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Introduction:

I was born in Jallandhar, Punjab in April 1949, two years after my parents migrated from Pakistan during partition of India. My parents had settled in Jallandhar after leaving fully furnished houses in Sialkot, Pakistan. They were looking after four younger brothers and one sister and were almost living hand to mouth. I stayed in various cities of Punjab till 1958, when my father was transferred to Chandigarh. The Chandigarh of late 1950s was all jungle with bushes all around. The monuments like central secretariat and Assembly Hall was only partially built. I remember having played on the partially constructed 6th floor of central secretariat. A large number of senior bureaucrats and officials were going to the offices on cycles. There were hardly any cars. All the trees around various roads which are in full bloom now and give a characteristic green appearance to Chandigarh, were being planted at that time. I started my schooling from 5th class onwards from D.A.V Higher Secondary School, Sector 8, Chandigarh. It was an interesting phase, as I had to study Hindi and English, where as in my formative years I had studied in only Punjabi. I picked up fast and was always amongst first 2 or 3 boys in the class. I was fourth in the Punjab University in 10th and second among the Medical batch in the 12th Class. At that time Punjab University was the only university for Punjab, Haryana and Himachal combined.



Schooling under Punjab University with merit

Graduation and Post-Graduation:

I was first in the family to join a medical course, in 1966 at Medical College Rohtak (Punjab, now in Haryana). The experience in Rohtak was really great, which culminated in M.B.B.S degree in 1971. The post-graduation was again in an institute where everyone dreams to be there, that is, Post Graduate Institute of Medical Education & Research Chandigarh. The PG course at that time, in PGI was of four years i.e. one year house job and three years of M.D / M.S. I chose M.D Medicine just because I thought at that time, that a person with M.D can start his practice anywhere without needing an operation theatre or hospital.

We know that time flies, but it flies so fast that events that happened 50 years ago appear to have happened in the recent past. Using a retrospectroscope, I vividly remember the day of my entry to Postgraduate Institute of Medical Education And Research Chandigarh on 1st of January 1972. It was a dream fulfilled. I had a chance to see in person the doyens of Medicine, Surgery and basic Sciences (Dr. P.N Chhuttani, P.L Wahi, Dr. J.N Beri, Dr. Santokh Singh, Dr. Aikat), and learned the advances in various specialties. Two Clinico Pathological Conferences (CPCs), two clinical meetings and a mortality meeting, every week, were the hallmark of the PGI teaching program, which would start exactly at 8AM. The Director and the Dean would attend the meeting every day along with all junior and senior faculty members.

Introduction to Neurology:

My introduction to Neurology started in 1973, when I was given my MD Medicine Thesis entitled “Studies on Blood Coagulation and Fibrinolysis in Young Hemiplegics”, with Dr J.S. Chopra. The 1975 Annual Conference of Neurological Society of India at Chandigarh, was a booster dose. The young Neurologists of that time discussed clinical neurology and clinical signs. Electrophysiology was in its infancy. Everyone was afraid of Dr Chopra. Two PG students, before me could not complete the thesis with him. I was forewarned. I, somehow stuck to the thesis. There were no computers at that time. Dr Chopra would make innumerable corrections and the whole material had to be typed again and again. I typed my thesis seven times.



