Tribute to the legend in Neuropathology: Prof SK Shankar

Prof SK Shankar left us on Teacher's Day - September 5th 2022, at the age of 75. A legend in the field of neuropathology, he left an indelible imprint in the field of pathology, and neuropathology in particular. An inspiration to generations, his contributions in establishing the specialty of neuropathology in this country will never be forgotten.

Born into a highly cultured, progressive vedic family on January 27th 1947 in Vishakapatnam, he was the first of seven siblings. His father Mr S Gopala Sastry was a Civil Engineer, Entrepreneur, social activist (Karma Yogi), and freedom fighter and his mother Mrs Sitadevi, a gentle but learned lady.

His life was a veritable lesson in overcoming adversity……..

His trials began on Day 1 of life when he was born with a meningomyelocele and operated on day 3 of life. The surgeon who operated on him informed the family that he is not likely to live. He defied fate and the same defiance, resilience, grit and determination remained as his closest companions through all the trials and tribulations he had to face throughout his life.
The early formative years he spent under the tutelage of his revered scholarly grandfather, Sri Susarla Surya Bhagavat Shankara Sastry, who taught him Sanskrit and the vedas. A strict disciplinarian, he instilled the values of honesty, discipline, rigor and pride in Indian culture that ingrained into him, the values that he lived his life by.

The early days….

After his 12th standard, it was his dream to become a doctor. He applied for a medical seat in Andhra Medical College. Being a ranker, he was called for the interview. He limped into the interview room with his certificates clutched in his hand. In his customary way, he responded to all questions asked by the panel. But, one of the interviewer refused to allow him entry into the medical college saying "he cannot even stand properly" and summarily rejected his application. Deeply disappointed, he started to walk out of the room dragging his right leg with his head down. He was called back by a neurologist Dr. Balaparameswara Rao in the panel, who asked him to wait outside the rom. He strongly supported his application saying that a candidate cannot be refused admission on the ground of disability. His application was approved. He graduated from Andhra Medical College in 1969 as best outgoing student. If it wasn't for the timely intervention of his benefactor, the world would have lost a great doctor, neuropathologist and researcher.

From then on, there was no looking back. He did his postgraduation in Pathology from AIIMS, New Delhi (1971-74) and worked for another 5 years as a Research Associate. He remains a superstar here and is fondly remembered by all his colleagues, juniors and allied disciplines for his ever present support, teaching, and photographic skills. Photographs for almost every thesis in Pathology, Surgery and neurosurgery was taken by Dr.Shankar.

He would often recall that there were three people during these early formative years, who influenced him– Dr Baldev Singh fondly called "Papa Neuron", Father of Indian neurology; Dr PN Tandon who fuelled his passion for research and Dr MG Deo who was his guide and who taught him to question everything. These early lessons, it seems, shaped him to be what he was known for - never tire of asking questions, and would quite happily denounce the printed text, while everyone around him would be conscientiously quoting the textbooks.

His appetite for research was kindled very early on, during his MD by his guide Dr MG Deo. His thesis titled "Cell to cell interaction in immune response. A study of turnover of B and T cells and 19s and 7s antibody forming cells" received the coveted Khanolkar Award for the Best Research paper for the year 1973, from the Indian Association of Pathologists and Microbiologists. He registered for PhD but never completed it. It was Dr MG Deo, Sir would often recall fondly, who taught him to question everything and "not to believe in textbooks". He also taught him to look for phenomenology and not merely pathology. It is by looking for "commonalities" in varied disease processes that one can understand pathophysiology, he would often say. It is probably the reason he would always ask "why this, why that", challenging what is in the textbooks, always exhorting "how did they know that!".

In June of 1979 he interviewed for faculty position at NIMHANS. Here too the then Director expressed doubts whether he would be able to do autopsies! How utterly wrong he was proven to be….it was precisely Sir's untiring passion for autopsies that helped him establish two facilities, that proved beneficial for the entire nation: the Brain bank and the Brain Museum. He joined NIMHANS as a Tutor in 1979 and would spend the next 34 years at this Institute. In a career that would span nearly four decades, he put the department on the national map to earn global recognition as a centre of excellence in neuropathology.

