Fortunately, timely treatment using the

CLOCKWISE FROM RIGHT: A village health guide accompanying diarrhoeal children at a health clinic; Big containers with ORS prepared in bulk in a hospital setup; A mother preparing ORS in a village.

newly introduced ORS formulation ensured that most lives were saved, and for the second time in India ORS was used to circumvent what would have otherwise been a fatal situation for many. By documenting this phenomenon, NICED was able to further extend the credibility of ORS in the country, and ushered in a new phase where it showed that what was earlier considered a life-threatening situation could now be treated by simply consuming the affordable ORS.

Since then, NICED has been actively engaged in ensuring that Indians, as well as those residing beyond the country, avail the most effective ORT. For instance, physicians found that while the standard ORS successfully replaced fluid and electrolyte losses, it was not able to reduce the volume and duration of diarrhoea, which was in fact sometimes increased. This was frightening and discouraging for the parents, and even for doctors and nurses who were not completely familiar with ORT. Scientists, thus, searched for alternative ORS formulations, which could help reduce duration of diarrhoea and volume of stool. In 1980s, WHO too launched several studies to develop an 'improved ORS' formula.

It was found that changes in the concentrations of glucose and sodium in the ORS mixture altered the absorption efficiency, and consequently the effectives of the rehydrating solution. Clinical trials showed that the solution made by reducing the concentrations of glucose (to 75–90 mmol/l) and sodium (to 60–75 mmol/l) was more effective than standard ORS in the treatment of diarrhoea in children. It reduced stool output and decreased the need for unscheduled intravenous infusion. Children consuming the new formula also experienced less vomiting.

NICED also documented the superiority of this formula by carrying out a study on dehydrating persistent diarrhoea. This led to the WHO/UNICEF adopting a policy for the safe use of the new ORS

formula containing 75 mmol/l of sodium and 75 mmol/l of glucose in children and adults suffering from cholera as well as non-cholera diarrhoea. This new formula was launched by the WHO and its partners during UN General Assembly's Special Session on Children in May 2002. The improved ORS is now made available through government and private sector channels in all the poor- and middle-income countries of the world where diarrhoeal disease burden is high. Owing to WHO's recommendations, individuals residing in developing countries, who face the highest risk of diarrhoeal deaths, are now able to safely enjoy the benefits of the improved solution.

Beyond bio-medical research on ORS containing non-toxic amino acid or ORS prepared by rice powder, scientists at NICED have also undertaken various community-level interventions to address the issue of diarrhoeal deaths – given that many in India continue to succumb to diarrhoea despite the option of an easily manageable treatment, especially in rural settings.

During the early part of 1980s, scientists at NICED realized that there was a distinct imbalance between ORS production and requirement. To overcome the shortage of ORS production, the scientists recommended the implementation of a 3-tier strategy of ORT at the community level. They found that home available fluids (HAF) – like sharbat, lassi, and rice water – were equally effective as ORS for children with mild diarrhoea without any dehydration. Thus, in the first tier, mothers were required to give adequate amounts of locally available fluids. In the second tier, dehydrated patients were to be treated first by village-level health workers with ORS. In the final tier, patients with severe dehydration were treated with intravenous fluid and/or ORS at the nearest health facility. Thus, NICED ensured that diarrhoea patients, despite the shortage of ORS, could be safely treated, and ORS was supplied to those who needed it most.

Apart from the ORT research, other research contributions of ICMR-NICED include discovery

of new serotype *Vibrio cholerae* O139, Bengal having potential to cause and spread of cholera epidemics. Early identification of multidrug resistant *Shigella dysenteriae* serotype 1, and *Salmonella* Typhi causing devastating outbreaks during 1980s and 1990s helped delivering efficient management and control of these diseases.

Epidemiological research documenting high prevalence of HIV among injecting drug users (IDUs) in the north-eastern states of India received worldwide acclaim and recognition. Supplementation trials of zinc, Vitamin A and other micronutrients, probiotics in diarrhoeal diseases are a few examples of clinical therapeutic intervention.

Successful completion of operational research on efficacy trials of oral cholera vaccine, typhoid Vi polysaccharide vaccine and rotavirus (Rotarix®) vaccine helped policy makers to make informed decisions on vaccine implementation.

FIGHTING MALNUTRITION

Providing Nutrition to Children through 'Balamrutham'

NATIONAL INSTITUTE OF NUTRITION, HYDERABAD

With the second largest population in the world, India's performance on socio-economic indicators has a considerable impact on the region and across the globe. The country has made significant gains in tackling the poverty challenge – it has been able to successfully realize the Millennium Development and Sustainable Development Goals (MDGs and SDGs) on poverty. However, the target of halving the proportion of people suffering from hunger remains unfulfilled. Upon the ratification of MDGs in 1990, the proportion of underweight children below 3 years in India stood at 52 per cent. In 2015, this fell to 33 per cent, meaning India fell short by 7 percentage points in meeting its target. It remains home to 'one quarter of the world's undernourished population, over a third of the world's underweight children, and nearly a third of the world's food-insecure people.'

In this context, the work undertaken by ICMR's National Institute of Nutrition (NIN) is seminal and plays a critical role in India's endeavours towards tackling the fight against hunger and malnutrition in children.

A key intervention of NIN was the review of the Supplementary Nutrition Program of Integrated Child Development Services (ICDS), focusing on the accessibility to right kind of nutrients in the state of undivided Andhra Pradesh.

Andhra Pradesh is one of the richest states in the country. Agrarian in character, the state is blessed with fertile land, water, and favourable agro-

Development of Ready-to-Eat milk-based supplementary food 'Balamrutham' for children has high acceptability (86.8 per cent) in Telangana and is similar to commercial baby foods available in the market, but at a much lower cost.

DR T. LONGVAH
Director in-charge, NIN, Hyderabad

An Anganwadi centre where 'Balamrutham' is distributed; FACING PAGE: 'Balamrutham' Take Home Ration (THR) 2.5 kg packet and its nutrition information printed on the packet, manufactured by Telangana Foods (a Govt enterprise).

'My son prefers Balamrutham in the form of powder twice a day. After eating once he usually demands another serving, and I have also observed an increase in his weight.'

– MADHAVI, MOTHER OF A 3-YEAR-OLD

climatic conditions. In addition, the state is mineral rich, has robust infrastructure, and a well-developed R&D culture. And yet, on nutrition indicators much is left to be desired here. The global MDG required India to reduce its child mortality rate (CMR) from 52 per thousand live births in 1990 to 42 per thousand live births by 2015. In the then combined state of Andhra Pradesh (now divided into Telangana and Andhra Pradesh), one-third of the children under the age of 3 years were found to be suffering from malnutrition, with 29.8 per cent of them underweight, 38.4 per cent stunted, 14.9 per cent wasted, and 79.6 per cent anaemic (data as of 2015). Despite more than a quarter of the under-3 year children being malnourished, the state had experienced only a minor reduction of 4.4 per cent in underweight children between 1998–99 and 2005–06.

In order to address the nutrition challenge among children, the government took up the enterprise of developing a wholesome food supplement. Earlier, the former state of Andhra

Pradesh provided Modified Therapeutic Food (MTF) – a fortified soy-based cereal-pulse/legume blend – to manage under-nutrition among children in the age group of 6–35 months for the Supplementary Nutrition Program of the ICDS Scheme (SNP-ICDS). After several consultations, a decision was taken to introduce a new enhanced formulation.

It was suggested that Ready-to-Eat (RTE) milk-based Supplementary Foods (RTESFs) will be developed as an alternative to the fortified cereal-pulse/legume-blended flours. This is because the milk-based supplements had four inherent advantages – first, they have a better amino acid profile, ensuring adequate access to proteins; second, they provide a healthy dose of bio-available calcium and potassium; third, they do not contain any anti-nutrients that could potentially interfere with the absorption of nutrients; and RTESFs are associated with improvements in linear growth – a primary indicator of children's health and well-being.

Given these benefits, the State Nutrition Expert Committee, which included key experts from the NIN, formulated and developed two novel skimmed milk-based ready-to-eat supplementary food products. These supplements contained different cereals, pulses, skimmed milk powder, a balanced sugar and milk-based fat, and were fortified with micronutrients.

AT A GLANCE

In 2015, in the then undivided Andhra Pradesh, one-third of the children below 3 years were found to be suffering from malnutrition, with 29.8 per cent of them underweight, 38.4 per cent stunted, 14.9 per cent wasted, and 79.6 per cent anaemic.

To manage under-nutrition, former Andhra Pradesh provided Modified Therapeutic Food (MTF) – a fortified soy-based cereal-pulse/legume blend – to children in the age group of 6–35 months under the Supplementary Nutrition Program of the ICDS Scheme (SNP-ICDS).

After several consultations, it was suggested that a new enhanced formulation, Ready-to-Eat (RTE) milk-based Supplementary Foods (RTESFs) will be developed, as it had more nutritional benefits. The State Nutrition Expert Committee, with key experts from National Institute of Nutrition (NIN), formulated two skimmed milk-based RTE supplementary food products.

An NIN study comparing the new products with the existing MTF led to the introduction of a superior food supplement – Telangana Foods' milk-based RTE supplements for 6–35 month-olds in Telangana under the product name 'Balamrutham'. In view of its increasing demand, the supplement is currently being supplied to over 10 lakh children.

Mothers of 6–35 months old children with 'Balamrutham' THR for their children, for one month of food supplementation. The product has witnessed immense popularity – other states are also requesting Telangana Foods for the supply of 'Balamrutham'.

Following the development of these two new products, NIN conducted a research study comparing these products with the existing soy-based one (MTF). This analysis was carried out in two ways. First, a sensory test was conducted for two groups which included evaluation of taste, smell, colour, texture and overall appearance of the products. An assessment of the products was also sought from mothers/primary caregivers of the ICDS children. Both the sensory evaluation results, and the assessment from mothers/primary caregivers, showed that Product 1 was considerably more popular than Product 2 or the earlier used MTF.

Second, acceptability, in terms of the proportion of product consumed, was gauged using a centre-based 3-day test meal feeding trial, as well as through a take-home ration/home use 2-week feeding trial among 12–35 months-old ICDS children. While results from the 3-day test meal feeding trial found the three products to be equally acceptable, in the case of the take-home ration/home use trial, Product 1 appeared to be the best accepted.

Apart from the overall acceptability of Product 1 over others, focus group discussions with mothers and primary caregivers provided certain key details related to product attributes and delivery. Firstly, children's preference of Product 1 emanated from the fact that it tasted sweeter and much better than the other two. Secondly, the supply of food products in individual packets was perceived to be more hygienic and hence emerged as the favoured system for regular consumption. Lastly, communication by project staff related to the handling, usage and storing of supplements improved adherence and compliance. It was noticed that post these inputs, beneficiaries were more willing to use the food product.

Children eating 'Balamrutham' food supplement at an Anganwadi Centre on one of the demonstration days. The supplement is currently being supplied to over 10 lakh children.

Service providers further corroborated these views. They emphasized the great ease and logistic feasibility that these packets provided, in distribution as well as storage. They also shared the view that the individual sealed packets would have more acceptability with the community, and consumers would be more willing to adhere to the set standards.

The recommendations of NIN's study have led to the introduction of a superior food supplement. As per the new recipe, Telangana Foods is producing and supplying the milk-based RTE supplements to 6–35 months old children in the state of Telangana under the product name 'Balamrutham'. The product has witnessed immense popularity. In view of its increasing demand, the supplement is currently being supplied to over 10 lakh children. The popularity is so much that other states are now requesting Telangana Foods for the supply of 'Balamrutham' in their states.

A multiple micronutrient powder (MNP) containing 7 micronutrients (Iron, Zinc, Folic Acid, Vitamin A, B2, B12 and C) for food fortification of Supplementary Nutrition Programme (SNP) has been developed and available as a low-cost product. Also, technologies of Double Fortified Salt (DPS) and fortification of wheat with vitamin A and Folic acid have been transferred to industry. Dietary Guidelines for Indian (DGIs), Food Composition Table are important contributions of NIN. National Nutrition Monitoring Bureau (NNMB) initiated in 1972 provided data on dietary pattern across the diverse population of the country for corrective measures.

CONTROLLING MALARIA

Eco-friendly and Effective Alternatives to Fight Malaria

NATIONAL INSTITUTE OF MALARIA RESEARCH, NEW DELHI

Malaria has long been a cause of morbidity and death in India. At the time of Independence, about 75 million people – out of a total population of 330 million – were affected by malaria, and 0.8 million of them were estimated to succumb to the disease every year. Even today, malaria remains one of the primary killers affecting a large proportion of the Indian population in tribal forested areas. According to the World Health Organization, 95 per cent of the Indian population lives in malaria-endemic areas, and 75 per cent of all malaria cases in South-East Asia are found in India. Further, most of the affected individuals belong to low-income households, with little to no financial capacity to obtain treatment, and reside predominantly in rural hinterlands, where access to medical facilities is generally not easy.

Given the prevalence of the disease, the Government of India launched the National Malaria Control Programme in 1953. This was built upon the enhanced effectiveness of the chemical-based DDT (dichloro diphenyltrichloro ethane) and BHC (benzene hexachloride) in combating malaria. Post the demonstrated success of DDT indoor spray, the National Malaria Control Programme was expanded and changed to the National Malaria Eradication Programme in 1958. However, the malaria epidemic of 1976, which led to 6.4 million cases, highlighted the need to look beyond mechanisms such as the DDT, which have adverse side-effects on humans as well as the environment. This prompted a pivot in the malaria control strategy to one that stressed on bio-environmental

NIMR demonstrated control of malaria by reducing vectors through environmental management and use of biological control agents. This approach will be very much required in very low endemic areas in the wake of elimination call.

DR NEENA VALECHA
Director, NIMR

NIMR's network of well-developed laboratories carry out research on the various aspects of malaria, further supported by its field units in malaria-endemic zones, which serve as testing grounds for new technologies. BELOW: Rearing of mosquitoes in a laboratory; FACING PAGE: Cages for holding mosquitoes.

control, and ICMR's National Institute of Malaria Research (NIMR) has led this process.

The primary task of the Institute is to find short- and long-term solutions to the range of challenges posed by malaria in India. NIMR has a network of well-developed laboratories in Delhi carrying out research on the various aspects of malaria, and is further supported by its field units in malaria-endemic zones, which serve as testing grounds for new technologies and facilitate transfer of know-how.

The concept of bio-environmental control for malaria first came to India in the early 1900s. This approach targets the malaria-carrying mosquitoes at the larval stage. During this stage, the mosquito larvae live in water and come to the surface to breathe. Bio-control uses other organisms or natural methods to control the proliferation of mosquito larvae – thereby offering a safe alternative to chemical-based strategies. However, this method only gained traction post the malaria epidemic of 1976. The concept of bio-environmental control of malaria was re-introduced in the mid-1980s and became the central feature of India's combating-malaria strategy. Various strategies for bio-environmental control of malaria were adopted and practised at the various NIMR field stations as a part of the Integrated Disease Vector Control (IDVC) project.

One such strategy was the use of larva-eating fish. In the mid-1990s, a primary health centre (PHC) highly affected by malaria, in the Kamasamudram region, Karnataka, was selected

as a demonstration site to evolve a non-insecticide method of malaria control. Scientists at NIMR carried out a geographical survey to identify and locate potential mosquito-breeding habitats. Results showed that wells, ponds and streams were the main breeding grounds. Villages surrounded by wells and ponds were found to be more vulnerable than those located near streams.

Based on the findings, the larva-eating fish Poecilia (locally known as Guppy) was introduced in the breeding habitats, especially in ponds and wells in 1994. This led to a 50 per cent reduction in the incidence of malaria in just a year. However, the institute's post-intervention monitoring showed that Poecilia was not as effective in ponds. Thus, NIMR included an additional variety of fish to augment

AT A GLANCE

At the time of India's Independence, about 75 million people – out of a total population of 330 million – were affected by malaria, and 0.8 million of them were estimated to succumb to the disease every year.

According to the WHO, 95 per cent of the Indian population lives in malaria-endemic areas, and 75 per cent of all malaria cases in southeast Asia are found in India.

The Government of India launched the National Malaria Control Programme in 1953, using chemical-based DDT and BHC in combating the disease. The Programme was expanded and changed to the National Malaria Eradication Programme in 1958.

After the malaria epidemic of 1976, ICMR's National Institute of Malaria Research (NIMR) led an approach stressing bio-environmental control, offering safe alternatives to chemical-based strategies.

Bio-environmental approach targets malaria-carrying mosquitoes at the larval stage. It was adopted by the various NIMR field stations as part of the IDVC project.

A PHC in Kamasamudram, Karnataka, was examined by NIMR scientists and larva-eating fish Poecilia (Guppy) was introduced in mosquito-breeding habitats in 1994. This led to a 50 per cent reduction in incidence of malaria in just a year.

