

SAMAVEDHAM SRINIVASA SRIRAMACHARI

(25 June 1925 - 25 December 2009)

Biog. Mem. Fell. INSA, New Delhi 38 91-101 (2010)





S. Sri Ramakrishna



SAMAVEDHAM SRINIVASA SRIRAMACHARI

(1925-2009)

Elected Fellow 1975

EDUCATION AND FAMILY

SAMAVEDHAM SRINIVASA SRIRAMACHARI was born on the 25th June 1925 into a scholarly Tamil family settled in Andhra Pradesh. His father was SS Applachariar. His early education was in St Joseph's Convent, Visakapatnam and Maharaja's College, Vizianagaram. He took his BSc degree specialising in Chemistry with Mathematics and Physics in 1943. He took his MBBS degree in 1948 and MD (Pathology and Bacteriology) in 1955 both from Andhra University. He subsequently obtained his DSc in Pathology from the same University in 1961. He was abroad on TCM Fellowship during 1954 specialising in Neuropathology and on WHO Fellowship in 1962 specialising in scientific microscopy and medical education Technology. He was awarded honorary doctorates by Sri Venkateswara University in 1975 and Andhra University in 1978.

Professor Chari has one daughter and two sons. His daughter Sandhyamani followed her father's footsteps to become a pathologist. His sons Murali and Krishna are doctors. His wife Pushpa had died a decade ago due to drug reaction and is remembered by a memorial lecture instituted by Chari.

PROFESSIONAL CAREER

Professor Chari joined as House Surgeon in King George Hospital, Visakapatnam in February 1949. He became Lady Tata Memorial Research Scholar, Andhra Medical College, Visakapatnam in July 1950. He worked as Assistant Research Officer in ICMR Research Laboratory, Coonoor between December 1951 and May 1954. Professor Chari's mother tongue is Tamil. It is only during this short spell in his career he served in Tamil Nadu. He proceeded to the US on TCM Fellowship in 1954. He joined as Associate Professor in Neuropathology, All India Institute of Mental Health, Bangalore in 1959. He acted as Director of this Institute between June 1961 and July 1962. Four months during this period, he visited USA, Great Britain, Hungary and Switzerland as a WHO fellow. He worked as Deputy Director (Technical) ICMR between 1962 and 1965. He served as Director, ICMR from 1965 till his retirement in 1987. He was an honorary Professor of Neuropathology at the All India Institute of Medical Sciences, New Delhi during 1966-67. After retirement, he



was INSA Senior Scientist between 1989 and 1992. He was an Honorary Scientist during 1999 and 2002.

MAJOR ACHIEVEMENTS

Dr Sriramachari made significant contribution to pathology and toxicology of Bhopal Gas Tragedy. In collaboration with his colleagues of the Medico Legal Institute, and Institute of Pathology, detailed histopathological studies were carried out under Light and E&M, on around 150 human autopsies. They encompass acute phase of severe Pulmonary Edema and Emphysema, often accompanied by Cerebral Edema and Hemorrhages. Subsequent autopsies showed sub acute phase of Bronchiolitis and Pneumonia followed by chronic phase of interstitial Pneumonitis and pulmonary Fibrosis. In one of his investigations, the entire spectrum of lesions was reproduced experimentally in laboratory animals exposed to single sub lethal doses of MIC and its aqueous derivatives. He has guided six PhDs, has over 140 original papers in National and International Journals in specialised branches of Clinical and experimental Pathology related to Nutrition, Liver diseases, especially Kwashiorkor and Indian Childhood Cirrhosis, Osteopathology, Neuropathology, low cost medical Educational Technology, Human Environmental Bio monitoring of Inorganic and Organic pollutants in human placenta. Dr Chari developed the Institute of Pathology from a two room accomodation (when he took over as Chief) in 1965 to a six floor Institute (IOP) which conducts research in cancer, leishmania, chlamydia, and placement models for pollutant monitoring in about 20 years time.

Dr Sriramachari made equally far-reaching contributions on toxicology of MIC exposure. He postulated two major hypotheses: The first is based on estimation of urinary thiocyanate levels, before and after sodium thiosulphate therapy. The vexed issue of toxic cyanide toxicity was upheld by providing a scientific basis for successful therapeutic intervention through several thousands of SCN estimation, apart from the independent proof of raised levels of blood cyanide. The second series of contributions relate to histotoxic anoxia. A marked reduction of end terminal amino groups by TNBS technique was traced to N-carbamylation of Valine residue of Hb by MIC, leading to blood gas disturbances, temporary elevations of 2-3 DPG levels, as in high altitude Pulmonary oedema.