The corner room that was his office for almost 3 decades

In 1985, he travelled to NIH on a Fogarty International Fellowship. He worked in the Nobel laureate Carlton Gadjusek's lab at Fort Detrick, NIH for two years from 1985-1987. It was perhaps during this time that his interest in prion diseases was triggered.

Fort Detrick, NIH 1985-87: worked in Carlton Gadjusek's lab

In 1992, he spent 6 weeks in Michael Palkovic's lab in Dept. of Anatomy, Simmelweiss University, Budapest, Hungary, as part of the Inter Science Academy Exchange Programme. It was during this time that he learnt the art of whole brain sectioning. and introduced large mount sections of the brain which remains a unique unsurpassed art in the Brain Bank.

Budapest – Michael Palkovic's lab

As a pathologist….

The most important lesson I learnt from him was that pathology cuts across disciplines. We are clinicians…equally essential for clinical care. Clinical colleagues would often seek him out for advice. We would attend classes in neurology and case discussions in neurosurgery and radiology. No one would ask us "why are you here" like they do now. It was in fact expected that we should be there. That was the foundation of healthy interdisciplinary communication that he laid and is responsible for the enormous respect we enjoy from our clinical colleagues even today. Academies of Neurology and Neurosurgery sought him out for presidency of their respective societies; the greatest honor they can bestow on a pathologist. That in itself speaks volumes on his enormous knowledge of the subject that seamlessly cut across disciplines.

In pathology he was a legend. An astute diagnostician and a wonderful teacher. He led by example, always participating in everything. He loved the simple act of grossing, and would often fight with me to do grossing of surgical biopsies even when he was head of department. No job was below his dignity. Even cleaning of instruments and the grossing area in the lab or in the Mortuary, he would insist on doing it himself and not leave it for the attenders. Documentation was an obsession with him, much to annoyance of everyone. Everything had to be documented, and this was much before anything such as NABL existed. But it was precisely this practice that made it so easy when we enrolled for NABL accreditation. We were amazed that almost alldocumenttaion that NABL required, was already in place!

Watching him gross tissues was a learning experience.

The Master at work

The reverence with which he handled tissues, the excellent descriptions (be it gross or histology), refreshingly unbookish remains a great source of learning. It was always an untarnished description of what he saw, scrupulously honest. "Don't try to fit your observations to a diagnosis, faithfully put down what you see..." was his constant refrain. He would always urge you to look around the lesion and marvel at how the tissue is responding to the pathology. I secretly believed that the cells talked to

him….and the stories he created were always captivating. Of course by the time he got down to seeing the slide, it would have to be spotlessly scrubbed clean of DPX, dust, etc…It always irritated him to have even "microscopic" dust or wax on the slide. The surgical blade was his inevitable companion, that would be perched on the microscope behind the eyepiece. He had so terrorised us into obsessively following this procedure that residents would come early hours of the morning just to scrub slides, rather than see slides!!!

The reports that he drafted, till today remains a beautiful document to read. Results of immunohistochemistry was always carefully observed and documented. Having introduced this technique to the department and standardised it himself, he was very good at trouble shooting. No finding could be dismissed as background/non specific on immunohistochemistry. When we would rather dismiss inconvenient findings, he would admonish saying – "document what you see. Don't dismiss a finding just because you don't understand what it means. It is telling you something which you are not able to understand." He encouraged independent thinking and enjoyed speculation. Publications that only reiterated what was already documented, he would call "*Tatastu* science".

His greatest passion was microphotography. He took immense pleasure in taking photographs for everyone and wouldn't allow anyone else to do so. Watching him take photographs was a great learning experience. Each slide was first immaculately cleaned, making sure there was not even a spot of dust or wax on it, the slide would then be scanned for hours until the perfect field was captured, carefully written down in a notebook, labelled with biopsy number and short description of findings. The number of dissertations and publications he has taken photos for is countless.