NIMR released approximately 500 Gambusia fish in the main channel of Kamasamudram tank, resulting in elimination of malaria over the next 15 years.

NIMR recommendations – use of sloping roofs in railway stations and residential buildings, and installation of mosquito-proof overhead tanks – were taken into account by the Konkan Railway Corporation.

Various strategies for bio-environmental control of malaria were adopted and practised in NIMR field stations. One such strategy was the use of larva-eating fish. Transportation of larvivorous fish (below); Release of larvivorous fish in a pond (far below).

As per a recent study USD 1.94 billion is the cost borne by the Indian economy for malaria alone.

the control strategy – in 1995, approximately 500 Gambusia fish were released in a ditch connected with the main channel of Kamasamudram tank. This resulted in the elimination of malaria in this area over the next 15 years. Following the demonstrated success of the programme, bio-control through the use of larvivorous fish was extended to the entire state of Karnataka.

Another noteworthy intervention by the institute took place in the mid-1980s at the Kheda district of Gujarat. Several rivers run through Kheda, thus the district experiences regular floods. It is also home to multiple irrigation projects, leading to further accumulation of water. Almost 70 per cent of the Kheda population is dependent on agriculture and several agricultural workers from neighbouring areas like Dahod, Godhra and Ahmedabad migrate to the district. The migrant workers generally reside in peripheral areas and sleep in open spaces. The many stagnant water bodies, along with the largely humid and hot climate provide ample breeding grounds for malaria-carrying mosquitoes.

Given the disproportionate burden of malaria in Kheda, ICMR's malaria institute conducted detailed surveys and strict surveillance. Many unused ponds and village tanks were renovated and aquatic weeds were removed. Moreover, significant amount of edible fish were cultivated in these tanks, which became an additional source of income for the owners. However, what set this programme apart was the active involvement of the local community at the grassroot level, generating funds from the local resource, and inspiring confidence in the community. Community members undertook *shramdaan*, which involved voluntary contribution of labour, filling numerous unused ditches, pools and drains, and converting these into playgrounds. To make the programme more attractive and sustainable, NIMR went on to incorporate the use of solar cooker and solar-based energy at village level.

In addition to malaria-endemic geographical areas, the institute has also engaged in specific contexts with large malaria vulnerability. For instance, NIMR collaborated with the Konkan Railway Corporation

Officials imparting health education to the locals. Involvement of the community is one of the important aspects of NIMR's strategies.

to combat malaria in one of the corporation's major construction projects connecting Roha in Maharashtra to Mangalore in Karnataka, through a 760 km long coastal railway line. Due to heavy rainfall in the Konkan region and possible obstructions to the natural watershed caused by the project, many feared outbreaks of mosquito-borne diseases due to the project's activities. During the construction phase, Infrastructure Development Corporation field unit, in collaboration with Goa's Directorate of Health Services, Konkan Railway Corporation engineers, and a team of Goa field unit of Malaria Research Centre carried out detailed surveys in all railway project sites in Goa. Their recommendations – such as the use of sloping roofs in railway stations and residential buildings, and the installation of mosquito-proof overhead tanks – were taken into account by the Konkan Railway Corporation and implemented in the entire Goa Sector.

A similar exercise was carried out at the BHEL industrial complex which covers an area of 25 km², housing the main and ancillary industrial units, staff and labour colonies. The main strategy involved filling and levelling mosquito-breeding zones. One of the highlights of this project was community involvement. Participation was witnessed from all sections of society, including those from low-income groups, and from government and voluntary agencies. This made the vector control programme a people's movement, promoting self-help, health awareness and improved sanitation and environmental conditions.

To ensure that India meets its development prerogatives, the country must first work towards augmenting the health and well-being of its population. As per a recent study, malaria alone costs the Indian economy around USD 1.94 billion (Rs 11,640 crore), as 95 per cent of the population lives in malaria-endemic areas. In this context, the work undertaken by NIMR is critical as the success of its operations will directly contribute towards India's economic and development agenda.

FILCO MOVEMENT

Community-based Approach for Filariasis Control

VECTOR CONTROL RESEARCH CENTRE, PUDUCHERRY

Lymphatic filariasis is a mosquito-borne disease caused by the filarial worms, *Wuchereria bancrofti* and *Brugia malayi*. Filariasis – or what is generally called elephantiasis – is an extremely painful and disfiguring disease, usually acquired in childhood, which steadily progresses and can result in severe swelling of certain body parts, such as the arms, legs or genitals.

In India, it is a major public health problem affecting more than 1.2 million individuals. ICMR's Vector Control Research Centre's (VCRC) endemicity map, updated in 2000, shows that as many as 257 of the 289 districts surveyed were found to be filariasis endemic. Seventeen states and six union territories were identified to be endemic with about 553 million people exposed to the risk of infection. While the *W. bancrofti* worm is responsible for 98 per cent of total filariasis infections in India, *B. malayi* was also found present in six states, with the largest occurrence in the central coastal part of Kerala.

VCRC, situated in Puducherry, has played a critical role in responding to the evident requirement for focussed efforts on filariasis control. Filariasis control, however, calls for customized solutions due to different parasite-vector combinations that occur in different environmental settings. This warranted thorough investigations on the epidemiology, mosquito biology and specific modes of transmission. Thus, VCRC's first focus was on addressing the issues in the most endemic areas of Puducherry and Kerala. The findings were then used to carry out large scale control of filariasis across the nation.

I cried more because of the social stigma, rather than the actual physical pain. During social events, I faced humiliations. After coming to VCRC clinic at Cherthala regularly for two years, I recovered completely.

A PATIENT

AT A GLANCE

Also called elephantiasis, lymphatic filariasis is a mosquito-borne disease caused by the filarial worms, *Wuchereria bancrofti* and *Brugia malayi*.

ICMR's VCRC, Puducherry, has played a critical role in filariasis control. In 2000, it identified 17 states and 6 union territories as filariasis endemic, with about 553 million exposed to the risk of infection.

Puducherry, with a Human Development Index score of 0.725, suffers disproportionately from filariasis caused by the *Culex quinquefasciatus* mosquito carrying *W. bancrofti* worm.

VCRC adopted an Integrated Vector Management (IVM) strategy – using efficient waste water management, use of insecticides and mosquito larvae-eating fish, and education and communication campaigns.

A 1986 survey showed that people in Cherthala, Kerala, were staying near water bodies infested with aquatic plants and weeds supporting *Mansonia* vector mosquitoes. Cherthala provides an area of 16.50 sq. km for mosquito breeding.

Students' Filariasis Control Clubs (SFCCs) were created in about 30 secondary schools, with over 3,000 student volunteers, in Cherthala, educating children about various aspects of filariasis,

A combined physiotherapy and chemotherapy intervention was practised at the VCRC Clinic at Cherthala, helping youngsters minimize the swelling from filariasis.

For mass-sensitization, a Malayalam documentary film *Yudham* ('The War') was produced, with a captivating story of a filariasis victim.

VCRC's FILCO established a filariasis control movement in Cherthala. It launched the sale of salt medicated with DEC, an effective treatment for filariasis, to eliminate remaining traces of infection.

One of VCRC's success stories was witnessed in Puducherry. The union territory is one of the highest ranked Indian provinces on the Human Development Index, with a score of 0.725. And yet, this picturesque region suffers disproportionately from filariasis caused by the *Culex quinquefasciatus* mosquito carrying *W. bancrofti* worm. Thus, VCRC adopted an Integrated Vector Management (IVM) strategy, which aimed at reducing the transmission of filariasis by lowering the *Culex* mosquito density to the minimum level possible. Through a multi-layered intervention – including efficient waste water management, long-term planning of waste water disposal systems, the judicious use of insecticides and mosquito larvae-eating fish, and education and communication campaigns – the project achieved drastic reduction in mosquito population and has maintained it. Human-biting density was reduced almost completely (93.7 per cent). Children born during the project period were free from filarial infection. A total of 9 lakh people benefited from this programme. Following the immense success of the project, the strategy was handed over to the State Health Department and since then it has been implemented in various parts of Puducherry.

Given that filariasis caused by different worms, and affecting different settings, requires varied solutions, the Centre adopted a distinct approach in the Cherthala region of Kerala, which is affected by the second type of filarial worm – *B. malayi*. The Cherthala taluk lies in the low land region sandwiched between the Vembanad Lake in the east and the Arabian Sea in the west. Spread over an area of about 304 sq. km, with a population of over 400,000, Cherthala has over 75,000 domestic ponds, besides a number of canals and vast areas of seasonal water collections – providing a total surface area of about 16.50 sq. km for mosquito-breeding. These water bodies are heavily infested with floating water plants. Vectors of Brugian filariasis, *Mansonia* lay their eggs beneath the leaves of the plants and the larvae attach themselves to their roots for respiration. Hence, control is possible only

LEFT: Research and development of bio-pesticides against mosquito larvae; RIGHT: The NABARD sponsored the concept of 'agriculture' for 'health', including composite fish – fast-growing and weed-eating edible fish – for mosquito control

93.7 per cent reduction in mosquito human-biting density achieved through VCRC's strategy and 9 lakh people benefited.

through the removal of such weeds. Local people of Cherthala, however, often use the weeds for many purposes. For instance, they are deliberately grown to be used as green manure. Moreover, the presence of these weeds is known to keep the water cool and clean. Thus, any control mechanism needed the active involvement of the community right from the very beginning.

Besides, many misconceptions prevailed among the people regarding the cause and transmission of filariasis, which again demanded a community-based approach. A survey carried out in 1986 showed that 82 per cent of the people in Cherthala had misconceptions – meaning that rooting out of these beliefs was a primary prerequisite.

Keeping in view the overall situation in Cherthala, VCRC introduced a multidimensional concept on filariasis through different media at various strata of the community. As human factors played a large part in the transmission, the role of health education was found vital. Student's Filariasis Control Clubs (SFCCs) were created in about 30 secondary schools, with over 3,000 student volunteers. With full co-operation of the department of education, children were educated on various aspects of the disease as a part of the club activities.

Another intervention was carried out for removing the deep-rooted stigma associated with filariasis in Cherthala. Victims of filariasis and their families are often shunned by society, particularly

1.2 million are affected by filariasis in India. The economic and social impact of filariasis could lead to an annual loss of USD 1 billion, affecting economic activity up to 88 per cent.

when trying to establish matrimonial relationships. To address this challenge, a combined physiotherapy and chemotherapy intervention was practised at the VCRC Clinic at Cherthala, which helped hundreds of youngsters minimize the swelling caused by filariasis. Further, to create mass-sensitization, a documentary film *Yudham* ('The War') was produced in Malayalam, with a captivating story based on the sufferings of a filariasis victim.

Perhaps one of the greatest achievements in Cherthala has, however, been the mobilization of the local people through Filariasis Control Movement (FILCO). The FILCO has evolved into a self-reliant body with multifaceted activities conducted towards vector control, parasite control and dissemination of filariasis control messages through public information campaigns.

The floating vegetation were removed from domestic water bodies through *shramdaan* (voluntary labour) by FILCO volunteers. Almost

LEFT TO RIGHT: 'Mosquito' dance – delivering health education on filariasis transmission; SFC Club members engaged in 'weed removal' from canal through 'shramdaan' (voluntary labour); Trained FILCO volunteers distributing anti-filarial drug ('Mass drug administration')

all villages of Cherthala were equipped with a Filariasis Detection and Treatment Centre owing to FILCO member organizations. Composite fish culture of fast-growing and weed-eating edible fish was introduced. Subsequently, the cultivation of leguminous plants was promoted as an alternate source of green manure to dispense with the practice of maintaining aquatic weeds in ponds. Thus, mosquito control becomes a by-product of the daily activities of the people. In fact, the National Bank for Agriculture and Rural Development (NABARD) has sponsored this concept of 'agriculture' for 'health' by providing financial assistance to all those who adopted this strategy.

Trained FILCO volunteers in Cherthala are also engaged in mass administration of DEC (diethylcarbamazine citrate), an effective treatment of filariasis. In a later stage, FILCO launched the sale of salt medicated with DEC in the hope of eliminating the remaining traces of infection. DEC is a safe and effective drug used widely for the prevention and treatment of filariasis. In a country such as India, with inadequate funds for sustained vector control and lack of effective governmental machinery for conventional drug distribution, DEC medicated salt seems to be the only effective method of eliminating microfilaria from the community and preventing the occurrence of new cases.

It is estimated that in endemic countries, the economic and social impact of the disease could lead to a potential annual loss of USD 1 billion, adversely affecting economic activity up to 88 per cent. To achieve its ambition of becoming an economic superpower, India must ensure it has a healthy population; and eradicating a disease like lymphatic filariasis must be central to this goal. Thus, VCRC continues to carry out extensive field, community and health system-oriented operational research to support the national and global programmes towards filariasis elimination.

TARGETING KALA-AZAR ELIMINATION

Multi-pronged Approach to Control a Neglected Tropical Disease

RAJENDRA MEMORIAL RESEARCH INSTITUTE
OF MEDICAL SCIENCES, PATNA

Kala-azar is ranked the second largest parasitic killer in the world – second only to Malaria. It is considered as one of the most dangerous neglected tropical diseases (NTDs). Transmitted through the bite of a female sand fly, the disease manifests itself as fever, weight loss and the swelling of the spleen or liver, and generally proves fatal without timely treatment.

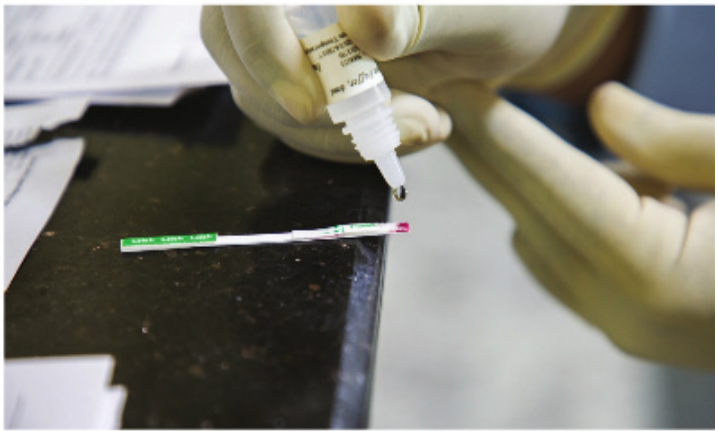
India, Nepal and Bangladesh harbour 67 per cent of the global burden of kala-azar. Among these, India emerges as the most vulnerable, with majority of the cases now concentrated in the four-state group of Bihar, Jharkhand, West Bengal and Uttar Pradesh. The first reported occurrence of kala-azar in the country is dated more than one-and-a-half centuries ago in the Burdwan area of West Bengal. In 1854, when the disease was initially reported, it was termed *Burdwan fever* by the local community. Given the high prevalence of the disease in India, it was known by multiple names depending on the area it affected – Kala-Dukh, Dum-Dum Fever and Kala-Jwar, to name a few. Finally, in 1882 it was reported as kala-azar in Assam.

Since then, kala-azar epidemic outbreaks were reported at regular intervals – in 1891, 1917 and 1933 – and the disease remained prevalent until 1950. However, with the introduction of DDT sprays under the National Malaria Eradication programme in the 1950s, incidence of kala-azar decreased sharply between 1951 and 1970 – in fact, reported cases for kala-azar were close to zero until 1975. But 1975 onwards, India is experiencing a resurgence of kala-azar, with cases detected mainly in Bihar, Jharkhand, West Bengal and eastern Uttar Pradesh –

Long back when I suffered from kala-azar, the test was very painful. I spent a lot of money in getting the injection daily for about one month. Now, a one-day treatment is enough after a simple and quick test, and all these are available free of cost at a nearby hospital.