NSI 1988 Group Photo

I joined DM Neurology course of PGI Chandigarh in 1976, being the first regular student to join the course after two army sponsored stalwarts Brig. BR Kumar and Brig. PVS Rana. Dr Wahi, the then Dean of PGI and Head of Internal Medicine, did not allow me to join Neurology after my MD (Medicine). He wanted me to do Senior Residency in Medicine before starting DM Neurology. He thought there was no scope for Neurology and by doing Senior residency in Medicine, I will be better prepared as a physician. There were no stroke registries or epidemiological studies. All research was on hospital based data. There were no MRI's or CT Scans. Interventional radiology did not exist and Neuroradiology was restricted to direct puncture carotid angiograms, pneumoencephalograms, myelograms and ventriculograms. The D.M Neurology training in PGI, Chandigarh was tough with teachers like Profs. D.R Gulati, JS Chopra, VK Kak and D. Rout. The teaching by Doctors B.B Sawhney, N.R.Rao and Chakravati, were in different style. There was no internet and we had to review the literature from volumes of Index Medicus and then try to get copy of the articles from various libraries in the country which would take even up to a month. Sometimes we had to visit the National Medical Library, Delhi to get one article. The time spent in rounds with all the consultants mentioned above was very difficult and demanding. The emphasis was on clinical Neurology and localisation. However once we were in the coffee room all the teachers were more than friends. Long coffee sessions, were in fact, informal teaching sessions in Neurology, Sociology and Political Science.



IAN Presidential Oration 2014

Contribution to Neurosciences:

I have seen the growth of Neurology from the so called Dark Ages of Neurology to the present era. In this write up I will touch upon the growth of Neurological Sciences with special reference to work done by me along with my colleagues in PGI Chandigarh from 1978 to 2014, which is the golden

period of Neurology. Though there has been progress in various fields, I would be discussing my contribution in the advancements in Stroke, Motor Neuron Disease and Dementia.

From the Dark Ages of Neurology, when NSI had 200 members with less than 100 Neurologists, and Neurology was synonymous with “no treatment”, to the present period of gene therapy a lot has changed. The future is where Molecular Biology and experimental Neurology are guiding research and the management of neurological disorders, by more than 2000 Neurologists.

Stroke in young was the priority area of investigation at that time. PGI under Dr. J.S Chopra was one of the major centers doing work on Stroke in young. Stroke prevalence rate at that time was 127-200/ 100,000, with case fatality of 41% Stroke in young was reported in 15-35% of hospital data. Work was initiated to find out the etiology of Stroke in young by studying thousands of cases. We had a very good pathology department where majority of the patients who died, had to undergo autopsy. The learning from postmortem studies is something which was the highlight of PGI training.

In a necropsy study, by Dr. A.K. Banerjee, Intra cerebral hemorrhage was seen in 138 out of 362 cases, arterial thrombosis in 101, cerebral embolism in 89 & CVT in 34. 37% were <40yrs of age. Dr. Dalal from Bombay, questioned the reported high incidence of stroke in young in India. However, data from various centers suggested that stroke in young was a problem needing investigation. Vascular endothelial growth factors (VEGF) and Monocytochyme Attractant Protein 1 (MCPI) levels were

found to be unaltered in plaques of patients from north India. Using bubble technique on TCD, high prevalence of cases of patent foramina of Ovale was detected in young patients with stroke.

The management of stroke in 1970's consisted of direct carotid artery puncture followed by conservative measures. By 2014 IV tPA had become the treatment of choice in ischemic strokes. At PGI in a period of 42 months, 502 patients of acute ischemic stroke were seen. 347 were eligible for IV tPA, however, only 130 received tPA. Better experience, multidisciplinary approach and community awareness programmes have improved the rates of tPA infusion. Mechanical devices like Merci, Penumbra, Solitair, Trevo, Revive have become available and thrombectomies are being undertaken.

From desk to bedside:

I tried to bring in the concept of a good clinical research laboratory at PGI, Chandigarh. Clinical research always goes hand in hand with experimental research. With the help of the research team of Neurology research lab, a mouse model of Middle Cerebral Artery occlusion was created. This was later used to study role of stem cells in experimental stroke model. Neurology department of PGI, under Dr. S. Prabhakar was part of DBT sponsored multi-institutional study to investigate intravenous autologous bone marrow mononuclear stem cell therapy for ischemic stroke. It was concluded that, under the condition of 'Invest' trial BMSC is safe but ineffective in the treatment of moderately severe subacute ischemic stroke. Until ongoing or further randomized trials show efficacy, this treatment should not be used in clinical practice, and patient should not accept such therapy without question.