Photography, his passion…

As the boss…

He was always the first to enter the department and the last to leave. You could set your watch to 8.00am when he got out of his car. A strict disciplinarian, he expected everyone

to follow suit. All of us were always on tenterhooks, wary of when he would get upset, as his temper was shorter than him! His dressing down was legendary and no one (if we could help it) wanted to be on the wrong side. His brand of speech was jokingly termed as "ballistic" in private! Quality of work was paramount. Technicians would go that extra mile just to please him. Praise from him made all the efforts worth it. But praise was never easy coming unless absolutely deserving and that's what made it all the more precious! Delays were not tolerated and cleanliness was mandatory.

As an administrator….

He headed the Department of Neuropathology from 1998-2010. His drive, energy, uncompromising demand for perfection, earned the Department the high reputation and respect that it enjoys till date, both in the country and abroad. In fact, calls come in asking is it "Dr Shankar's department?" rather than neuropathology! When it came to patient care, he was unforgiving in demand for quality and insisted on what he would always call "zero error!" A strict disciplinarian, he drove himself and others in the pursuit of perfection. His motto was emblazoned on his wall…

An astute administrator, he occupied the highest administrative positions including Dean (2009-2010), followed by incharge Director and Vice Chancellor of NIMHANS from Feb-Jun 2010. He discharged his duties with elan and was known for the instant decisions, a razor sharp mind and quick grasp of matters. Despite the short tenure, the Institute vastly benefited from the introduction of a slew of digitization initiatives that proved a turning point. He set forth the vision and mission of NIMHANS during his tenure as Director.

He was unique - endowed with extraordinary vision, fierce determination, indomitable will, and magnanimity to further, not his personal interests, but the requirements of the department, and the nation at large; his contributions were enormous.

For the Department, he was instrumental in achieving several milestones, that have become flagships of the Institute and the nation as well – initiating the Transfusion Medicine Centre, the state-of-art Mortuary (1976), setting up Electron Microscopy facility (1982), Human Brain Tissue Repository (Brain Bank) and Brain Museum (1995), facilitating establishment of advanced labs in Neurobiology Research Centre – including Neurooncology (2010), Neuromuscular Lab (2012), Proteomics Lab (2012) and theAutoimmune lab.

A great visionary, he was endowed with the ability to presage the needs of the community, decades into the future. Often times, to us mere mortals, his ideas would seem radical and implausible. But at the end, he was always proven right. For instance, decades ago, he urged us that space physiology is important to initiate and even put it into the Vision and Mission statement of NIMHANS. Many dismissed it then, and today it's the need of the hour.

One of his accomplishments was the Neurobiology Research centre that now house 15 high end research labs – translational psychiatry, neurooncology, stem cell biology, glial biology, proteomics, molecular biology, molecular genetics, neuromuscular lab, autoimmune lab, flow cytometry, and even music and cognition lab – way back in 2010, that today has so much relevance. His mission was simple – provide high end infrastructure to be a central facility to be shared and provided to all researchers thereby providing opportunity to perform high class basic and translational research. The deeply ingrained sense of sharing was again clearly evident in this enterprise.