A KALA-AZAR PATIENT

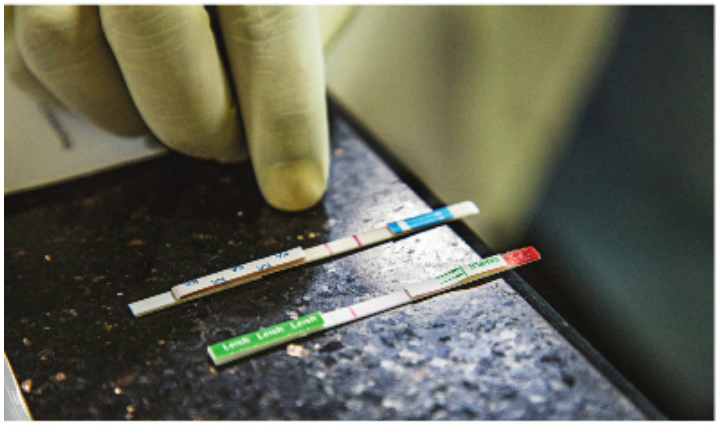
BELOW: rK39 strip testing for kala-azar – a rapid diagnostic tool which is easy to perform with serum or blood sample, within just ten minutes
FACING PAGE ABOVE: rK39 strip testing for kala-azar; BELOW: Estimation of insecticide in sprayed wall samples using Insecticide Quantification Kit

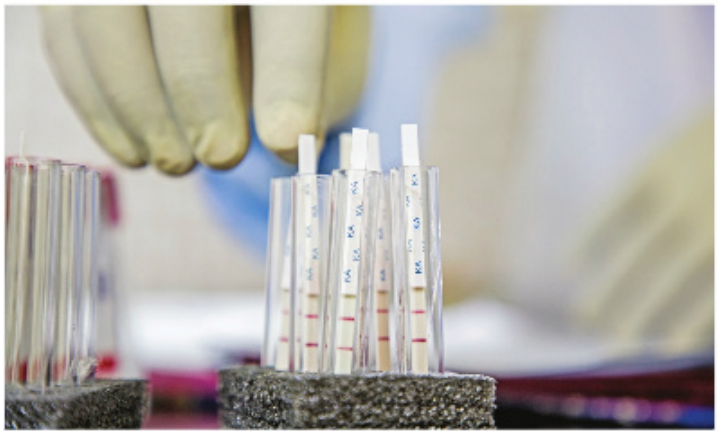


altogether 55 districts are identified as high endemic zones, and a total of 152 million individuals are at risk of this disease. Bihar alone contributes about 80 per cent of the Indian case load. Sporadic cases of kala-azar have also been reported in other states, such as Assam, Himachal Pradesh and Sikkim.

Considering the prevalence of kala-azar and its severity, India launched a targeted kala-azar elimination programme in 2003. Further, during the World Health Assembly in 2005, India, along with Nepal and Bangladesh, committed to tackle the disease through strategies of mutual cooperation. ICMR's Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), in Patna, is at the centre of India's kala-azar elimination initiative – in multiple areas such as disease surveillance, diagnosis and treatment, prevention and vector management, and clinical research.

RMRIMS's in-depth review of India's kala-azar control programme, for instance, has played a crucial role in understanding the strength and gaps in its design – thereby facilitating the improvement of policies to ensure effective kala-azar elimination. One such study was conducted in 2007 in the highly-endemic areas across the four affected states of India. This brought out certain fundamental weaknesses. First, the utilization of government healthcare facilities for the diagnosis and treatment of kala-azar was found to be significantly low. Despite availability of competent screening tests at





government health units, about half of the patients had gone to private set-ups for tests. This prompted a focused investigation into the low-uptake of government services – a trend that is especially worrisome, given that kala-azar primarily affects the poorest communities, who generally depend on borrowings or sell their limited assets to obtain healthcare, pushing them into further poverty.

Another aspect highlighted was the issue of community participation. The infectious nature of kala-azar means that the effectiveness of any elimination strategy fundamentally hinges on its ability to mobilize the affected community. To understand the level of community awareness and uptake of treatment, RMRIMS conducted various

AT A GLANCE

Kala-azar is considered one of the most dangerous neglected tropical diseases (NTDs) and is the second largest parasitic killer in the world.

Transmitted through the bite of a female sand fly, it manifests itself as fever, weight loss and swelling of spleen or liver, and can be fatal if not treated timely.

India, Nepal and Bangladesh harbour 67 per cent of the global burden of kala-azar. India is most vulnerable, with majority of the cases in Bihar, Jharkhand, West Bengal and Uttar Pradesh.

The first reported occurrence of kala-azar in India was more than one-and-a-half centuries ago in the Burdwan area of West Bengal, and was called *Burdwan fever*.

After 1975, there was resurgence of kala-azar mainly in Bihar, Jharkhand, West Bengal and Uttar Pradesh. Bihar alone had 80 per cent of the cases.

ICMR's Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), in Patna, is at the centre of India's kala-azar elimination initiative.

RMRIMS's 2007 study in the highly-endemic areas showed under-utilization of government healthcare facilities, especially among the poorest communities who went to private set-ups.

Between 2003 and 2010, RMRIMS's data showed significant under-reporting of the disease – four to eight fold – few people sought treatment at PHCs.

RMRIMS's noteworthy intervention has been the development of a rapid diagnostic tool for kala-azar, rK39 – easy to perform with serum or blood sample, within just ten minutes.

RMRIMS suggestion to use compression pumps, as opposed to stirrup ones, for indoor spraying of DDT, has been included in the national road map 2014 in the endemic districts of Bihar.

80 to zero – decline in deaths caused by kala-azar after RMRIMS's intervention. The cases also reduced from 33,187 in 2011 to 6,221 in 2016.

studies in different endemic areas between 2003 and 2010. For example, it carried out extensive door-to-door surveys in certain highly-endemic districts of Bihar. When the data was cross-matched with recorded kala-azar cases in the associated primary health centres (PHCs), significant under-reporting of the disease was seen – highlighting the fact that very few from the local community actually sought treatment at the PHCs. As per the studies, the level of under-reporting was four to eight fold.

Intensified research blended with high political commitment led to tuned-up surveillance and control strategies in light of the gaps identified. The WHO–TDR sponsored study on the different implementation strategies for kala-azar-control is a major landmark in this area. In order to ensure early diagnosis and treatment, RMRIMS carried out various surveillance techniques. For example, a

LEFT TO RIGHT: Project discussion with scientists and technical staff; Staff nurse swabbing the abdomen of a suspected kala-azar patient prior to splenic aspiration; Technician performing test at the central diagnostic facility for biochemistry; Doctors examining a patient in the OPD.

medical camp was set up in an endemic village so that individuals with kala-azar symptoms could get themselves checked and treated. Other tools included the index-based approach or the blanket house-to-house search. Based on RMRIMS studies, the camp approach was found with higher kala-azar case yield, and it has been taken over by state government on a pilot basis.

RMRIMS has also made certain critical contributions through clinical and operational research. One such noteworthy intervention has been through innovation in the existing rapid diagnostic tool for kala-azar. There are a few screening tests available for kala-azar – such as DAT, ELISA, DOT-ELISA. But these tests could not be introduced as a part of the Indian programme as they required high technical skill, equipment, and more importantly, took a protracted period of time. Thus, the development of rK39 is considered a boon, and has drastically eased the diagnosis of kala-azar. Today, screening is easy to perform with serum or blood sample at doorstep, within just ten minutes. However, rK39 suffers from certain shortcomings – in spite of its high utility in early diagnosis, it can neither be used as a confirmatory test of cure nor can it be used in cases of re-infection. In this regard, ICMR's continuing efforts in the form of the antibody-based test, developed by the National Institute of Pathology, and the red blood cell-based version, developed by RMRIMS, could further help strengthen the diagnostic capabilities.

Another key contribution of RMRIMS is demonstrating the efficacy of Miltefosine – the first ever oral drug for kala-azar. Earlier, all the drugs available were either in injection or infusion form, and thus Miltefosine was proved to be a revolution

The first ever oral drug for kala-azar, Miltefosine has 94 per cent cure rate with absolutely minimal side effects.

ASHA workers assembled at a primary health centre for training. To ensure early diagnosis and treatment, RMRIMS carried out various surveillance techniques, for example setting up medical camps where individuals with kala-azar symptoms could get themselves checked and treated. FACING PAGE, CLOCKWISE FROM RIGHT: Drugs given to a patient at an ART centre; Alphacypermethrin spray with Hudson pump; The survey team moving around in the study village; Door-level investigation of kala-azar by rK39 strip test; A kala-azar patient sleeping inside KO-TAB-123 impregnated bed net.

in the treatment. The 28-day-long home-based treatment with Miltefosine was, consequently, introduced in national kala-azar elimination programme as the first-line drug. It was found to be quite effective (with a final cure rate of 94 per cent) and safe with minimal side effects in few cases. Besides its use in treatment of kala-azar, Miltefosine is also the first-line drug used in the national programme for the treatment of Post Kala-azar Dermal Leishmaniasis (PKDL) – the recurrence of kala-azar as skin lesions. Presently, single-day treatment with AmBisome (10 mg/kg body weight) is the first-line drug for Kala-azar treatment under programme mode.

Given the transmission of kala-azar by the sand fly, vector-control is one of the major interventions contributing to kala-azar elimination. Indoor spray of DDT emerged as one of the primary vector-control methods after the resurgence of kala-azar in 1962, and RMRIMS has played a key role in enhancing the effectiveness of the strategy. For instance, India continued to use stirrup pumps for DDT spray for a significant period of time. However, an RMRIMS study found that compression pump, as opposed to stirrup, was more user-friendly as it was lighter in weight, easier to operate, with lower operation cost, and demonstrated higher safety and better coverage. Eventually, it has been included in the national road map 2014 for use in the endemic districts of Bihar.

The impact of the improved kala-azar elimination strategy can be envisaged by the fast-declining record of kala-azar cases and deaths in India. The total number of cases came down from 33,187 in 2011 to 6,221 in 2016, and during the same period, deaths due to kala-azar have declined from 80 to zero. However, kala-azar is still a threat in the endemic regions, and RMRIMS's initiatives will be crucial in implementing more targeted interventions.

COMBATING JAPANESE ENCEPHALITIS

Effective Diagnosis and Fighting the Disease

REGIONAL MEDICAL RESEARCH CENTRE
(NORTHEAST REGION), DIBRUGARH

Japanese encephalitis (JE), a mosquito-borne infection, is a leading cause of viral encephalitis in Asia. Globally, about 30,000 to 50,000 cases are reported every year, mostly among children, and 10,000 of them succumb to the disease annually. In endemic areas, like India, the annual incidence of the disease ranges from 10 to 100 for every 100,000 individuals. Majority of the people living in JE-endemic areas are infected with the virus before the age of 15 (85 per cent). However, less than 1 per cent of people infected with JE virus develop clinical illness. In persons who develop symptoms, the incubation period (time from infection until illness) is typically 5–15 days. Initial symptoms often include fever, headache, and vomiting. Mental status changes, neurologic symptoms, weakness, and movement disorders might develop over the next few days; these could prove to be fatal. Seizures are common, especially among children.

Further, about half of those who survive the disease are left with serious neurological and psychiatric impairment including brain damage and paralysis.

In India, the first clinical case of JE was reported in 1955 at Vellore, Tamil Nadu. Since then, subsequent cases of JE have been recorded across the southern, northern and eastern regions of the country. According to recent data from the National Vector Borne Disease Control Programme, 21 Indian states are endemic to JE.

India's northeastern region continues to face a disproportionate burden of the disease. The situation is particularly severe in the case of Assam – it was the

The use of insecticide treated bed nets for control of JE in Assam has been internationally applauded and accepted as a low-cost, environment-friendly, easy-to-use tool. ICMR's efforts also led to the development of Early Warning System and an indigenous vaccine JENVAC for JE control.

DR KANWAR NARAIN
Director, RMRC, Dibrugarh

A perennial breeding habitat for JE vectors; FACING PAGE: Rain-fed paddy field – the most important breeding habitat for JE vectors (above); Pig-rearing in close proximity to human dwellings (centre); Insecticide-treated net being put around a pigsty (below).

10 to 100
in every 100,000
individuals is the
annual incidence
of JE in India, with
majority infected
before the age of 15.

first state to observe high morbidity and mortality rates due to the JE virus back in 1976. Since then, Assam's Upper Brahmaputra valley has experienced recurrent JE episodes on an annual basis. Over the last few years, JE has also spread to newer areas of Assam causing great concern among public health authorities of the state. Data from the region show that the disease claims a considerable number of lives in the state, particularly during the periodic outbreaks. The latest epidemics of 2014 and 2015 acutely affected the two highly endemic contiguous districts of Assam, Dibrugarh and Sivasagar.

ICMR's Regional Medical Research Centre for the Northeast (RMRC, NER), located at Dibrugarh was the first laboratory to undertake diagnosis and research on JE in the northeastern region. The centre has been actively involved in investigating every outbreak and providing diagnostic services for JE.

AT A GLANCE

The first clinical case of Japanese Encephalitis (JE) in India was reported in 1955 at Vellore, Tamil Nadu. According to recent data from National Vector Borne Disease Control Programme, 21 Indian states are endemic to JE.

ICMR's Regional Medical Research Centre for the Northeast (RMRC, NER), located at Dibrugarh, Assam, was the first laboratory to undertake diagnosis and research on JE in the northeastern region.

In collaboration with the Northeast Space Applications Centre, Shillong, RMRC, NER developed an Early Warning System for JE (JEWS). By using technologies like Remote Sensing (RS) and Geographic Information System (GIS), every year the JEWS helps identify villages at risk two to three months prior to the actual outbreak season.

RMRC promotes the use of Insecticide Treated Mosquito Nets (ITMN). An RMRC study conducted during 2003–2006 revealed that localities using nets for both humans and pigs were better protected (72 per cent protection) than those that limited usage to only humans (67 per cent) or only pigs (56 per cent).

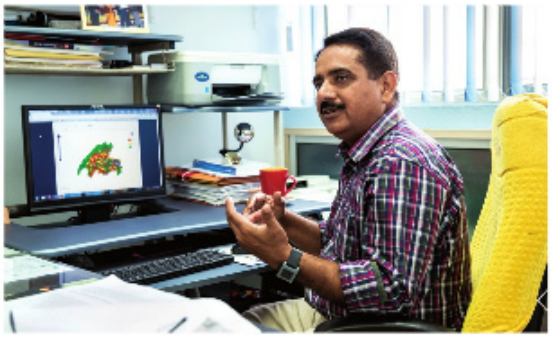
To address the issue of JE in adults, the government initiated a vaccination programme for the age group 15 to 65 years for the first time in Sivasagar, Assam in 2011. RMRC conducted a study to assess the safety, immunogenicity and effectiveness of this vaccine, which was found to be 90.14 per cent effective and provided protective antibodies over the 12 months' post-vaccination study period.

With the Sivasagar district immunization programme, JE incidence rate fell to 43 per million in 2012 – as opposed to the expected incidence of 112.8 per million, based on earlier trend.

CLOCKWISE FROM TOP LEFT: Dusk hour collection of mosquitoes in and around a cow shed; Collected adult mosquitoes being transferred to a Barraud cage for transportation to the laboratory; Sorting of immature mosquitoes for transfer to the laboratory; Dr Siraj A. Khan, a scientist, demonstrating the JEWS model for early warning of JE; Serological testing for JE; Immature stage (larvae and pupae) mosquito collection from an irrigation canal.





Given that there is currently no curative treatment for the disease, RMRC, Dibrugarh, has taken the lead to develop a spectrum of early management strategies – the only recourse for JE.

For the highly JE endemic district, Dibrugarh, the research centre in collaboration with the Northeast Space Applications Centre, Shillong, developed an Early Warning System for JE (JEWS). By employing technologies like Remote Sensing (RS) and Geographic Information System (GIS), in conjunction with the epidemiological risk factors specific to the JE endemic areas of Assam, the JEWS helped identify the villages at risk almost two to three months prior to the actual outbreak season on an annual basis. The model has also been able to provide an estimate of cases that could occur during

The Acute Encephalitis Syndrome (AES), JE and Rickettsial Diseases team of ICMR–RMRC, Dibrugarh.

the year. Following the high precision of the warning system, the model has now been adopted in two additional JE endemic districts of Assam – Tinsukia and Sivasagar. With the aid of the centre's forecast system, health authorities now have enough time to take necessary control measures in the high-risk areas by pooling the limited men and material at their disposal, and prevent large-scale sufferings and deaths due to the disease in the community.

Another key area of RMRC Dibrugarh's JE intervention approach is the promotion of Insecticide Treated Mosquito Nets (ITMN) – one of the most effective prevention strategies given that JE is a mosquito-borne disease. The JE virus is known to affect both humans and animals, particularly pigs. Pigs act as amplifying hosts for the JE virus; thus, communities with infected pigs are even more vulnerable to the disease. The Centre's study evaluating the efficacy of ITMNs in JE-prone areas of Assam during the period 2003–2006 revealed that localities using nets for both humans and pigs were better protected (72 per cent protection) from human JE infections than those that limited net usage to merely humans (67 per cent) or to only pigs (56 per cent). RMRC Dibrugarh's seminal investigation then led to the incorporation of the use of mosquito nets for pigs as a preventive measure for JE in Assam government's JE prevention strategy.

Any JE prevention campaign would be incomplete without the inclusion of an effective vaccination strategy. The Government of India initiated a mass JE vaccination campaign in the worst affected JE endemic districts of Assam, Dibrugarh and Sivasagar, in 2006 for children below the age of 15. This programme was further

Through extensive research at NIV and vaccine development by Bharat Biotech, India introduced its first ever JE vaccine – JENVAC – in 2013.

extended to cover children from remaining districts of Jorhat and Golaghat in 2007; Dhemaji and Tinsukia in 2008; Kamrup, Lakhimpur and Sonitpur in 2009; and Nagaon and Udalguri in 2010. They were immunized with the live attenuated SA-14-14-2 JE vaccine.