In short, Dr Sriramachari made significant contributions towards a proper multi-disciplinary understanding of the health effects of the greatest chemical disaster of the world.

RESEARCH CONTRIBUTIONS

Sriramachari's contribution covers a wide spectrum of fields. (i) nutritional pathology, (ii) histochemistry, (iii) osteopathology, (iv) medical educational



technology, (v) hypoxic pathology, (vi) neuropathology, (vii) pathological and toxicological aspects of Bhopal gas disaster, (viii) tissue trace elemental analysis. He has published over 140 original papers.

(a) Nutritional Pathology

Sriramachari started as a Lady Tata Research Scholar under Professor Ananthachari. He was among the earliest workers to carry out liver biopsy studies in India in 1950-51. He studied the pattern of biochemical and histopathological changes in adult suffering from malnutrition in comparison with those with cirrhosis.

Working in the Nutrition Research Laboratory, Coonoor as Assistant Research Officer, he published a series of papers on a wide range/variety of pathology of nutritional disorders. The papers on pathology of Kwashiorkor are among the first reports from India. It was here that some of the best work on Kwashiorkor and protein was undertaken by Ramalingaswami, Gopalan and Chari. With the corresponding experimental studies in animals subjected to protein or combined caloric deficiency, he differentiated a fatty liver from a merasmic liver. This work is considered to be of importance even today in understanding protein energy malnutrition. He and his associates made a very important observation, based on an eight year follow up study, that none of the cases of kwashiorkor ended up with hepatic fibrosis non progressed to cirrhosis.

Professor Chari carried out an extensive study of different types of fatty livers caused by protein and lipotrope deficiency and obtained histopathological evidence for distinct periportal or centrilobular changes in the liver in the same animal species viz. rat. He clarified the pathogenesis of fatty livers of kwashiorkor. Besides he participated in some crucial experiments of Late Patwardhan and Late Phansalkar, both experimental and clinical (as a human volunteer), in their pioneering studies on the beneficial effects of diet based on mixtures of vegetable proteins.

Professor Chari investigated the long term sequel of protein deficiency fatty livers. He found under the influence of continuing protein deficiency, even after hepatic fibrosis or cirrhosis developed, the same effects are not sustained. Through a well planned series of toxic liver injuries induced by carbon tetrachloride, he established the theory of reversibility of experimental cirrhosis, both dietary and CCl₄ induced toxic origin, under the overall influence of concurrent protein deficiency. Thereby he was able to explain certain anomalous clinical situations as to why children with kwashiorkor never progress to cirrhosis, unlike the well fed children with Indian childhood cirrhosis. This broad area of his DSc thesis received recognition by people like Roy Cameron and VR Khanolkar.



(b) *Other Nutritional Disorders*

In addition to liver, other organs such as aorta and the cardiovascular system and the endocrines, are severely affected in experimental protein deficiency. Some of the important findings were confirmed from time to time, including the more recently described condition of clinical or experimental model of mucoid vasculopathy, in Kerala, by his daughter Sandhyamani. The studies on nutritional pathology of Vitamin A deficiency in the early fifties in which he was associated with Professor Ramalingaswami and Dr Leach of Oxford University, provided the first evidence of an anatomical basis for the retinal involvement in Vitamin A deficiency in young monkeys. Subsequently, along with Professor Ganguly and Dr Juneja, he studied the differential effects of the alcohol, aldehyde and acid forms of Vitamin A on the male and female gonads of the rat. While retinol had all round protective effect, retinoic acid, resulted in gonadal damage.

(c) *Histochemistry*

As a Lady Tata Research Scholar, Sriramachari working with carbowaxes was perhaps the first medical scientist to exploit the principles of histochemistry. Subsequently, he used several other enzyme histochemical techniques and tetracycline labelling in problems of osteopathology such as mode of action of Vitamin D in new bone formation, neuromuscular disorders and experimental brain oedema.