But the most evocative example is his greatest triumph- the Brain bank. This mission he embarked on in the early 1980s, when the concept of tissue banking was not just in its infancy, but little known even amongst researchers. It was, to put it simply, a Herculean task. Many dismissed the proposals as sheer fantasy. But he was so convinced of its need for the scientific fraternity, he just never gave up, despite several setbacks and disappointments. And achieve he did, against all odds, to set up the one and only "Human Brain Tissue Repository" (Brain bank) in 1995 with joint funding from DBT, DST and ICMR. But it took him another decade to convince researchers in India to use the material! And what a resounding pay off…..it's the crowning glory for the Institute and the Nation boasts of it. It was a superhuman effort, and all for the needs of the neuroscience research community, rather than for his own advancement…. Almost every neuroscience researcher in the country has benefitted and several epoch making discoveries, indigenous kits, and patents were made possible. The Brain Bank in the last 27 years of existence has supported >50 projects of researchers, with >300 high impact publications including in ***Nature***, and several dissertations from the use of material from the Brain Bank. Significant scientific work with wide ranging application resulted. In the field of neurochemistry, for the first time in literature, it was demonstrated that major drug metabolizing enzymes Cytochrome P450 and flavin monooxygenases (FMO) were found in human brain tissues. Dysfunction of serotonin (5HT) 2A receptors was found in psychiatric disorders like depression. In neurodegenerative diseases, role of trace metals like aluminium, magnesium, sodium, etc in regulating metabolism and DNA topology in neurodegenerative disease were evaluated. In epilepsy, a novel gene responsible for the Lafora body disease (Laforin) was discovered and localized to Chromosome 6q24. In India, there is significant demographic and ethnic variability with implications in biology. Ethnic differences were discovered with lower numbers of nigral neurons In Indians with increasing age in contrast to the West. Similarly, we found that the APOE e4 genotype

was not associated with poor survival following neurotrauma, in contrast to Western studies.
He was also instrumental in setting up the CJD Registry in India along with Dr P Satishchandra that recorded all cases of CJD reported in India from 1969 onwards.

As a researcher, he was par excellence. His unique approach of trying to understand "phenomenology" as he called it, set him apart from everyone. Always probing, fearlessly questioning, inducing people to think beyond the book were quintessential characteristics that drove him. Stringent academic honesty was his second nature. His interests were wide, but his passion was in neuroinfections, epilepsy, prion diseases and brain development.

His lifelong passion for autopsies helped him make valuable contributions to neuropathology. During the Japanese encephalitis epidemic, he described in detail the neuropathology of JE, the "necrolytic" lesions, and noted for the first time the occurrence of cysticercosis with JE which went onto become an easy biomarker on CT scans for diagnosis. His careful histopathological evaluations of each autopsy also revealed that necrolytic lesions were greater on the side of the cysticercal cyst. He proposed that there is successful parasitism between the JE and cysticercus. The cysticercus opens up blood brain barrier permitting entry of the JE virus. He was very keen on experimental neuropathology. His work on pigs infected with cysticeri ("measly" pork) provided the pioneering findings on the biology of cystcerci. The mechanisms of immune subversion by the parasite, its expression of choline esterase enzyme and production of an ACTH like substance was disclosed using available histochemical stains, and is a landmark contribution.

In neurotuberculosis, he meticulously catalogued the "kaleidoscope of neuropathological changes" (as he liked to call it) in the largest series of brain autopsies. He documented hypothalamus and brain stem infarcts as the cause of sudden death in tuberculous meningitis. Using elegant immunohistochemical studies to document the "immune architecture" of tuberculomas, he brought out commonalities between tuberculosis and cysticercosis that explains the common cross reactivity between these two infections. The role of immune responses to antigenic mycobacterial components, and it secretory antigens in propagation and maintenance of the disease process was elucidated.

Sinners do not die!

During the HIV epidemic, he fearlessly carried out autopsies. These were valuable lessons for us. He would often jokingly declare "sinners don't die"… nothing will happen, we need only universal precautions. As always, he was right… nothing happened to any of us, including the Mortuary staff who willingly participated as he led by example and would be garbed and amongst us. The payoff was staggering. We banked brain tissues

and CSF from the HIV/AIDS cases which helped decipher neurobiology unique to Subtype C. It was established that the most prevalent subtype causing AIDS in the Indian subcontinent is subtype C, thus generating epidemiological data. A novel indigenous PCR test for HIV clade subtyping was developed and validated. In addition, molecular heterogeneity of toxoplasma gondii has been evaluated utilising human tissues. This experience helped us to do our bit during COVID19 pandemic and create a biorepository of COVID19 biospecimens for research. In fact it was the same mortuary staff who urged me to start autopsies of patients succumbing to COVID 19! We hope it made Sir proud!