The JE vaccination campaign among the young population of Assam facilitated a dramatic decline in the prevalence of paediatric JE. Subsequently, the vaccine has been incorporated into the routine immunization programme among children in JE-endemic areas throughout the country. However, JE cases in adults were still quite high, and in fact exhibited an increasing trend. To address this issue, the government initiated the adult JE vaccination programme for the age group 15 to 65 years for the first time in Sivasagar district of Assam in 2011. RMRC Dibrugarh, in tandem, conducted a pilot

Administration of JE vaccination with the live attenuated SA 14-14-2 vaccine. The RMRC conducted a study to assess the safety, immunogenicity and effectiveness of this vaccine in the age group 15 to 65 years in Sivasagar, Assam in 2011 – it was found to be 90.14 per cent effective.

study to assess the safety, immunogenicity and effectiveness of the single dose of live attenuated SA 14-14-2 JE vaccine in adults. This vaccine was found to be safe and effective (90.14 per cent) and provided protective antibodies over the 12 months' post-vaccination study period.

With promising outcomes of the Sivasagar district immunization programme in 2011, JE incidence rate fell to 43 per million in 2012 – as opposed to the expected incidence of 112.8 per million according to the earlier trend. The single dose vaccination programme has subsequently been further expanded to other JE endemic parts of the state among the adult population.

Demonstrating the exceptional coordination among the different arms of ICMR, one of the most noteworthy interventions in the area of JE vaccination has emerged from another ICMR institute – National Institute of Virology (NIV) located in Pune. Through extensive bio-medical research on the various strains of the JE virus at NIV and vaccine development by Bharat Biotech, India introduced its first ever indigenous vaccine – JENVAC – in 2013. Prior to this, India had to depend on Chinese-manufactured live attenuated vaccines to address domestic JE epidemics.

JENVAC possesses a distinct superiority over other vaccines. Live attenuated vaccines are created using live pathogens with reduced virulence. As opposed to these, JENVAC comprises 'killed' pathogens and are safe to be administered even during epidemics, where the target individuals are generally less healthy. With the launch of JENVAC, the Indian government can now use a safe and effective solution to protect its vulnerable population from JE infection.

IMPROVING CHILD HEALTH

Developing National Rotavirus Surveillance Network

NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

Rotavirus-induced diarrhoea is one of the most common health issues among infants and young children across the globe. Resulting in gastroenteritis – or what is commonly known as stomach flu – this viral infection often leads to severe diarrhoea and dehydration. While it is largely manageable in developed countries, it still poses significant threat to life for most young ones in the developing world. In countries like India, dehydration due to diarrhoea emerges as the major cause of death among children below five years of age. In India, rotavirus makes up for about 40 per cent of the diarrhoeal admissions. Every year about 9 lakh young children are admitted to hospitals due to rotavirus diarrhoea; an additional 3.27 lakh children get treated as outpatients for the same disease; and 80,000 to one lakh children suffering from rotavirus diarrhoea die every year.

ICMR's National Institute of Epidemiology (NIE), located in Chennai has played an instrumental role in battling this disease. Through extensive nation-wide surveillance, it has been able to systematically estimate the prevalence of rotavirus-induced diarrhoea in the diverse pockets of India, underscoring the need for introduction of an effective intervention.

Despite the prevalence of rotavirus diarrhoea across countries, it was first discovered only in 1973 and the first reported case of the disease in India was in 1977. Since then, several premier research centres across the country –

It is exciting to know that rotavirus surveillance data from NRSN has contributed to the introduction of rotavirus vaccine in UIP. With access to this powerful intervention, we can look forward to see betterment in health of our young children all across India.

DR MANOJ MURHEKAR
Director, ICMR-NIE, Chennai

Diarrhoeal stool specimens being stored in wide-mouthed containers, to estimate the prevalence of rotavirus-induced diarrhoea; FACING PAGE ABOVE: The Rotavirus ELISA kit and test plate; BELOW: A dehydrated child receiving IV fluid. ICMR's surveillance demonstrated that children below two years exhibited highest vulnerability to rotavirus disease.

9 lakh children are admitted to hospitals every year; additional 3.27 lakh get treated as outpatients, and 80,000 to 1 lakh die due to rotavirus diarrhoea.

such as ICMR's National Institute of Cholera and Enteric Diseases located in Kolkata, the Christian Medical College, Vellore and the All India Institute of Medical Sciences, New Delhi – have conducted a string of bio-medical studies. However, national-level data, capturing the overall burden of the disease, was still not available due to variability in the parameters used in these studies.

In 2001, ICMR, in collaboration with the Centers for Disease Control and Prevention (CDC), Atlanta, USA, began planning for a rotavirus surveillance network spanning the whole of India. This led to the birth of a two-phased national surveillance, under the coordination of NIE. The first phase, called the 'National Rotavirus Surveillance Network' (NRSN), was conducted across seven different regions of India within a four-year period from 2005 to 2009, and covered over 7,000 children. In November 2011, the NRSN was expanded to generate pan-India data. This phase was carried out between September 2012 and August 2016, and covered over 21,000 children from 17 states and two union territories.

ICMR's surveillance, for the first time, brought out certain key issues in the state of child health in India. It demonstrated the high prevalence of rotavirus disease in the country, with children below two years exhibiting the highest vulnerability to the virus. It also showed that more than half of the children afflicted by the infection were suffering from the more severe form of the disease. ICMR's surveillance, thus, underscored the necessity for the introduction of a rotavirus vaccine that could benefit all – irrespective of affordability.

The two international rotavirus vaccines – *Rotarix*, marketed by the UK pharmaceutical

AT A GLANCE

In India, rotavirus makes up for about 40 per cent of the diarrhoeal admissions. ICMR's National Institute of Epidemiology (NIE), Chennai, has been instrumental in battling rotavirus diarrhoea.

Rotavirus diarrhoea was first discovered in 1973 and the first reported case of the disease in India was in 1977. Several premier research centres, such as ICMR's National Institute of Cholera and Enteric Diseases, Kolkata, the Christian Medical College, Vellore and All India Institute of Medical Sciences, New Delhi, have conducted bio-medical studies.

In 2001, ICMR, in collaboration with the Centers for Disease Control and Prevention (CDC), USA, planned a rotavirus surveillance network spanning across India. This led to the two-phased 'National Rotavirus Surveillance Network' (NRSN).

ICMR's surveillance demonstrated high prevalence of rotavirus disease, with children below two years exhibiting highest vulnerability; and more than half of them were suffering from the more severe form of the disease.

The high prices of existing vaccines for rotavirus diarrhoea, *Rotarix* and *RotaTeq*, resulted in the clinical trials of Indian-made and cheaper version, *Rotavac*. By 2013, results demonstrated its safety and efficacy.

In 2014, National Technical Advisory Group on Immunization (NTAGI) recommended the introduction of *Rotavac* vaccine. The Ministry of Health and Family Welfare (MoHFW), Government of India, announced the incorporation of the vaccine into the national immunization programme.

On 26 March 2016, India became the first country in Asia to launch an indigenous rotavirus vaccine in the Universal Immunization Program.

As part of the pilot phase, *Rotavac* has since been introduced in four states: Haryana, Himachal Pradesh, Odisha and Andhra Pradesh.

company GSK Biologicals, and *RotaTeq*, marketed by the American company Merck and Co. – were the only versions available in India. These vaccines were being used by some of the big private hospitals and were also a part of the optional vaccines recommended by the Indian Academy of Paediatrics. However, the high prices of *Rotarix* and *RotaTeq* meant that a substantial proportion of the population could not avail the benefits of these drugs. The prohibitive price was the primary reason behind a large population of children continuing to get infected and consequently developing severe diarrhoea. This was also supported by NIE's surveillance data, where only a small fraction of the children attending various hospitals had a history of rotavirus vaccination.

With a birth cohort of 27 million, introducing the vaccine free of cost in India's Universal Immunization programme also posed a serious financial challenge: thus began the search for a safe and optimally effective indigenous rotavirus vaccine. Around the time of the first phase of the NIE surveillance, the Indian-made and cheaper version, *Rotavac*, was showing promising outcomes in the ongoing clinical trials. By 2013, results from the completed clinical trials for *Rotavac* demonstrated the safety and efficacy of the indigenous vaccine.

Data from these trials, along with the national rotavirus disease burden information from ICMR's National Rotavirus Surveillance Network, were then presented to the National Technical Advisory Group on Immunization (NTAGI), and in 2014, the Advisory Group recommended the introduction of the rotavirus vaccine. Following this, the Ministry of Health and Family Welfare (MoHFW), Government of India, announced the incorporation of the rotavirus vaccine into the national immunization programme. On 26 March 2016, India became the first country in Asia to launch an indigenous rotavirus vaccine in the Universal Immunization programme.

As part of the pilot phase, *Rotavac* has since been introduced in four states: Haryana, Himachal Pradesh, Odisha and Andhra Pradesh. The life-saving vaccine will not only check diarrhoeal deaths, but is expected to enhance overall child health, and address issues of malnutrition and delayed physical and mental development among children. By offering the vaccine free of charge, it is also expected to help offset the high medical bills that often push millions of Indians into abject poverty.

International experience with the rotavirus vaccines shows that vaccination had a large impact on mortality, hospitalizations and outpatient visits in countries that integrated the vaccine into their national immunization programme. For instance, Mexico experienced a 46 per cent decline in diarrhoeal related deaths among under-five children post the launch of the rotavirus vaccine. Similarly, Brazil witnessed a 22 per cent fall in deaths.

Going forward, the vaccination programme must be expanded to other parts of the country to ensure that the benefits reach every infant in the country. For this next step, the NIE has been entrusted to carry out the review of the first phase of vaccine rollout, and field surveys have already been initiated. As with the national rotavirus surveillance programme, NIE's review will go a long way in ensuring the delivery of evidence-based health interventions – so that life-saving medications can be made available to the right individuals at the right time.

CLOCKWISE FROM BELOW LEFT: Equipment for performing ELISA test; A mother with an infant suffering from acute diarrhoea; Case recruitment form filling by surveillance team; FACING PAGE: A patient filling a form for written informed consent process.

ADDRESSING OCCUPATIONAL HEALTH PROBLEMS

Creating Safe Work Environments

NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH, AHMEDABAD

India is among the fastest growing economies of the world today. It is the seventh largest economy in terms of nominal GDP, and the third largest in terms of purchasing power parity. Behind the imposing figures, however, is a gigantic workforce – many of whom are employed in small- and medium-sized enterprises with a largely informal set-up or are engaged in farming activities. These individuals are often unaware of the exposure to potential hazardous substances at their workplaces and generally lack agency to tackle the issue. The National Institute of Occupational Health (NIOH), Ahmedabad, was established in 1966 by the ICMR to ensure the physical, mental and social well-being of workers in all occupations.

A key intervention by NIOH is in the case of silicosis – one of the most common and serious occupational diseases. About 10 million people working in mines, ceramics, potteries, foundries, metal-grinding, stone-crushing, agate-grinding, and the slate-pencil industries are exposed to free silica dust. Inhalation of this white powder – popularly known as the powder of death – leads to the incurable respiratory disease, silicosis. Because the symptoms – including shortness of breath, drastic weight loss, and difficulty in performing the simplest of physical activities – may take anywhere between months to a couple of years to manifest, workers in these industries generally do not realize the consequences until it is too late.

Health of the workforce is of paramount importance in any country's economy. The institute endeavours for safe work and healthy workforce through prevention, preservation and promotion of health, safety and work environment.

NIOH TEAM

A worker manually segregating metal raw materials before they are transferred to the kiln in an iron foundry.
FACING PAGE: A worker in an agate factory. About 10 million workers are exposed to free silica dust, or so-called 'powder of death', that causes silicosis.

The town of Khambat in Gujarat is known for its booming export-oriented agate industry. However, grinding of the agate stone produces a substantial amount of silica – making the agate workers extremely vulnerable to silicosis. An NIOH study in 1988 showed that 38 per cent of the workers suffered from silicosis. NIOH notified the diagnosed individuals to the chief inspector of the factories, helping the victims of silicosis secure compensation as per law. The watershed study was not only able to create awareness among the agate workers, it also catalyzed the creation of augmented stone-grinding machines aimed at checking silica emission. However, the new machines achieved limited success. Workers refused to use them, stating that they consumed more power and suffered from significant speed variation. Thus, in close consultation with the workers, NIOH introduced a modified dust-control device, consisting of blowers and bag filters, which could be attached to the traditional machines.

Detailed tests prior to the official introduction showed that the modified machines successfully brought down silica emission by 93 per cent, thereby ensuring that more than 300 workers of Khambat and their families were insulated from the risk of contracting silicosis. Scientists at the NIOH went a step further and took the lead in establishing the *Akik Kamdar Kalyan Trust*, facilitating workers to purchase the modified machines at subsidized rates – 500 such machines have now been installed at several units. The findings of the Institute's study based on the modified machines have prompted the amendment of the Gujarat State Factory Rules. Thus, this industry, primarily a cottage industry, has been brought under the legislation, and agate stone grinders now enjoy a much safer workspace.

NIOH has also made great strides in checking silicosis in the quartz-crushing industry. The quartz-crushing hubs of Godhra and Balasinore in Gujarat provide employment to many local communities and an increasing proportion of migrant workers. Truckloads of quartz are collected from the nearby open areas, crushed into white powder, bagged and sent to glass factories and other silicate industries. While few of the crushing units have adopted mechanized systems, majority of them continue to employ some form of manual labour. Every year during the lean agricultural period, thousands of tribals from Madhya Pradesh travel to these towns to fill crushed quartz stone in bags – working 8 to 12 hours a day. Quartz-grinding is one of the deadliest occupations, which causes exposure to almost 100 per cent free silica leading to silicosis in a matter of few months. Thus, silicosis has emerged as a major cause of death in, for instance, Alirajpur of Madhya Pradesh – home to many migrant workers.

80–96 per cent reduction in respirable airborne dust levels was observed in factories post interventions by NIOH.

AT A GLANCE

The NIOH was established in 1966 by ICMR in Ahmedabad.

About 10 million people working in mines, ceramics, potteries, foundries, metal-grinding, stone-crushing, agate-grinding, and the slate-pencil industries are exposed to free silica dust, which leads to respiratory disease like silicosis.

An NIOH study in 1988 showed that 38 per cent of the workers suffered from silicosis in the agate industry in Khambat, Gujarat.

NIOH successfully brought down silica emission by 93 per cent through their dust-control device in Khambat, ensuring safety of more than 300 workers and their families.

NIOH established *Akik Kamdar Kalyan Trust* in Gujarat, facilitating workers to purchase modified machines at subsidized rates – 500 such machines have now been installed at several units.

Every year during the lean agricultural period, thousands of migrant workers travel to quartz-grinding hubs to fill up crushed quartz stone in bags – working 8 to 12 hours a day.

Quartz-grinding is one of the deadliest occupations, which causes exposure to almost 100 per cent free silica leading to silicosis.

NIOH scientists have identified sources of dust generation in quartz-crushing units and have recommended enclosure of dust sources and use of powerful exhausts.

NIOH assisted in the cancellation of the registration of the deadly Methomyl by the Pesticide Registration Committee, thus ensuring the safety of cotton farmers.

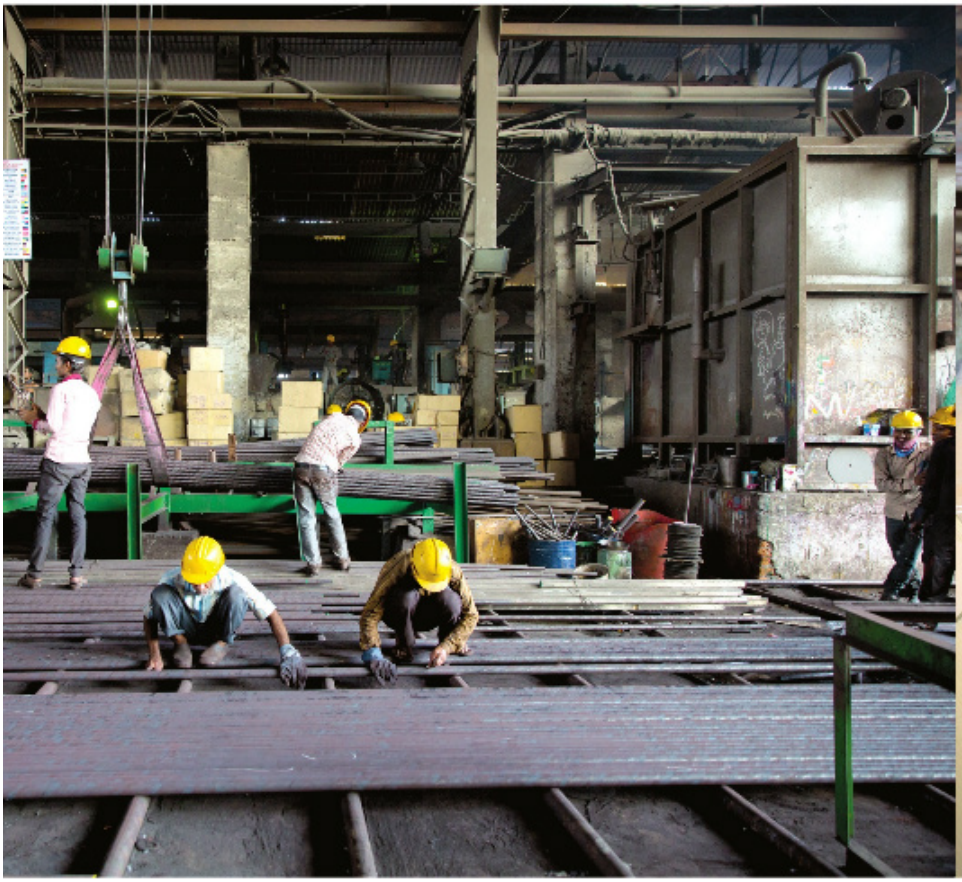
NIOH's recommendation of wearing nylon gloves for tobacco cultivators has helped circumvent acute nicotine toxicity and green tobacco sickness.