(d) *Osteopathology*

Professor Chari contributed to an exhaustive histochemical study on the mode of action of Vitamin D and the sequences of mineralisation of the rachitic epiphyseal cartilage under the influence of Vitamin D and starvation. The early demonstration of non calcific phase as a result of glycogenolysis of chondrocytes, immediately followed by the calcific phase is of basic significance. In recent years, Professor Chari was involved in a new approach towards the crystalloid colloid interaction of fluoride ion and its implications in the epidemiology of the disease confined only to certain vulnerable segments of the community, while sparing others on more wholesome dietaries. The results of a promising study of the physical chemistry of such interactions with tea and tamarind were presented at the Indian Science Congress (1983) in Tirupati.

(e) *Hepatic Pathology*

Apart from nutritional disorders Professor Chari was engaged in the study of two other major diseases. One of them refers to life-time pursuit of ICC, in collaboration with the Madras group represented by Late STAchar and his associate Late Dr V Balagopala Raju and Dr N Sundaravalli. It resulted in an exhaustive cross sectional and long term clinic



pathological follow up study of a disease entity unique to India. Ever since 1961, studies based on serial liver biopsies focussed attention on the changing dynamic pathology, particularly under the influence of prolonged steroid therapy. It was repeatedly demonstrated that, contrary to the general belief that the disease was invariably fatal, several cases had indeed recovered and returned to normalcy. It is a matter of satisfaction that generally other centres were also veering around to the view advocated by the Madras group, in spite of initial controversy. The actual cause of this unique disease is still a mystery. The current theory of exogenous dietary copper toxicity suggested by the Pune group, attributed the condition to the alleged use of copper yielding vessels in the preparation of infant foods. However such a view was not substantiated by ICMR multicentric study on ICC carried out during 1984-87. Professor Chari reexamined this problem from the point of view of trace element profile of hepatic tissue in cases of ICC and allied liver disorders. This work was undertaken with the help of Dr Jagjeet Kaur and Dr AK Jain of the IOP and Dr Gangadharan and his colleagues in the analytical division of BARC. Multivariate discriminant analysis revealed distinct patterns and there were varying degrees of increase, not only in hepatic copper but also in zinc, in ICC as well as in other liver disorders in childhood. These changes appeared to be the consequence of underlying liver damage and mediated by hepatic metallothionein under the influence of hitherto unrecognised home remedies, containing potential hepatotoxic agents. The problem was further clarified by developing a suitable rat experimental model. The preliminary results were encouraging.

Professor Chari also undertook a study of pathology of non cirrhotic portal fibrosis wherein he observed that as opposed to the generally held view of 'obliterative' or 'occlusive', changes in the portal veins at all stages of disease is actually a dilatation. Under the auspices Prof Chari published an illustrated atlas of 'histopathology of the liver' with particular reference to hepatitis, cirrhosis and ICC.

(f) Medical Educational Technology

Professor Chari was instrumental in the Institute of Pathology undertaking the task of mass production and distribution of low cost teaching aids in the field of pathology comprising sets of 35mm colour and black and white transparencies of pathological specimens. The background involved innovation in a variety of subjects like microscopic and photographic objects, photochemistry and processing of colour films. This unique facility, which continues to enjoy good reputation for over 25 years, is a significant national contribution. In the process seven patents were taken in the name of the Indian Council of Medical Research.

NEUROPATHOLOGY

Professor Chari has made notable contribution in the study of brain tumours by conventional method and applications of hitherto unrecognised topographical

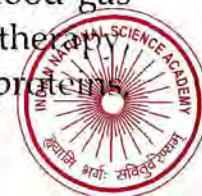


properties of biofilaments of certain brain tumours, such as collagen fibres by demonstrating birefringence and dichroism of native glial filaments. Professor Chari and his group, from the studies on experimental neurolethargy, demonstrated for the first time the direct damage of the anterior horn cells in the spinal cord of monkeys subjected to intrathecal administration of the active principle of *Lathyrus sativus* seeds. This work has a great bearing on the understanding of neurological evidence of potentially hazardous foodstuff. In central Indian cities like Nagpur, there was a potential problem of sudden illness and death of children in summer months. This was attributed to a variety of reasons, notably virus infection. However, Chari and Paatoria studied the brains of 15 children who had died and showed that there was no viral infection. It was a manifestation of acute deaths due to heat hyperpyrexia in unprotected urban children.

With increasing vehicular accidents, the pathogenesis, sequelae and reversibility of global or widespread cerebral oedema assume great importance. In spite of therapeutic advances, the underlying mechanisms are poorly understood. Much of confusion in the available literature is due to inappropriate experimental model for the study of experimental cerebral oedema, employing the mouse or rat or unnatural methods such as localised cold injury. In association with Professors Pathak and Bilani, an extensive study was carried out employing more than 370 monkeys. The study has brought to light that oedema is essentially of a watery or saline nature and results in complete reversibility of the lesions if treated promptly by procedures such as release of compression, hyperosmotic agents or corticosteroids.