Similarly several new insights into rabies viral pathogenesis and subacute measles encephalitis were reported. The tissues stored proved a valuable treasure trove when new techniques like proteomics, genomics and transcriptomics emerged. Proteomics and transcriptomic studies were performed in temporal lobe epilepsy, rabies, tuberculous meningitis, cryptococcal meningitis and toxoplasma encephalitis. A proteome map of human brain at different ages is in progress. The influence of post mortem delay in mitochondrial function was evaluated. Role of mitochondrial dysfunction in traumatic brain injury and neurodegenerative diseases has been studied.

Following his superannuation in 2012, he started his second innings as Emeritus Professor.

In recognition of the valuable material collected, ICMR, Dept of Health Research, Ministry of Health and Family Welfare, Govt of India funded establishment of a Centre for Advanced Research For Innovation In Mental Health And Neurosciences. The mission statement of this project was “to be a leader in the field of mental health and neuroscience and evolve state of the art technology and innovation and translational research and develop critical mass of manpower to meet national needs by scientific collaboration and co-operation”.

In keeping with this, the Neuropathology Brain Museum was renovated to occupy 1200sq feet with LED lighting. It was also thrown open to public and school children as his mission was to spread “N-literacy” (Neuroscience literacy) as he called it. He wanted to “sow the seeds of neuroscience in young minds”. He spent hours passionately and tirelessly teaching the wonders of the brain to public and children. The Brain Museum became a household word and the footfalls tremendously increased. It became a popular tourist spot and features on the google maps as “a must see” in Bangalore. Its now part of the Museums of India circuit! Despite all the digital displays that we tried to procure, what always held the fascination of visitors was the chance to “hold and touch a real brain” which Sir would do in his usual flamboyant style….



Doing what he loved most, enthusing and inspiring children

In keeping with the mandate of developing neuroscience education material, he developed a unique 'Histological Atlas of the Common Infections of the CNS' that had a set of 48 histological slides. He painstakingly described each slide, took beautiful photographs of the pathological features and prepared a CD containing the Text and Photographs. To this day, this has remained an invaluable teaching resource among the medical colleges teaching postgraduate students of pathology, microbiology and neurology and neuropathology.

Always ready to help, he generously helped everyone who came to him – be it with antibodies (expense was never a concern), material or just ideas – each interaction with him was invaluable. Scientific fervour was in his blood…he gave freely of his ideas, and time to enthuse everyone to do research. It didn't have to be in the hallowed precincts of a committee room, in fact, most science happened, as he would say, "in the corridors or over a coffee". He abhorred protocol and hierarchy. Everyone was important….and no one would be kept waiting. A prolific writer, he took great pleasure in publishing. With more than 400 publications in 4 decades, he was cited as one of the 3 researchers in the Country with the highest citation index! He would always urge everyone to publish, would often happily rewrite papers that came to him for review. A master at the art of editing, he was much sought after by all. As a strict rule, no manuscript that came to him took more than 24 hours to complete.

But he was also a highly principled man and expected everything to be done on time. He never minced words and freely expressed his mind. This typed sheet that adorned his wall said it all…

Lack of planning
(on your part)
Should not be cause for emergency
(on my part).

As a teacher….

As a teacher, he reigned supreme in the hearts of students. His classes for residents of neurology, neurosurgery and pathology in Anatomy and Museum were legendary and never forgotten. The class would always be on Sundays, and last for at least 3 hours. His enthusiasm and energy would never flag and would only rise with every passing minute. Even till the end of his career he would take classes with the same degree of enthusiasm. His mood after each class would always be buoyant. It would always amuse him how students would tire but not him! He was instrumental in shaping the lives and career of many.

The Neuropathology Society of India…

APCON Dec 2006, first resolution to have Neuropathology Society

To establish a Society for Neuropathology in the Country was his fond dream. He laid the initial stepping stone for this in 2006. His handwritten notes on the Constitution I still have preserved with care. I am only happy that with Dr Chitra Sarkar's drive we could realise his dream in 2015 when the Society was born. His last presentation was the Presidential oration in NPSI at PGIMER, Chandigarh in 2018…and his last public appearance at a conference too was at the last NPSICON in 2019.