Around 5 lakh people die due to indoor air pollution in India every year.

NIOH scientists have been able to identify specific sources of dust generation in the quartz-crushing units and their recommendations, such as the enclosure of dust sources and the use of powerful exhausts, have been incorporated. NIOH's industrial hygiene survey conducted thereafter in six factories showed that respirable air-borne dust levels have been reduced by 80–96 per cent. The Institute has also developed a battery-operated cooling garment (jacket) for labourers working in heat-stressed environments.

Beyond industry-sectors, NIOH has actively engaged in creating safe agricultural practices. India is currently the world's largest producer of cotton and also comes at the top in terms of land

LEFT TO RIGHT: Surface temperature evaluation using infrared thermal imaging camera; Workers manually inspecting for the imperfectness of rolled-on iron bars and polishing before packaging; Self-sewed gloves made from jeans used by the workers in ceramic tiles industries. Workers use these gloves for collecting baked tiles coming out of the kiln on conveyor belt rollers.



area under cotton cultivation. Several states in the northern, central and southern parts of India have significant amount of land and labour dedicated to cotton cultivation. However, cotton yield continues to suffer owing to pest issues, particularly the ball-worm pest. In 1988–89, an insecticide – Methomyl – was introduced in India for the control of ball-worm pest on cotton. Soon after, an increasing number of farmers using the Methomyl spray lost their lives. For the first time, NIOH carried out a systematic study, and this led to the cancellation of the registration of Methomyl by the Pesticide Registration Committee. Timely action by NIOH, thus, ensured the safety of cotton farmers from the potential danger of exposure to the toxic compound.

Given the formidable task of creating safe work zones in a spectrum of occupations, NIOH is simultaneously engaged in multiple sectors. NIOH's recommendation of wearing nylon gloves for tobacco cultivators has helped circumvent acute nicotine toxicity and green tobacco sickness. The Institute's evaluation of various types of *chulhas* (stoves) have helped create awareness and bring down respiratory diseases, especially among rural women. NIOH has played a fundamental role in securing compensation for workers suffering from occupational asbestosis. Owing to its seminal work, the Supreme Court has identified NIOH as the final authority for diagnosis of asbestosis for compensation purpose.

Personal cooling garment for use in hot environments to protect workers from heat-related injuries. It is an affordable low-cost assistive device, consisting of silicone tubing embedded in cotton fabric vest covering the torso area. It has a rechargeable battery-operated system with different capacities of backpack containers.

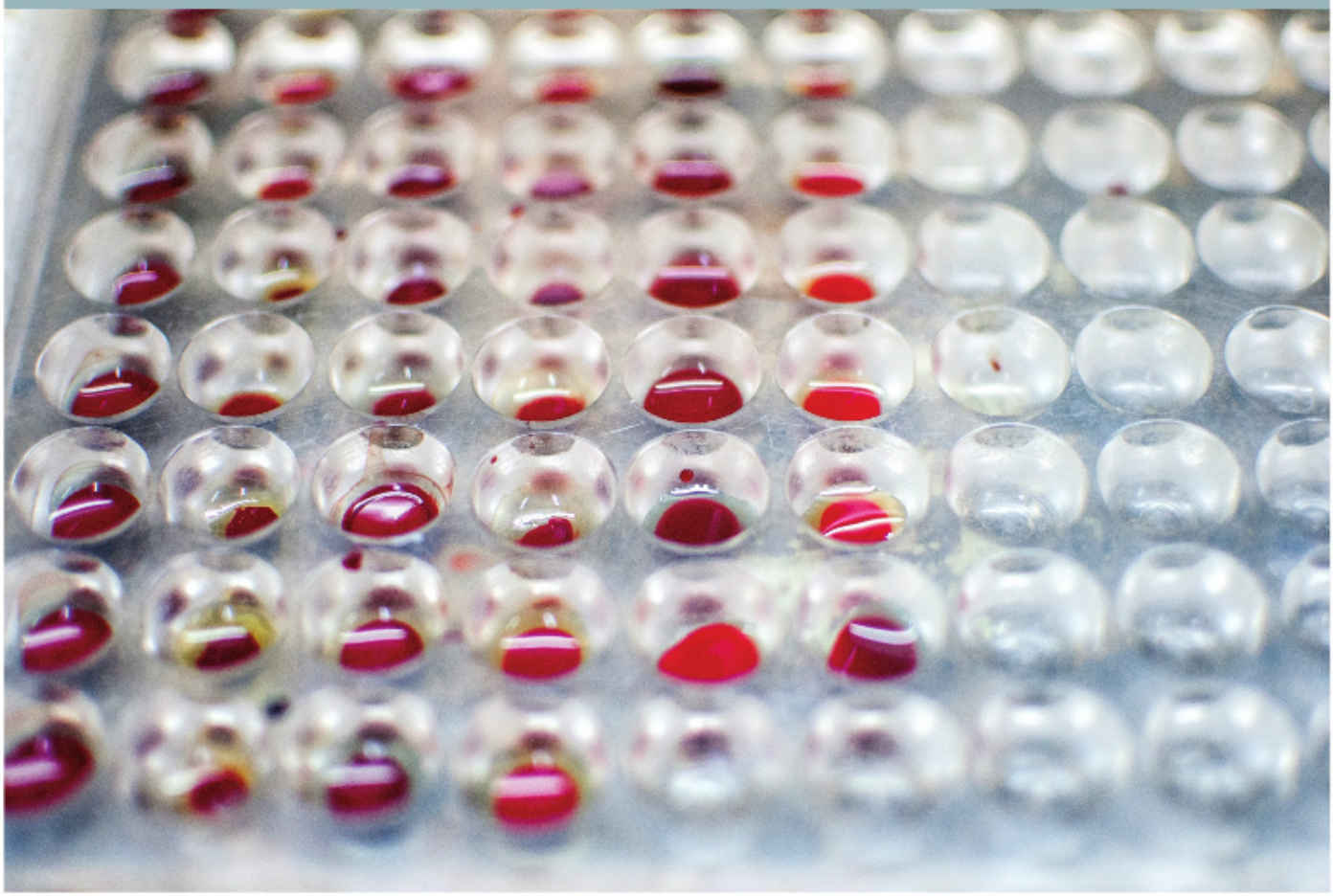
TOP LEFT: A worker being tested for isometric hand–arm–shoulder strength during wrist-twisting clockwise operation on a screwdrive; TOP RIGHT: A worker being interviewed to record self-reported information on occupational ergonomics; BOTTOM: The chromatography and mass spectrometry techniques, viz., single, triple, quadrupole and high-resolution mass spectrometry have been playing a significant role in health research. These techniques are beneficial for the determination of toxic chemicals (pesticides, PCBs, dioxins, PAHs, etc.) at trace level in biological, environmental and food samples, which are potential hazards to human beings.

As India continues to grow, the country is expected to experience more complicated occupational health concerns, which adversely affect the health of not only the workers associated with manufacturers but also of the general community residing nearby, as more industrialization brings with it a similar degree of pollutants. Increased use of pesticides will affect both agricultural and consumer products. Social developments like urbanization and mechanization will also contribute to more noise, air, soil and water pollution. In this context, NIOH's exhaustive approach to addressing these issues will continue to play a critical role in ensuring safe work and living spaces.

ENSURING SAFE BLOOD TRANSFUSION

Tracking the Bombay Phenotype

NATIONAL INSTITUTE OF IMMUNOHEMATOLOGY, MUMBAI



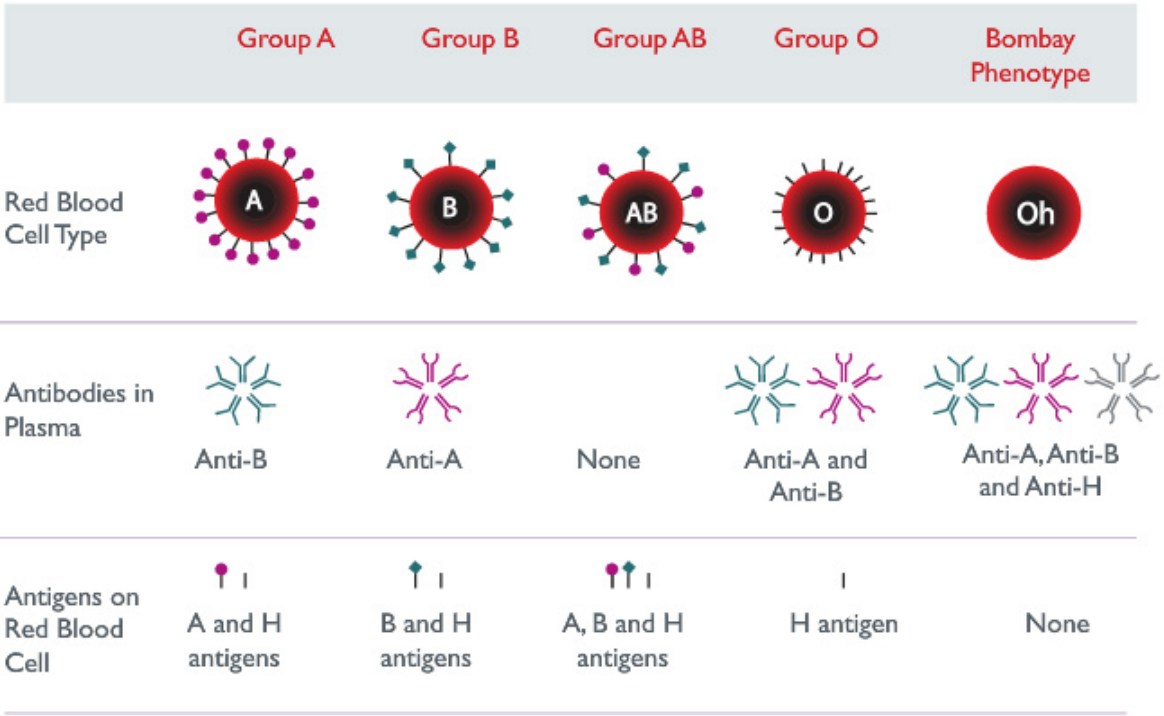
The discovery of the Bombay phenotype was a watershed moment in the field of Immunohematology. Discovered by accident in 1952 – more than six decades ago – in a blood bank of a general hospital in Bombay (now Mumbai), even today it is popularly known as the 'Bombay' phenotype among the scientific community, named after the city where it was first discovered.

The ABO blood group classification is critical in human blood transfusion. For all individuals, the H-antigen is the first antigen formed on red blood cells (RBCs) which then gets chemically modified to either A or/and B antigens. Based on the presence of either A or B or both antigens, individuals are then categorized into separate blood groups – A, B and AB. If the H-antigen does not get transformed, then the individual is labelled as 'O' blood group. Receiving blood that contains a foreign antigen can cause acute haemolytic transfusion reaction – the clumping and subsequent destruction of RBCs. Thus, it is important to determine the ABO blood group status of all blood donors and recipients for safe blood transfusion.

The Bombay phenotype blood cells do not express the H-antigen in the first place. This means that they cannot synthesize either A or B antigens. The H-deficiency in itself does not entail any ill-effects. However, by routine blood-grouping techniques it is (mis)identified as O group, but when cross-matched with O group red cells, they are incompatible due to presence of anti-H antibodies in the serum. These antibodies react with the H-antigen present on the RBCs of a normal O group individual. For many years, this fact remained unknown in transfusion medicine. It was detected 52 years after the discovery of ABO blood group system.

During antenatal checkup often pregnant women were identified with Bombay phenotype. In one case of caesarian section, blood units were supplied and the operation was successful. The woman's mother thanked the scientists.

SEEMA JADHAV
Technical Officer from Department of Transfusion Medicine, NIIH Mumbai
DR K. VASANTHA
Ex-HoD, Department of Transfusion Medicine, NIIH Mumbai



ICMR's National Institute of Immunohematology (NIIH) and its scientists have played a central role in the detection of the Bombay phenotype – from its initial discovery to the current surveillance of individuals with this rare blood group. Dr Harkisan Motiram Bhatia, the first director of the Institute of Immunohematology (now NIIH) was, at the time, a postgraduate student at the Department of Pathology and Bacteriology at Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital. He, along with Dr Y. M. Bhende, who was heading the department, identified the new blood type for the very first time.

In December 1951, on one of his shifts Dr Bhatia came across a railway accident victim who required blood transfusion. Despite being identified as an O+ blood type, his serum kept reacting with multiple group O samples during the cross-matching stage. Eighty additional group O samples were further tested with the serum and the same results were obtained. Therefore, merely the plasma – and not the remaining blood cells – was transfused. In January 1952 again, another patient exhibited the same reaction. Both individuals apparently were of the O blood group, but their blood samples could not be cross-matched with any other O group samples. Interestingly, samples from the two individuals were completely compatible with each other. Following this, the doctors conducted a deliberate screening of hundreds of people and 160 blood donors. After eight months of this exercise, they finally encountered a first-time blood donor who showed similar blood group patterns. Three samples of the donor's blood were then referred to the Blood Group Research Unit at the Lister Institute of Preventive Medicine, London for further analysis.

Through extensive studies conducted by Sanger, Race, Morgan and Watkins at the Lister Institute, it was finally established that this was a new blood group character related to the ABO blood system.

'Study of Blood Group Substance H' – Dr H.M. Bhatia's doctoral thesis submitted to the University of Mumbai; FACING PAGE: The various blood groups.

They also suggested that the phenotype might not be uncommon in India. The discovery of the new phenotype led to a flurry of research closer home. For example, in the article titled 'Rare blood groups and Consanguinity: Bombay phenotype,' Bhatia and Sanghvi found that the gene responsible for it was present mainly in Marathi-speaking people around Bombay. The increasing attention and scientific scrutiny paved way for several surveillance programmes in the Marathi-speaking region.

From the year 1956 onwards, routine screening tests were put in place to understand the incidence of individuals with this rare blood type. Blood samples from the Human Variation Unit of Cancer Research Institute, Mumbai, and those collected from antenatal women attending the Nowrojee Wadia Maternity Hospital, Mumbai, were screened. Whenever possible, samples from newborn babies as well as their fathers were also tested. This exercise led to the screening of a total 42,297 samples – out

AT A GLANCE

A chance discovery in 1952 in a blood bank of a general hospital in Bombay, the 'Bombay' phenotype was named after the city where it was first discovered.

ICMR's National Institute of Immunohematology (NIIH) has played a central role in detection of Bombay phenotype – from its initial discovery to surveillance of individuals with this blood group.

Dr Harkisan Motiram Bhatia, the first director of the Institute of Immunohematology (now NIIH) came across victims in December 1951 and January 1952 with a rare blood group, and samples from both were found compatible with each other.

After eight months, NIIH got a first-time blood donor with the rare blood group. Three samples, two patients and one donor were referred to the Blood Group Research Unit at the Lister Institute of Preventive Medicine, London for further analysis. It was finally established that a new blood group had been discovered.

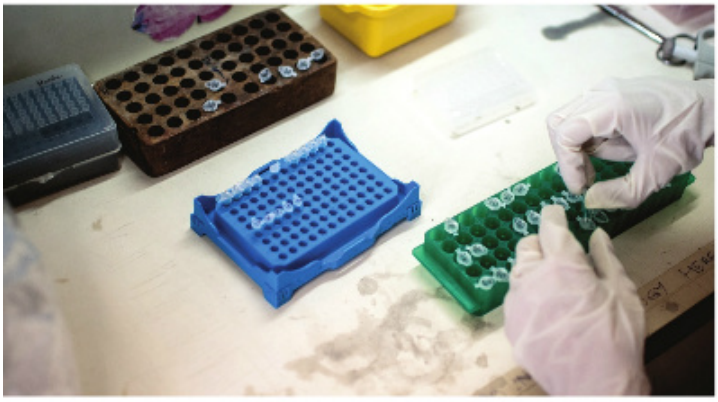
In the article titled 'Rare blood groups and Consanguinity: Bombay phenotype,' Bhatia and Sanghvi found that the gene responsible for it was present mainly in Marathi-speaking people around Bombay.