MOTOR NEURONE DISEASE

Till recently there was nothing possible, once a diagnosis of MND was made. Lot of literature had emerged regarding aetiology of MND, which included exposure to environmental toxins and chemicals, infections by viruses, immune mediated damage, pre-mature ageing of Motor Neurons, loss of growth factors required to maintain survival of motor neurons and genetic susceptibility. Glutamate excitotoxicity is also known to contribute to motor neuron damage. Riluzole has been the main stay of treatment of

MND. It blocks the release of Glutamate from neurons and prolongs median survival by 2-3 months. The effect is better if started early. I started the study of “Role of autologous bone marrow derived stem cell therapy in management of patients with Motor Neuron Disease” in a pilot Study, at PGI Chandigarh. 10 patients of amyotrophic lateral sclerosis (ALS), according to revised El Escorial criteria were recruited to determine the efficacy of autologous bone marrow derived mononuclear cells in improving outcome.

The primary objective was to compare ALS functional rating scale (ALSFRS) score at baseline (time of first presentation) to that as on 3 months, 6 months, 9 months and 1 year after injection of mononuclear cells derived from patients’ bone marrow in the sub arachnoid space at L 2/3 or L 3/4 spinal level. There was a definite decrease in rate of progression of disease after stem cell transplant from the initial presentation. There was a worsening after an initial stable period of 6 to 7 months after stem cell transplant. In a second part of the study, 30 patients who were clinically definite/ lab supported ALS, were studied between March 2012 and November 2013. Two intrathecal injections of autologous bone marrow derived stem cells were given, 6 months apart. Three monthly follow up till six months after second injection death/PEG/ or ventilator support was done. ALS FRS scores were assessed at base line, 3 months and historically 6 months prior to enrollment. Follow up of 1 year revealed that 18 of 30 were alive without PEG/ventilatory support

There was no significant worsening in total ALS/FRS score, ALS-FRS Bulbar score, upper limb FRS score, lower limb FRS score and respiratory score. Patients remained stable for about a year after the two stem cell injections. There was no definitive improvement. A Biomarker development program in ALS was also initiated in the Research lab of Neurology Department, in collaboration with Dr. Akshay Anand.

DEMENTIA

Prevalence of Dementia in Rural Indian population has been reported to be 3.39% - 8.4%. In Urban Population, it is 2.44 - 4.1% in West, 1.83% in North, 0.8% -1.28% in East and 3.6% in South. I was also involved in the study of Biomarkers for Alzheimer disease, Mild Cognitive Impairment, and vascular dementia. I always believed that Ayurvedic drugs like

BRAHMI, have lot of potential but have not been investigated scientifically. I studied the role of Brahmi (*Bacopa Monniera*) in the treatment of Dementia. In an experimental model of mouse the benefit was confirmed. This was later further studied as a double blind clinical trial in patients with Dementia, with promising results. Animal model was also developed with laser induced injury in mice and role of stem cells was studied

Conclusion:

When I superannuated in April 2014, I was a satisfied person. I had developed a Department with strong foundation, where every individual was given due respect for his or her capabilities, and where the prospective students, preferred a DM training from PGI. I was able to mentor more than 120 D.M. students and around 10 PhD students, who are well settled in India and abroad. In my journey from a general physician, to a satisfied senior clinical neurologist and researcher, I have been ably supported by my wife Dr Indu Prabhakar, who entered my life in 1975 and still continues to push me to do my best. She has given me two sons, Dr Sharad, Associate Professor Orthopedics at PGI Chandigarh and Dr Anuj, Assistant Professor in Interventional Neuro-radiology at AIIMS, New Delhi, who are enjoying their lives with their spouses (Gynaecologist and Radiologist respectively) and their sons and daughter.

I have followed the path shown by the young neurologists of 1970s who later became the pillars of Neurology in India.



Dr. Indu with Grandchildren