As a human being…

He **r**eigned supreme in everyone's hearts. His philosophy in life was always to "give, give and give". The morning coffee was shared with the sweeper who swept streets daily. His house, fondly termed "Shankar Mutt" was always open to visitors and food was always available to anyone anytime. He enjoyed feeding people. All residents in

department will fondly remember the “energy”, as he called it, every evening after working hours, when we would be plied with something every day - be it chikkis, jelebi, samosas….

Extremely protective of his staff, he would always make sure everyone left before he did. If we went out to attend conferences, the women residents were always dropped back safely. In short, he spoilt us. Was “Godfather” to us in every sense of the word (and he enjoyed being called that!)– protective, fatherly, ready to fight for rights of underprivileged, but at the same time would expect his instructions to be followed to the letter, no questions asked.

The much loved “punishment”….

He had a deep love for children. He had a gargantuan memory. The family of every person, staff, faculty, acquaintance is always remembered, particularly the names of their children, even what they are studying or working is always fondly remembered. He would without fail enquire about them. Small children who visited him were always “punished” - a euphemism for a chocolate which always miraculously appeared in his pocket. He always had an appropriate gift – at anytime, for any purpose and given at the right time with great deal of affection. I always wondered how he was everready!

He was human too…, loved music, movies and was especially fond of Jayalalitha! Music would always be playing in his room and if we hear music wafting from the room, you know all is well…Especially fond of Telugu movies, he enjoyed popular Hindi hits too on Sundays. A particular favourite that he saw many times and never tired of watching again and again was….Munnabhai MBBS!

He lost the battle to multiinfarct dementia. That robbed him of his prized possessions…..independence, freedom of movement, speech, and finally memory.

The number of people whose lives he touched are too numerous to count – people flocked to him from all walks of life; be it for advice on choice of career, house, colour or even life partner…it was all in his stride . The messages, the outpouring of grief, and the stream of visitors who came to see him on 5th of September were unstoppable, a mute testimony to the number of lives he touched. Each person had a story to tell of how he/she was helped by Sir…

It was very poignant that he left on Teacher’s day, a teacher incomparable…who truly embodied all qualities of a “Guru”. In Sanskrit, Guru stands for a "mentor, guide, expert, or master". In Indian tradition, a guru is more than a teacher: the guru is a reverential figure to the *shisya*, with the guru serving as a "counselor, who helps mould values, shares knowledge, is a model to follow, an inspiration, and one who helps in the spiritual evolution of a student". He was all of these to those who had the opportunity to know him.

Even in passing away, he continued to teach. He donated his brain to the Brain bank, the cause that he held dear to his heart!

I consider myself extremely privileged to have had the opportunity to shadow him for 24 years. My memory of him the first day I saw him, was this whirl of energy that whizzed past, throwing behind his shoulder the brusque "Yes?!" that I came to now so well…. he gave me everything, my first job, his Brain Bank, the Brain Museum, his room, his chair, even his quarters when he vacated, and most precious of all, his time for which I will be eternally grateful…..there has been no nobler person that walked this earth. He showed the world that he was much more "abled" than any of us and how!

You will live on in our memories Sir….I pledge to keep your dreams alive and take them forward. Every time a resident marvels at a gross specimen, every time a beautiful pathology description is written, in every microphotograph that's taken with pride, each time a scientist in India dares to dream, each time tissues from the Bank is used by a researcher, each time someone thinks of banking….you will be remembered….

Any number of adjectives from a dictionary would be woefully inadequate to do justice to him. In his honor, I can only hope to emulate his energy, and encourage my our junior colleagues to continue to learn and rejoice in Sir's legacy.

A eulogy to a legend whose contributions are larger than life!

Anita Mahadevan
Will forever remain, your indebted student

PS: To the reader, please excuse this rambling narrative, it did not pass through the hands of the Master editor ….