Today, NIIH has identified 268 Bombay phenotype cases so far. About 64 per cent of the cases have been reported in Maharashtra. It's incidence is 1:4500 in Konkan and Goa region, 1:6000 in Karnataka and 1:25000 in Tamil Nadu.

NIIH has been aggregating a list of all individuals with the Bombay phenotype. It has supplied blood to patients in other states, and sometimes also to other countries like Malaysia and South Africa.

Only 25 to 30 per cent of the listed individuals with the Bombay phenotype are active blood donors. NIIH plays a principal role in awareness creation.

CLOCKWISE FROM LEFT: Laboratory set up at KEM Hospital Blood Bank; Technician at KEM Hospital Blood Bank collecting blood from a Bombay phenotype donor; Department of Transfusion Medicine, NIIH, where extensive investigations on Bombay Phenotype and other blood groups are carried out; A laboratory at KEM Hospital; FACING PAGE: A technician carrying blood samples at the blood bank lab.



of these, three families were identified with the Bombay phenotype. Based on this study, it was estimated that roughly 1:13,000 individuals from Mumbai and about 1 in every 77 individuals in the Marathi-speaking area might be a carrier of the genetic allele responsible for the Bombay phenotype.

Subsequently, Dr Malti Sathe at Bombay Blood Group Center (BGRC) carried out a similar examination, but on a much larger scale – 1,67,404 blood samples from patients and voluntary donors at KEM Hospital Blood Bank and J.J. Hospital Blood Bank were tested between January 1968 and December 1972. Twenty-two cases of the Bombay phenotype were detected during this extensive survey. These findings facilitated a more accurate calculation of the prevalence of the phenotype – the incidence was revised to 1 in 7,600 individuals for the Mumbai region, and 1 in 2,573 for O group individuals. A second layer of investigation based on the details of the Bombay phenotype individuals – such as caste, native place and consanguinity – further revealed that 14 of the 22 cases of Bombay phenotype were from the Marathi community.

By this time, the NIIH had successfully aggregated a total of 58 blood samples of individuals with the Bombay phenotype. Of these, 29 cases were found to have originated from three districts of southwest Maharashtra (Raigad, Ratnagiri and Sindhudurg), collectively known as Konkan, and Goa. The disproportionate prevalence led to a survey to find out the exact incidence of this rare phenotype in this region – 24,085 unrelated individuals from more than 400 villages were tested and 6 cases of the Bombay phenotype were detected. Through

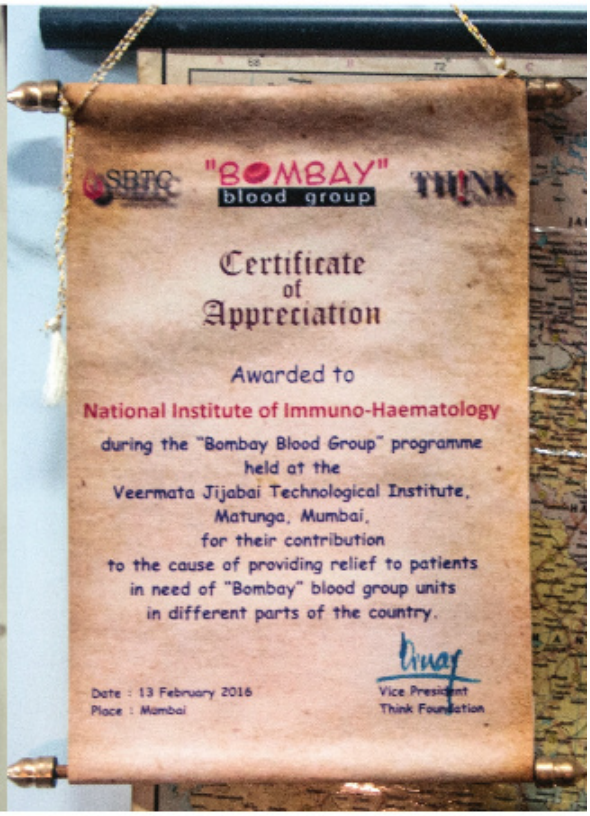
the targeted screening programme, the Institute was able to determine that 1 in 4,500 individuals in the Konkan and Goa region belong to the Bombay blood phenotype.

Today, the Institute has identified a list of 268 Bombay phenotype cases so far. Micro-mapping of these cases is continuously being carried out to understand the incidence. About 64 per cent of the cases have been reported in Maharashtra. Surveillance programmes have also been implemented in other states of India: incidence ranges between 1:6,000 in Karnataka to 1:25,000 in Tamil Nadu. However, the job is only half done. Considering the average incidence of the Bombay phenotype as 1:15,000 to 1:17,000 individuals, it is likely that India is home to about 30,000 to 40,000 individuals with this phenotype. Therefore, systematic screening for various castes and tribal groups in the different states of India need to be carried out.

Better understanding of the blood group and its incidence is only a means to the actual goal – safe and easy blood transfusion. While the mapping exercise allows the estimation of individuals with this rare condition, there is a simultaneous need to create a platform to link the Bombay phenotype blood donors to potential recipients. On 1 January 2015, a prominent national daily, the *Hindu* reported that an infant, Sandesh Kumar from Gorakhpur, Uttar Pradesh, had an inborn heart condition and was in dire need of surgery, which required blood transfusion. He was found to have a very rare blood type – the Bombay phenotype. Surgery could not be performed due to the non-availability of this rare blood type. This was also posted on the internet and 10 individuals with the phenotype came forward. The Think Foundation, a Mumbai-based NGO facilitated this process. It collected blood from three Bombay phenotype individuals in Mumbai. The blood was air-flown to Delhi where Sandesh's father received it and he was successfully treated. This highlighted a crucial gap – the need for a Bombay blood donor registry. Since its discovery, the NIIH has been aggregating a list of all individuals with

30,000 to 40,000 individuals in India are likely to have Bombay phenotype, blood average incidence is 1:15,000 to 1:17,000.

LEFT: The team of scientists working at the Department of Transfusion Medicine, NIIH. Standing left to right: Mrs Seema Jadhav (Technical Officer), Dr Ajit Gorakshakar (Scientist F and HoD), Dr Swati Kulkarni (Scientist C); sitting: Dr K Vasantha (Scientist E, Former HOD); RIGHT: Certificate of appreciation given to NIIH by Think Foundation during Bombay Phenotype Individuals Meet organized on 13 February 2016, for their contribution in addressing transfusion needs of Bombay phenotype individuals and maintaining a donor registry.



Over 800 medical officers and technicians from blood banks across India have been trained by NIIH.

the Bombay phenotype. In several instances, it has supplied blood to the patients in need for this blood type. On some occasions, the blood has also been delivered to patients in other countries like Malaysia and South Africa.

Apart from maintaining a repository and actively supplying blood, the NIIH is also involved in capacity building. It has been conducting training for blood bank medical officers and technicians since 1961. So far, more than 800 medical officers and technicians from blood banks across the country have been trained. Today, majority of the blood banks in the country have either medical officers or technicians trained at NIIH. During this programme, along with routine blood bank procedures, emphasis is made on resolving discrepancies in grouping, detection of weaker variants of A and B blood types, and

LEFT: Mr Pravin Shinde (left) with Mr Mahesh Ghag (right), Bombay Phenotype donors; RIGHT: Mr Vinay Shetty from Think Foundation who has been actively involved along with NIIH in arranging Bombay phenotype donors.

the identification of the Bombay phenotype. The training programme has enabled a great proportion of blood banks to directly identify and confirm Bombay phenotype cases, as well as maintain their own lists. These blood banks and NGOs such as the Think Foundation and Sankalp Pratishthan, Bengaluru, have been supplying blood to patients as and when required.

Creating awareness is another area in which the NIIH plays a principal role. Only 25 to 30 per cent of the listed individuals with the Bombay phenotype are active blood donors. Thus, three-fourth of them are currently not donating blood. It was thus felt that there is a need for better education on the considerable benefits of donating this rare blood group. A meet was organized by Think Foundation and NIIH, under the aegis of State Blood Transfusion Council, in February 2016 at Veermata Jijabai Technological Institute, Mumbai, to resolve queries and create general awareness on the importance of Bombay phenotype blood donation.

The NIIH was designed for two broad purposes. First, to conduct clinical research on the various aspects of Immunohematology – a core component of this being the mapping and tracking of rare bloods. Second, it was meant to build capacity and create an efficient and accessible blood banking system. The Institute's contribution in the case of Bombay phenotype exemplifies both objectives. It has been able to successfully survey the prevalence of the blood type, train immunohaematologists across the country and supply blood when required.

TACKLING FLUOROSIS

Simple Solution to a Complex Problem in Tribal Hinterlands

NATIONAL INSTITUTE FOR REASEARCH IN TRIBAL HEALTH, JABALPUR

Groundwater is the most common source of drinking water across India. With an ever-growing population and consequently falling groundwater tables, one has to dig deeper and deeper to pump out fresh water. The groundwater in many parts of India, however, is rich in the naturally occurring mineral, fluoride. The consumption of fluoride in small quantities is beneficial for the body, for instance, it helps prevent dental cavities and tooth decay. On the other hand, when taken in significant amounts (about 2 to 5 mg per day, or more), it leads to a disabling disease that may cause weak teeth, or stiffness of the muscles and joints, and ultimately leading to crippling fluorosis.

Fluorosis has, thus, emerged as a critical public health concern in India – it is estimated that over 62 million people in the country are exposed to high fluoride and are at substantial risk of developing fluorosis. Of these, 6 million are children below the age of 14 years.[1] Madhya Pradesh in particular is severely affected – most of the eastern, southern and western districts of the state have excess fluoride in ground water, and the tribal populations inhabiting these areas have been found to be the worst impacted.

The National Institute for Research in Tribal Health (NIRTH), a permanent ICMR institute, has made crucial headway in the field of fluorosis – not only by correctly identifying the disease in the tribal hinterlands of Madhya Pradesh,

The problem of fluorosis started gradually in 1994 in Tilaipani village. Scientists from ICMR helped in diagnosing and developing effective strategies for its mitigation. I accompanied the team to the affected villages. Had it not been for ICMR intervention, many children would have been crippled.

MR SANTLAL MARAVI
Health Supervisor, Padri Patpara, Mandla

AT A GLANCE

The consumption of fluoride in small quantities is beneficial, but when taken in significant amounts, it may cause weak teeth, or stiffness of the muscles and joints, and ultimately leading to crippling fluorosis.

In India, of the 62 million people who are exposed to high fluoride and are at substantial risk of developing fluorosis, 6 million are children below the age of 14 years.

The National Institute for Research in Tribal Health (NIRTH), an ICMR institute, started its work on fluorosis in 1995, correctly identifying the disease in the tribal hinterlands of Madhya Pradesh, and providing customized solutions.

In a detailed door-to-door study conducted in villages in MP, NIRTH found that deformities due to fluorosis were further complicated by nutritional deficiencies. To address this, it proposed water and nutritional intervention models.

To provide clean and fluoride-free drinking water, NIRTH focused on renovating traditional wells, initiating the supply of piped water, and diluting fluoride-contaminated water with rain water. It also recommended the intake of a local shrub called *Chakoda Bhaji* (Cassia Tora), which contains three of the four essential micronutrients (Calcium, Vitamin C and Iron).

A five-year gap after NIRTH's intervention revealed that the prevalence of knock-knee deformity had reduced drastically among the most-affected age group (under 20) – from 51 per cent at baseline to 2.6 per cent.

UNICEF included NIRTH's intervention models in their 'International Learning Exchange Programme' from their Geneva Office in 2007 and 2008.

but also introducing customized solutions as per local requirements. Upon the request of the Chief Medical & Health Officer (CMHO), Joint Director and Collector Mandla, NIRTH started its work on fluorosis in 1995 – at a time when the understanding of fluorosis in India was almost non-existent.

In the 1990s, the villages of Tilaipani and Hirapur in Madhya Pradesh were experiencing grave ramifications of a mysterious disease. The children in the two villages were seen stumbling about awkwardly knock-kneed and with discoloured teeth – signs of fluorosis. Children with more advanced form of the disease were often confined to their homes, unable to attend school or play with their peers. Parents too complained of extreme muscle and joint pains. However, in the late 1990s, doctors often misdiagnosed it as simple arthritis, polio or rickets – thereby failing to make the vital connection

LEFT TO RIGHT: ***Chakoda Bhaji*** (Cassia Tora) shrub, which contains three of the four essential micronutrients (Calcium, Vitamin C and Iron) to check fluorosis; Children with knock-knees in a fluoride-affected village – 6 million children under the age of 14 are at a risk of developing fluorosis; An X-ray of knock-knees.

Over 62 million people in India are exposed to high fluoride and are at substantial risk of developing fluorosis.

between the symptoms and the consumption of the so-called safe water from the multiple bore wells across the village.

NIRTH's door-to-door study was finally able to identify the root of this mystery. A medical officer, accompanying the surveying team, also carried out detailed clinical examinations. A 24-hour dietary survey was conducted to evaluate food consumption patterns and nutrient intake; blood samples were collected for biochemical analysis; and drinking water samples were taken to estimate fluoride presence. Further, radiological examinations were conducted for most of the severely affected children.

The detailed study also found that deformities due to fluorosis were further complicated by multiple nutritional deficiencies. To address the issue, NIRTH proposed two remedial measures – water and nutritional intervention.

FROM ABOVE TO BELOW: Clinical examination being conducted in a tribal village – this includes a dietary survey to evaluate food consumption patterns and nutrient intake, blood samples collected for biochemical analysis, and drinking water samples taken to estimate fluoride presence; A counselling session at NIRTH clinic; A technician working in a NIRTH laboratory.

Given the importance of providing clean and fluoride-free drinking water, the first measure of water intervention focused on renovating traditional wells, initiating the supply of piped water, and diluting fluoride-contaminated water with rain water. A meeting was convened at the office of district magistrate and a plan was developed to provide safe drinking water to the affected villages. The Public Health Engineering Department (PHED) – the government agency responsible for providing safe drinking water – proposed a plan for safe drinking water supply, which was subsequently approved. With financial assistance from the Rajiv Gandhi National Drinking Water Mission, a programme under the Ministry of Rural Development, the plan was initiated.

The second mode was nutrition-based. It was found that residents of the two villages were suffering from severe dietary deficiencies of micronutrients essential for checking fluorosis – Calcium, Vitamin C, and Iron. In order to ensure greater acceptability of the treatment among the native population, the Institute recommended the intake of a locally available shrub called *Chakoda Bhaji* (Cassia Tora). This shrub was found to contain three of the four essential micronutrients (Calcium, Vitamin C and Iron), and was being used by the tribals as part of their diet during rainy season, when fresh leaves are easily available.

Chakoda Bhaji, however, was not consumed frequently; like most vegetables, it was seasonal in nature. NIRTH, thus, took an additional step and facilitated awareness among the affected tribal population. Through group meetings coordinated by Anganwadi workers and female health workers, the tribal women were advocated to increase the intake of *Chakoda Bhaji* from once a week to at least four to five times a week, all year round.

After a five-year gap, an impact evaluation of the two interventions revealed that the prevalence of knock-knee reduced drastically among the most affected age group (under 20) – from 51 per cent at base line to 2.6 per cent after intervention. There was also a slight reduction in the prevalence of dental

An awareness programme being undertaken by the centre. Through such awareness programmes, NIRTH proposed water and nutritional intervention models to check fluorosis.

51 to 2.6 per cent reduction in knock-knee cases after NIRTH's intervention.

fluorosis in the same age group. Assessment for certain individual cases also showed partial reversal of the fluoride-cased bone deformity in most cases and complete reversal in certain instances.

Due to the highly successful nature of NIRTH's intervention models, they were adopted by UNICEF Bhopal and implemented in Dhar and Jhabua regions of Madhya Pradesh. Post a year of implementation, an independent evaluation found a 30 per cent reduction in skeletal and non-skeletal fluorosis. Later, UNICEF also included this model in their 'International Learning Exchange Programme' from their Geneva office in 2007 and 2008.

India's economic success will hinge on its ability to build a healthy community. Illnesses such as fluorosis, which have identifiable causes and remedies, must be tackled on priority. In this context, the work undertaken by NIRTH is seminal and will continue to play a crucial role in India's overall development.