STUDIES OF BHOPAL GAS LEAK DISASTER AND OTHER DISASTERS

Professor Chari would be best remembered for his research on the infamous Bhopal Gas Tragedy. He participated as an observer in conducting of autopsies of bodies washed offshore near Cork where the Air India plane crashed in 1985. He had the opportunity to study a wide range of gross pathological changes due to sudden decompression following exposure at various altitudes and the peculiar type of impact injuries due to crash landing of the bodies on the surface of the ocean. He was also involved in the scientific investigation relating to Bhopal gas leak disaster as one of the representatives of ICMR. He participated in several projects relating to immediate autopsy studies as well as toxicological investigations with a bearing on subsequent health of survivors. Most of the work was carried out in collaboration with Heeresh Chandra, Director, Medico Legal Institute, Bhopal. With the help of Dr Saxena, the spectrum of early and late histopathological changes including pulmonary fibrosis was delineated. Within weeks of the disaster, a number of studies on clinical and forensic toxicology were mounted. Some of the problems were successfully tackled. The issues such as chronic cyanide toxicology, blood gas analysis, pulmonary function tests, DPG estimations, sodium thiosulphate therapy, urinary thiocyanate estimation, carbamoylation of haemoglobin and tissue proteins



comparative chemical analysis of autopsy tissue and tank residue were satisfactorily resolved. Experimental studies were undertaken at DRDO Gwalior to determine the extent of chronic toxicity due to MIC, and its derivatives like methylamine.

AWARDS AND HONOURS

Professor Chari was elected Fellow of Indian National Science Academy in 1975. He was Vice President of INSA during 1983-84. He was elected Fellow of the Indian Academy of Sciences in 1967. He became Member, Neurological Society of India in 1959 and its President in 1969. He was elected Fellow of the National Academy of Medical Sciences in 1962. He was elected Fellow of the Andhra Pradesh Academy of Medical Sciences in 1976. He has taken seven patents along with his colleagues.

Professor Chari was awarded Shakuntala and Basanti Devi Amirchand Prize of ICMR in 1975, RV Rajam Oration Prize (National Academy of Sciences) in 1978. He was the recipient of JC Bose Award in Life Sciences of UGC in 1979 and BC Roy Award in Neuropathology of MCI in 1979. He received INSA BN Chopra Memorial Award 1983 and INSA SK Mitra Memorial Award in 1998. He was awarded *Padma Shri* by the Government of India in 1985.

AS A PERSON

Professor Chari was soft spoken, unassuming and simple. He was present in all the scientific meetings organised by INSA in New Delhi even after his retirement from active service. The author had the opportunity to meet him and talk to him on several occasions. He was committed to his profession. He was well versed in Sanskrit. His loyalty and commitment to ICMR was legendary. *Patrika* of Indian Academy of Science, March 2010 reports "When the world and the country were making ceremonial tributes for the 25th Anniversary of the Bhopal Gas Tragedy, Chari spent the terminal period of his life driving himself to complete the ICMR report. Worried about Chari's health but nevertheless wishing to pay homage to the victims of the gas tragedy, ICMR and Vijayan, the Director of VP Chest Institute who was also his treating physician held a special function on the premises of the hospital in Delhi on 3rd December 2009. It seemed as if Chari had willed himself to live for that day and he gave a memorable lecture sitting in a wheel chair connected to oxygen supply and surrounded by anxious physicians. He deteriorated physically thereafter but his mind was razor sharp and he out-argued his younger colleagues in the intensive care ward" Professor Chari breathed his last on 25th December 2009.