1. N. Arlappa, Aatif Qureshi, and R. Srinivas, 'Fluorosis in India: An Overview', *International Journal of Research & Development of Health*, http://www.ijrdh.com/files/11.Fluorosis.pdf.

DETECTING LEPTOSPIROSIS

Diagnosis and Control of Zoonotic Infection in the Andamans

REGIONAL MEDICAL RESEARCH CENTRE, PORT BLAIR

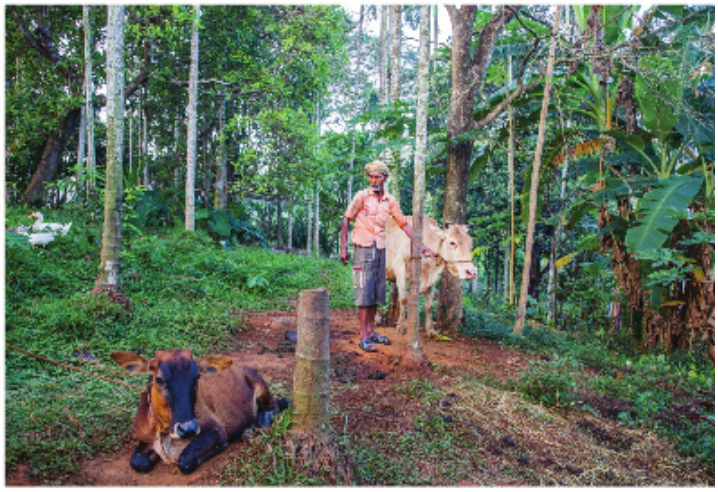
Leptospirosis is a zoonotic infection caused by the *Leptospira* bacterium. (Zoonotic diseases are those transmitted from animals to humans.) It is generally transmitted through the urine of various 'host' animals – such as rats, cattle, pigs, dogs and cats. Infection among humans occurs when they either come in direct contact with animal urine, contaminated water, or wet environment. Leptospirosis is particularly prevalent in warm and wet tropical zones – where the bacteria are able to thrive for a prolonged period of time. In such ecological niches, the disease is a common agent of fatal symptoms such as liver damage, kidney failure, severe bleeding from the lung, and multiple organ failure culminating in rapid death.

The Andaman Islands situated in the Bay of Bengal is, thus, one of the most endemic regions of leptospirosis in the world – given the year-round warm climate and long drawn-out monsoon season. The history of leptospirosis in the Andamans can be traced back to as early as the 1920s, when Taylor and Goyle initiated a study at Ross General Hospital at Port Blair to understand the cause of febrile jaundice with haemorrhages, commonly occurring among the free living convicts of the Andaman penal settlement. During a five-month period they were able to detect 64 confirmed cases of leptospirosis. After this comprehensive study conducted in 1929, however, little was known about the status of leptospirosis in the Andamans for the next six decades.

The number of deaths due to leptospirosis, which used to be 20–40 every year in the 1990s has come down to 2–3 during the last three years (2014–16) because of joint efforts – one health vision approach.

DIRECTORATE OF HEALTH SERVICES
Andaman and Nicobar Administration, Port Blair

LEFT TO RIGHT: Occupational activities posing high risk of exposure to Leptospira – fresh water fishing; Cattle are often carriers of Leptospira, making cattle farmers at high risk of leptospirosis; Bathing in ponds and streams, a common habit in the villages, can result in exposure to Leptospira as the water may be contaminated with the urine of carrier animals containing live bacteria.



RMRC is currently carrying out research on soil bacteria that may have an inhibitory effect on the survival of leptospirosis bacteria.

In the post-monsoon period of 1988, an 18-year-old girl was admitted to the G.B. Pant Hospital in Port Blair. Admitted with the complaint of fever and coughing of blood, she was diagnosed with miliary tuberculosis. She recovered completely and her chest X-ray became clear within a week of administration of anti-tuberculosis and other antibiotic therapy – a phenomenon that would have been impossible had she been actually suffering from miliary tuberculosis.

Soon, the disease – then locally referred to as the Andaman Haemorrhagic Fever (AHF) – spread to other parts of the union territory. For instance, several individuals at a forest labour camp in the south Andaman region were reported with similar symptoms – haemorrhages, fever and respiratory problems. A similar outbreak was also witnessed in north Andaman, about 300 km north of Port Blair. Doctors were able to successfully treat the mysterious AHF with antibiotics, and the outbreak subsided within a couple of months. However, it reappeared in the next season – for the next five years, the post-monsoon outbreaks continued while the cause remained elusive.

In 1993, the Regional Medical Research Centre (RMRC) at Port Blair – a centre specializing in health issues of indigenous tribes – started a detailed

investigation to analyse the annual outbreaks. The Centre carried out a systematic review of the islands' medical archives and clinical information curated during the previous five years and found leptospirosis to be the primary suspect. Attempts for further proof, linking AHF to leptospirosis were made; and in 1995, the diagnostic enigma of the mysterious haemorrhagic fever was finally solved by serological evidence during an outbreak in Diglipur in north Andaman. The bacteria were subsequently isolated from human patients.

RMRC's identification of the cause of AHF has contributed tremendously in addressing the spread of leptospirosis in the Andamans. Because of the many types of animals which carry the disease, leptospirosis is one of the most widespread zoonotic disease. By identifying the disease, and consequently the specific modes of transmission, RMRC has been able to make targeted interventions to effectively contain the problem.

Today, medical personnel as well as the Andaman residents are well aware of leptospirosis, prompting early detection of the disease when contracted and early appropriate treatment. Given the transmission through animals, the most effective containment strategy is through veterinary public health. The RMRC, in collaboration with the Directorate

AT A GLANCE

In 1993, the Regional Medical Research Centre (RMRC) at Port Blair – a centre specializing in health issues of indigenous tribes – started a detailed investigation to analyse the post-monsoon outbreaks of the mysterious Andaman Haemorrhagic Fever (AHF).

In 1995, RMRC accurately identified that *Leptospira* was the cause of the mysterious fever and that AHF was a clinical variant of the leptospirosis.

The RMRC, in collaboration with the Directorate of Health Services, the Department of Animal Husbandry and the Department of Agriculture, carries out regular awareness programmes among farmers, medical and paramedical professionals, and veterinarians in the Andamans.

RMRC has played an essential role in detecting post-disaster outbreaks of leptospirosis, and assisting State Health Departments in containing the outbreaks, such as after the Odisha cyclone of 1999 and Mumbai floods of 2000 and 2005.

The RMRC employs a multi-layered strategy to tackle leptospirosis, ranging from local solutions specifically for the Andamans, to national strategies and international collaborations.

Along with other international centres, RMRC is actively searching for an effective DNA vaccine for leptospirosis.

The establishment of the Port Blair institution has contributed in setting up reference and diagnostic laboratories for half a billion people in the Southeast Asia region, including India, where people are predominantly engaged in wet farming and are therefore at risk of leptospirosis.

LEFT TO RIGHT: A Leptospira repository at RMRC, Port Blair; A Leptospira bacteriology laboratory at RMRC, Port Blair; Bedside inoculation for blood culture of ***Leptospira*** at a primary health centre.

RMRC is also exploring technologies to effectively prevent the disease through bio-control.

of Health Services, the Department of Animal Husbandry and the Department of Agriculture, has been carrying out regular awareness programmes among the farmers, medical and paramedical professionals, and veterinarians. Further, the animals in the Andamans are regularly monitored for infection.

Apart from leptospirosis identification and treatment, RMRC is also exploring technologies to effectively prevent the disease – for instance, through bio-control. In the Andamans, leptospirosis peaks during two seasons: the rice-sowing month of July and the harvesting October–November period. This is because during this time a large section of the community is exposed to the waterlogged rice-fields – a fertile breeding-ground for the leptospirosis bacteria. Farmers also come in constant contact with cattle used for agriculture. Thus, the RMRC is currently carrying out research on soil bacteria that may have an inhibitory effect on the survival of *Leptospira*. Some of these inhibitory bacteria can also have a beneficial effect on farming as plant growth promoting factors.

Given RMRC's expertise on leptospirosis, it has also played an essential role in detecting and containing post-disaster outbreaks of leptospirosis. The first major instance was in the aftermath of the super-cyclone of 1999 in Odisha. Such epidemics have been detected subsequently post the Mumbai floods in 2000 and 2005, and in Kerala in 2001. Apart from identification of an outbreak, the Centre's efforts have also improved the preparedness of health systems to prevent such outbreaks. For instance, sensitive surveillance and effective public health preventive action by the Tamil Nadu Public Health Department thwarted a potential major

TOP TO BOTTOM: A girl being examined under community-based research initiative of RMRC, on the level of exposure to *Leptospira*; Community awareness programme on leptospirosis in an Anganwadi Centre in Andaman; Participants in a community awareness programme.

outbreak of leptospirosis in the aftermath of the Chennai floods in 2015.

The RMRC today employs a multi-layered strategy to effectively tackle the widespread problem of leptospirosis. The Centre's intervention ranges from local solutions crafted specifically for the Andamans, to national strategies, and international collaborations. For example, the RMRC, along with other international centres, is actively in search for an effective DNA vaccine. ICMR's efforts towards the establishment of one institution in Port Blair have contributed in establishing reference and diagnostic laboratories to address the challenge faced by half a billion people in the Southeast Asia region, including India. The people in this region are predominantly engaged in wet farming and are therefore continuously exposed to damp environmental conditions that pose the risk of leptospirosis.

UNVEILING THE MONKEY FEVER

India's Battle Against Kyasanur Forest Disease

NATIONAL INSTITUTE OF VIROLOGY, PUNE

ICMR's various institutes have played an instrumental role in correctly identifying and managing a range of diseases affecting the Indian population. One such disease is the Kyasanur Forest disease (KFD). Internationally, the KFD virus is ranked as one of the most high-risk categories of pathogens belonging to the Biosafety Level-4.

The KFD was first identified in the dense evergreen forests of Kyasanur, located in the Shimoga district of Karnataka. In April 1957, a team of field investigators from the National Institute of Virology (NIV), Pune – then known as the Virus Research Centre – were sent to Shimoga to check the cause of large-scale deaths of monkeys in the nearby forest. Closely following the death of the monkeys was the emergence of a mysterious disease in the neighbouring villages. Many villagers were falling ill with similar symptoms – the sudden onset of fever lasting about one to two weeks, headache, body ache, general weakness and sometimes diarrhoea, vomiting and pain in the abdomen. In 1957 itself, 500 individuals were affected by the disease, and 70 of them succumbed to it. It even earned a local name – monkey fever – given the close association of the strange disease with the death of monkeys.

Thanks to the scientists at the NIV, today we have a much better understanding of the disease – how it is transmitted, and through which animals. This understanding has played an important role in designing an effective prevention, control and treatment mechanism. First, the investigators

Since 1957, KFD has been prevalent in the Western Ghats. It is remarkable that under the aegis of ICMR, NIV, Pune carried out detailed ecological, entomological and virological studies, which unveiled the mysterious monkey fever and saved human life by developing a vaccine and diagnostic support.

DR DT MOURYA
Director, NIV, Pune

PREVIOUS PAGE: Collection of ticks/nymph using flag dragging method by NIV researcher in KFD-positive forest area.
LEFT TO RIGHT: Haemophysalis ticks distribution on leaves; Haemophysalis ticks waiting on apex of leaves for host to jump and attach to body; Ticks laying eggs in forest area.

ICMR, in association with the Department of Science and Technology, has established Asia's first Biosafety Level-4 laboratory at NIV.

started searching for the vector responsible for transmitting the disease from the monkeys to humans. Field investigators at the Shimoga forest initially suspected mosquitoes as the carrier of KFD virus. However, they could not find any trace of the virus in the mosquitoes inhabiting the area. Instead, the investigators noticed another potential vector – the dead monkey carcasses were generally infested by ticks. In fact, two of the investigators fell ill as they started gathering ticks from the dead monkeys. This helped determine the carrier organism.

Researchers at the Institute further went on to study the ticks. In order to locate their sources, the researchers attempted to retrace the path that the infected villagers took before they fell ill. Young girls were chosen as subjects of this investigation as they only ventured into the forest occasionally, and hence were able to retrace their steps back more accurately. Once the location was identified, the researchers sent the ticks to Pune for laboratory tests. This then finally illustrated a pattern. The tick, *Haemaphysalis spinigera*, tended to infest monkeys and bite humans as well. The larvae of the *Haemaphysalis spinigera* grew in number in September, once the monsoon season was over. During November and December it would grow to the adolescent stage, or what is called the nymph. At this stage the ticks would start feeding on multiple larger animals or hosts, until they matured to full-grown adult ticks in February–March. This explained why every year the KFD epidemic begins in October or November, peaks from January to May, and then declines by June and July.

Then, there was another important question –

if the monkeys were dying in such large numbers, how was the KFD virus being passed on from one generation of ticks to the next? In other words, where was the new generation of uninfected ticks getting the virus from? This meant that the ticks and the monkeys were picking up the virus from another source. The researchers then set up traps at various locations in the forest – such as in the forest undergrowth and hollow tree trunks – to catch smaller mammals that might be carrying the KFD virus. The researchers found that smaller mammal hosts, such as rodents, were keeping the virus alive between each season. Because the Shimoga area provided a fertile ecosystem – suitable climate, monkeys, small mammal hosts and ticks – the KFD virus was able to survive and infect humans.

By understanding the transmission cycle of the KFD, the local health and forest authorities now treat the forest floor with gamma-hexachlorocyclohexane or lindane. However, controlling the ticks is very difficult, given the huge population of ticks in the dense forest. In addition, the damage to the vegetative flora and the circulation of lindane in the food chain remains a challenge. To avoid tick bites, villagers are instead encouraged to use tick repellents like N, N-Diethyl-meta-toluamide and Dimethyl phthalate oil. Injection of Ivermectin

AT A GLANCE

Internationally, the KFD virus is ranked as one of the most high-risk categories of pathogens belonging to the Biosafety Level-4.

The KFD was first identified in April 1957 in the dense forest of Kyasanur, in Shimoga district of Karnataka, by a team of field investigators from the National Institute of Virology (NIV), Pune.

The tick, *Haemaphysalis spinigera*, infests monkeys and bites humans, causing KFD or monkey fever, as it was named locally.

To reduce ticks, the local health and forest authorities treat the forest floor with gamma-hexachlorocyclohexane or lindane; the villagers use tick repellents like N, N-Diethyl-meta-toluamide and Dimethyl phthalate oil; Ivermectin injection is given to cattle post-monsoon.

The ICMR has helped the state government to set up a Virus Diagnostic Laboratory in Shimoga. The KFD vaccine was manufactured here till 2001, then at the Institute of Animal Health and Veterinary Biological, Bengaluru.

In 1990, the Karnataka government initiated KFD vaccination campaign – two doses given to all persons aged 7–65 years, followed by a booster dose. Vaccine efficacy is low with 62.4 per cent for first two doses; which goes up to 82.9 per cent with booster dosage.

Since the discovery of KFD, nearly 400–500 cases have been reported annually. It has also spread in other states – Tamil Nadu, Kerala, West Bengal, Maharashtra and Goa.

Work on KFD was suspended until ICMR built a state-of-the-art facility Biosafety Level-3 laboratory, which became fully functional in 2006.

KFD vaccination drive in Shimoga, Karnataka in KFD-affected areas during year 1980s.

NIV has developed an inactivated chick embryo tissue culture vaccine – the first ever viral vaccine developed and produced entirely with Indian expertise.

to the cattle post-monsoon in the months of September–October is also promoted to reduce the tick burden on cattle stocks.

Apart from prevention, NIV has also developed an inactivated chick embryo tissue culture vaccine against KFD. This was the first ever viral vaccine developed and produced entirely with Indian expertise. The ICMR has helped the state government to set up a Virus Diagnostic Laboratory in Shimoga. The technology for the vaccine was then transferred to the laboratory, till 2001, when the responsibility was also given to the Institute of Animal Health and Veterinary Biological, Bengaluru.

Since 1990, the Karnataka government has

CLOCKWISE FROM TOP LEFT: KFD diagnosis training conducted by Dr Pragya D. Yadav, Scientist, NIV, Pune for staff of VDL, Shimoga, Karnataka; Researchers performing KFD virus propagation at maximum containment laboratory, NIV, Pune; Dr D.T. Mourya, KFD expert working in isolator in Bio-safety level 3 laboratory of NIV, Pune; Decontamination of vehicle by a researcher in appropriate personal protective equipment (powered air-purifying respirator).

initiated vaccination campaign in all endemic areas. Vaccination is usually carried out within a range of 5 km of the affected area. The schedule for vaccine is two doses at 0 and 1 month to all persons aged 7–65 years. This is followed by a booster dose at 6–9 months. Vaccine efficacy is low with 62.4 per cent for first two doses – however, with the booster dose efficacy goes up to 82.9 per cent. Hence, there is need for booster doses annually for 5 years. Since the discovery of the disease, nearly 400–500 human cases are reported annually. It has also spread widely along the Western Ghats – in Tamil Nadu, Kerala, West Bengal, Maharashtra and Goa – thus emerging as a grave public health problem in India. The ICMR has therefore made concerted efforts to ensure quick and accurate diagnosis of the disease.