V RAMAMURTI, FNA
Old No. 2, New No. 5
Fourth Main Road, Kasturbanagar
Chennai-600020 (TN)

Tel: 044-24412500
E-mail: ramamurti@hotmail.com



BIBLIOGRAPHY

- 1952 (With RAMALINGASWAMI V) Liver change in Kwashiorkor *Ind J Paedia* **20**: 1-6
- (With RAMALINGASWAMI V) Polyethylene glycols as embedding media in histochemical work *J Clin Path* **5**: 346-349
- (With RAMALINGASWAMI V) Liver changes in Kwashiorkor *Ind J Paediat* **20**: 1-6
- 1953 (With PATWARDHAN MV *et al.*) Nutritional factors in toxic liver injury, Part I *Ind J Medical Sci* **7**: 533-544
- 1954 (With ANANTHACHARI MD) Malnutrition and cirrhosis study of hepatic structure and function *Ind J Med Sci* **8**: 31
- (With PATWARDHAN MV *et al.*) Nutritional factors in toxic liver injury, *Ind J Med Sci* **8**: 31-44
- (With ANANTHACHARI MD) Malnutrition and Cirrhosis study of hepatic structure and function *Ind J Med Sci* **8**: 31
- (With RAMALINGASWAMI V and PATWARDHAN VN) Liver injury in protein malnutrition *Ind J Med Sci*, **8**: 433-441
- 1955 (With RAMALINGASWAMI V and LEACH EH) Ocular structure in the monkey *Qua J Expt Phy* **40**: 337-347
- 1956 (With PIRANI CL and HAYMAKER W) The effect of traumatic injury on the brain of Vitamin C deficient guinea pigs *Am J Path*, **32**: 131
- (With GOVINDA REDDY D) Histological changes in cirrhosis of the liver *Ind J Med Sci* **10**: 944-950
- 1957 (With GOPALAN C) Aortic changes in induced malnutrition *Ind J Med Res* **11**: 405-409
- 1958 (With SRIKANTIA SG and GOPALAN C) A follow up study of fifteen cases of Kwashiorkor *Ind J Med Res* **46**: 121-128
- (With SRIKANTIA SG and GOPALAN C) A follow up study of fifteen cases Kwashiorkor *Ind J Med Res* **11**: 405-409
- Nutritional factors in the pathogenesis of hepatic cirrhosis Part I *Ind J Path Bact* **1**: 27-34
- Nutritional factors in the pathogenesis of hepatic cirrhosis, Part II **1**: 35-44
- (With DIKSHIT PK and PATWARDHAN VN) Histochemical study of healing of rachitic epiphyseal cartilage of the rat *Ind J Path Bact* **1**: 105-113
- 1959 (With PATWARDHAN VN) Experimental production of periportal fatty livers in rats, *Ind J Path Bact* **2**: 166-175
- 1960 (With ACHAR ST and RAJU VB) Indian childhood cirrhosis *J Piedia* **57**: 7440-7458
- 1962 Review of experimental dietary cirrhosis *Ind J Med Res* **50**: 950-951
- 1971 (With MANI KS *et al.*) Experimental neurofathyrisim in monkeys, *Ind J Med Res*: **59**: 880-885
- 1976 (With PATORIA NK) Pathology of acute encephalopathy, syndrome in children in summer *Ind J Med Res* **64**: 296-313
- 1980 (With RAJU VB and SUNDARAVALLI N) Indian childhood cirrhosis some observations pathology and etiology *Ind J Paedia* **47**: 543-547



- 1981 (With BALANI DK and PATHAK SN) Pathology and pathogenesis of experimental extradural cerebral compression *Ind J Med Res* **74**: 438-461
- (With BALANI K and PATHAK SN) Reversibility or prevention of brain oedema *Ind J Med Res* **74**: 462-478
- 1986 Health effects of Bhopal Gas Tragedy, Indian Council of Medical Research, April, Editor
- 1990 (With SHARMA VK *et al.*) High performance liquid chromatographic estimation of carbamoylated amino acids *Curr Sci* **59**: 528-529
- 1991 (With RAO GH *et al.*) MS analysis of preserved tissue of Bhopal gas disaster: evidence of methyl carbamylation in post-mortem blood *Med Sc Law* **31(4)**: 289-293
- (With RAO GJ *et al.*) Bhopal gas disaster: Unidentified compounds in the residue of the MIC tank 610 *J Ind Acad Sci* 13-19
- 1993 Observations related to health effects of Bhopal toxic gas leak, IPCS/WHO International Toxicovigilance Conf Proc, Cardiff
- 1994 (With JEEVARATNAM K) Acute histopathological changes induced by methyl isocyanate in lungs, liver, kidneys and spleen of rats, *Ind J Med Res* **99**: 231-235
- 2004 The Bhopal Gas Tragedy: An environmental disorder *Curr Sci* **86**: 905-920
- 2005 Bhopal Gas Tragedy: Scientific challenges and lessons for future *J Loss Prevention in Process Industries* **18**: 264-267