Earlier laboratory tests for diagnosis of KFD were usually labour-intensive and time-consuming. This led to numerous infections among field investigators and laboratory personnel. Work on KFD was in fact suspended until ICMR built a state-of-the-art facility Biosafety Level-3 laboratory, which became fully functional in 2006. Today, ICMR, in association with the Department of Science and Technology, has established Asia's first Biosafety Level-4 (BSL-4) laboratory at NIV. This facilitated the development of the much needed, time-sensitive, cost-effective molecular and serological tests for the identification of the KFD virus. Diagnostic services provided by the Institute have helped in identification of KFD in five states of India. These diagnostic tests have now been transferred to Zydus Cadila and will be available in the market soon. This effort will not only go a long way in diagnosing patients but also understanding the prevalence of the disease in India and adjoining countries, if it exists.

DIAGNOSING PARAGONIMIASIS

Novel Interventions for Controlling Lung Fluke Infection

REGIONAL MEDICAL RESEARCH CENTRE, DIBRUGARH

Paragonimiasis is a food-borne disease caused by the parasitic lung fluke *Paragonimus*. It is usually contracted after the consumption of infected raw, pickled or undercooked crabs, crayfish and, in rare cases, frogs. These creatures are hosts to the parasite, which develops into its infective stage known as a metacercaria, thus causing the disease in crab-eating animals or man. Despite affecting individuals in several Asian countries, western and central Africa, and the Americas, paragonimiasis remains a relatively neglected disease with little public health awareness, especially in India. This, in turn, has left jarring gaps in both the understanding of the prevalence of the disease and medical knowledge regarding the infection.

For instance, initially paragonimiasis was often misdiagnosed as tuberculosis (TB) as both diseases exhibit similar clinical symptoms. Much like the case of TB, paragonimiasis-infected individuals suffer from chronic cough, coughing of blood-stained sputum, chest pain and laboured breathing. Thus, paragonimiasis patients were, in a majority of the cases, administered TB treatment, and they inevitably failed to respond to it. Apart from a significant over-estimation of the prevalence of multi-drug-resistant tuberculosis, the misdiagnosis had other far-reaching health implications.

This phenomenon – of misdiagnosing paragonimiasis as TB – was investigated through several surveys led by ICMR's Regional Medical Research Centre (RMRC) in Dibrugarh. Despite negative results in the sputum-based TB

RMRC's efforts helped in demystifying the misdiagnosis of pulmonary Paragonimiasis as TB and paved way for its correct diagnosis and effective treatment. This resulted in successful treatment of patients with lung fluke infection and improving their quality of life.

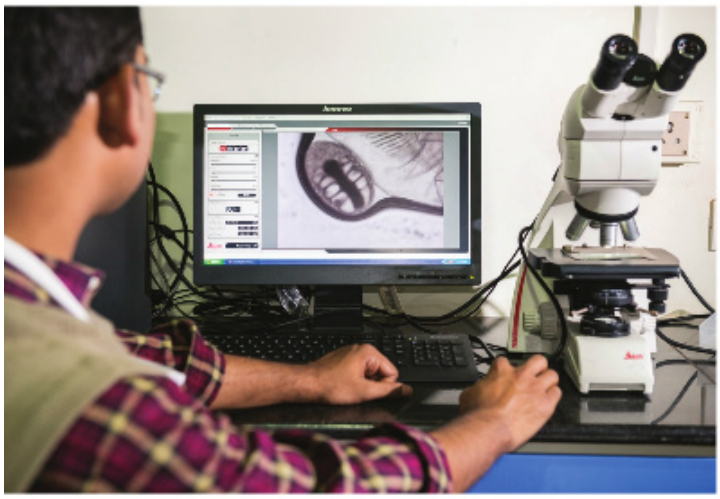
DR KANWAR NARAIN
Director, RMRC, Dibrugarh

People collecting freshwater crabs from hill streams for consumption. These crabs can harbour infective stages of lung flukes that can cause paragonimiasis if consumed raw, pickled, or undercooked.

755 of the 1007 crabs were carrying the infected parasite in Changlang, where 95 per cent of the population consumes them.

tests, individuals complaining of TB-like symptoms were often considered infected by TB by the local clinicians. This is because individuals with negative test results may develop bacteriologically positive disease at a later stage. The Centre's studies showed that in the states of Arunachal Pradesh and Assam there were multiple smear-negative patients who had been diagnosed with TB and treated under the DOTS programme. However, they did not respond to the treatment. This prompted the researchers at RMRC Dibrugarh to explore possible reasons for the treatment failure in such a large proportion of smear-negative TB suspected cases. Door-to-door interrogation and laboratory tests revealed that many of these individuals were, in fact, infected with lung flukes.

Examination of freshwater crabs in the laboratory of ICMR–RMRC, Dibrugarh for presence of metacercariae, i.e., infective stage of lung flukes.



AT A GLANCE

Paragonimiasis is a food-borne disease caused by the parasitic lung fluke *Paragonimus*. It is usually contracted by consuming raw, pickled or undercooked infected crabs, crayfish and, in rare cases, frogs.

These creatures are hosts to the paragonimus parasite, which develops into its infective stage known as a metacercaria, thus causing the disease in persons who consume these crabs.

Initially paragonimiasis was often misdiagnosed as tuberculosis (TB) as both diseases exhibit similar clinical symptoms. This misdiagnosing was investigated by ICMR's Regional Medical Research Centre (RMRC) in Dibrugarh. Door-to-door interrogation and laboratory tests revealed lung fluke infection.

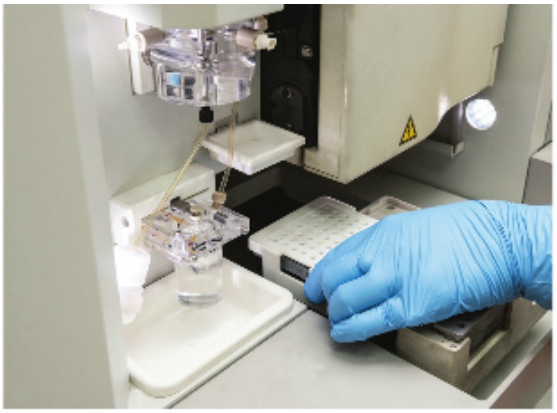
The disease was assumed to occur only in the state of Manipur, however, an in-depth investigation conducted by RMRC Dibrugarh revealed that the infection was prevalent in the northeast region of India, and cases had been detected in Arunachal Pradesh, Assam and Nagaland.

A community-based study to explore the potential prevalence of paragonimiasis in Changlang, Arunachal Pradesh, in 2002 found 95 per cent local residents consumed crabs and crayfish, either roasted, partially cooked, or raw.

Post the study in Changlang, the Centre collected sputum samples from 675 inhabitants and 72 cases of paragonimiasis emerged.

RMRC Dibrugarh also carries out targeted awareness and treatment interventions in endemic regions. It conducted a survey in the Changlang in 2011 that demonstrated a decline in the prevalence of paragonimiasis following treatment and community education.

Scientists at RMRC Dibrugarh, developed an enhanced diagnostic ELISA test kit to detect human paragonimiasis.



Team members from ICMR–RMRC, Dibrugarh involved in the study of lung fluke infection in the northeastern states of India
FACING PAGE LEFT: Highly sensitive and specific ELISA kit (below) developed by RMRC–ICMR, Dibrugarh, scientists; RIGHT: DNA sequencing for confirmation of lung fluke species (top two);Technician carrying out ELISA to detect paragonimiasis (bottom two).

The research centre's studies highlighted the need for a more effective diagnostic tool for paragonimiasis. At the time, sputum examination was the most effective method available for detection of paragonimiasis. However, this method was not very useful as the identification of lung fluke eggs in human sputum is less sensitive. This meant that many cases of paragonimiasis would go undetected or misdiagnosed as TB. Responding to this need, scientists at the RMRC Dibrugarh developed an enhanced diagnostic kit to detect human paragonimiasis. Instead of looking for eggs in the sputum, the new system focussed on identifying antibodies to *Paragonimus* in the human blood. This made it a much more sensitive and specific diagnostic kit. The indigenously-developed ELISA test kit was found to be highly useful in detecting both pulmonary and extra pulmonary forms of human paragonimiasis. This was described as a game changer as no such kits were available commercially. Given that pulmonary paragonimiasis and tuberculosis are overlapping public health issues in the northeast region of India, this kit is expected to address the issue of misdiagnosis to a considerable extent – especially among smear-negative TB suspects.

Another fundamental intervention by RMRC Dibrugarh relates to the prevalence of paragonimiasis. For a very long time, the disease was known to occur only in the state of Manipur, caused by a particular species called *Paragonimus westermani*. Human paragonimiasis in Manipur was first detected in 1982, following which several additional cases were diagnosed. However, an in-depth investigative research programme conducted by RMRC Dibrugarh revealed that the lung fluke

infection was in fact not as limited in distribution as it was earlier assumed. The researchers found that paragonimiasis had emerged as a much larger concern primarily in the northeast region of the country, and several cases had been detected in other states as well, such as Arunachal Pradesh, Assam and Nagaland.

Scientists at RMRC Dibrugarh during surveys in Arunachal Pradesh noticed a common practice among the local communities – crabs were often eaten raw or partially cooked. This prompted the launch of a definitive community-based study to explore the potential prevalence of paragonimiasis in the remote and hilly Changlang district of Arunachal Pradesh in 2007. The study found that 95 per cent of the local residents regularly consumed crabs and crayfish, which were either roasted and partially cooked, or eaten raw. Given this food habit, the Centre went on to investigate the actual prevalence of the disease among the inhabitants of the area. Sputum samples were collected from 675 inhabitants – out

of these, 72 cases of paragonimiasis emerged. The Centre further carried out an examination of the crabs found in the nearby water streams – 755 of the 1007 crabs collected were carrying the parasite in its infective stage or metacercaria.

To better understand the particular type of *Paragonimus* affecting the area, metacercariae collected from the infected crabs were also studied. The metacercariae were developed into adult lung flukes in laboratory rats, and it was identified as *Paragonimus heterotremus*, thus demonstrating not only the occurrence of paragonimiasis beyond Manipur, but also the occurrence of an additional species of the parasite in India. This played a crucial role in formulating an informed strategy to tackle paragonimiasis in the country.

RMRC Dibrugarh also carries out targeted awareness and treatment interventions in endemic regions. For instance, it conducted a survey in the Changlang district in 2011 that demonstrated a decline in the prevalence of paragonimiasis following treatment and community education in a hyper-endemic area. The result of this study highlights the success of the hotspot targeted – active case detection and treatment method – or what is popularly called the 'test & treat' strategy. It gives reason for cautious optimism that proactive case detection and paragonimiasis treatment, along with community education, can significantly reduce the food-borne disease in highly endemic and difficult-to-access areas. This could then ultimately contribute to complete elimination of paragonimiasis from the endemic zones of the country.

Credits

ICMR Team
Dr Soumya Swaminathan, Secretary DHR and Director General, ICMR – Overall Guidance and Supervision
Dr Sanjay Mehendale, Additional Director General, ICMR – Technical Guidance
Dr Rajni Kant, Scientist F and Head, RMPPC – Project Coordinator
Dr Enna Dogra Gupta, Scientist B – Technical Support
Dr Joyita Chowdhury, Consultant – Technical Support
Ms Rina Sinha, Consultant – Technical Support

Front Cover, Pages 2-5
Photographs: Anushree Bhatter

Back Cover & Introduction
Photographs: Anshika Varma, Anurag Banerjee, Anushree Bhatter, Karam Puri

NIRRH, Mumbai
Photographs: Anurag Banerjee
Contributing authors:
Dr Smita D. Mahale, Director and Scientist G
Dr Priyanka P. Parte, Scientist D
Dr Ikram M. Khatkhatay, Scientist F
Ms Priya Menon, Technical Officer

ERC, Mumbai
Photographs: Anurag Banerjee, Alamy
Contributing authors:
Dr Smita D. Mahale, Director and Scientist G
Dr Vinay K. Saxena, Scientist E

NIRT, Chennai
Photographs: Anshika Varma
Contributing authors:
Dr Srikanth Tripathy, Scientist G
Dr Mohan Natarajan, Scientist F
Dr Geetha Ramachandran, Scientist E
Dr Beena Thomas, Scientist E
Dr Luke Hanna Elizabeth, Scientist D
Dr Muniyandi M, Scientist C
Dr Uma Devi, Scientist D
Dr Rathinasabapati R., Senior Librarian and Information Officer

NICED, Kolkata
Photographs: Anushree Bhatter
Contributing authors:
Dr Phalguni Dutta, Former Emeritus Medical Scientist (ICMR) and Scientist G
Dr Shanta Dutta, Director and Scientist G

NIN, Hyderabad
Photographs: Courtesy NIN, Alamy
Contributing authors:
NIN-ICMR & DWCD, Government of Telangana Activity

NIMR, New Delhi
Photographs: Courtesy NIMR
Contributing authors:
Dr Neena Valecha, Director and Scientist G
Dr R.C. Dhiman, Scientist G
Dr S.K. Ghosh, Scientist G
Dr Anup R. Anvikar, Scientist F

VCRC, Puducherry
Photographs: Courtesy VCRC
Contributing authors:
Dr P. Jambulingam, Director and Scientist G
Dr S. Sabesan, Sr Consultant and Scientist G (Retd)

RMRIMS, Patna
Photographs: Anshika Varma
Contributing authors:
Dr Pradeep Das, Director and Scientist G
Dr Vidya Nand Rabi Das, Scientist F
Dr Krishna Pandey, Scientist F
Dr Vijay Kumar, Scientist E
Mr Rakesh Bihari Verma, Scientist B

RMRC (NER), Dibrugarh
Photographs: Anushree Bhatter
Contributing authors:
Dr Siraj Ahmed Khan, Scientist E
Dr Prafulla Dutta, Scientist G

NIE, Chennai
Photographs: Courtesy NIE
Contributing authors:
Dr C.P. Girish Kumar, Scientist E
Dr Manoj Murhekar, Director in-Charge and Scientist G
Dr Sanjay Mehendale, Additional Director General, ICMR, New Delhi

NIOH, Ahmedabad
Photographs: Karam Puri
Contributing authors: All scientists of NIOH & ROHC (E), Kolkata and ROHC (S), Bengaluru
Compilation and editing:
Dr Sunil Kumar, Director in-Charge and Scientist G
Dr Rekha Kashyap, Scientist F
Mr P.B. Doctor, Scientist E
Mr J. Majumder, Scientist C
Ms Shruti Patel, Tech. C
Mr P.M. Chacko, Private Secretary

NIIH, Mumbai
Photographs: Anurag Banerjee
Contributing authors:
Dr Ajit Gorakshakar, Scientist F
Harita Gogri, Senior Research Fellow
Ajay Donta, Senior Research Fellow

NIRTH, Jabalpur
Photographs: Courtesy NIRTH
Contributing authors:
Dr Tapas Chakma, Scientist G
Dr Neeru Singh, Former Director and Scientist G

RMRC, Port Blair
Photographs: Anshika Varma
Contributing authors:
Dr A.P. Sugunan, Scientist F
Dr P. Vijayachari, Director and Scientist G

NIV, Pune
Photographs: Courtesy NIV Pune
Contributing authors:
Dr D.T. Mourya, Director and Scientist G
Dr Pragya D. Yadav, Scientist E

RMRC, Dibrugarh
Photographs: Anushree Bhatter
Contributing authors:
Dr Kangjam Rekha Devi, Scientist E
Dr Kanwar Narain, Director




India became polio-free in 2011; it's first-ever scientifically documented test tube baby was born in August 1986; it became the first country in Asia to launch an indigenous rotavirus vaccine in the Universal Immunization Programme to curb diarrhoea in 2016 – all these, and many more outstanding achievements and innovative solutions to various ailments can be attributed to the Indian Council of Medical Research (ICMR).

One of the world's oldest medical research establishments, ICMR has been leading research and innovations in the field of medicine. Aligning its research goals and focus areas with national health priorities, it aims to provide unique solutions to medical issues especially designed to suit the local populations across India. This book brings together some of ICMR's landmark contributions in ensuring health for all.

With a dedicated team of scientists and pan-Indian institutional network, ICMR has been addressing wide-ranging medical issues such as nutrition, maternal and child health, infectious diseases, occupational health, and non-communicable diseases. This volume highlights the achievements and contributions of 15 institutes of the ICMR that have been working diligently to prevent, control and cure various diseases.

ISBN: 978-93-5194-198-9
9 789351 941989
SHOWCASE
Roli Books
www.rolibooks.com