



Profile

Stanley Appel: a life in Russian proverbs



For more on **expanded autologous infusions of Tregs in ALS** see *Neurol Neuroimmunol Neuroinflamm* 2018; 5: e465

"In 2009, I was asked to give the keynote address at a naturalisation ceremony in Houston for several thousand new American citizens—a great privilege for me, and a chance to remember and honour my own family and the drive, the dedication, and the hardships my father endured to reach this country and start a new life." (Stanley Appel. *From an e-mail to me. November 2018*). I wondered, when he wrote those words, if he knew how profoundly he was revealing who he is.

At 85 years of age, Stanley Appel—Co-Director of Houston Methodist Neurological Institute, Chair of the Stanley H Appel Department of Neurology and Peggy and Gary Edwards Distinguished Endowed Chair for the Treatment and Research of Amyotrophic Lateral Sclerosis (ALS) at the Houston Methodist Hospital in Houston (Texas), Professor of Neurology at Weill Cornell Medical College (New York), practising neurologist, teacher, and respected researcher, especially into ALS—is still honouring the dedication and drive that brought his father Joseph Appel to the USA as a Russian immigrant in 1930. Twenty years after most people have retired, Stanley still shows up for a work load that might daunt a man 40 years his junior—one requiring an effort that surely commemorates those his father made. "Dad's family moved to the USA when he was 7, but he was left behind because he had trachoma", he reveals. "With no immediate family behind him, and only a second-grade education, he managed to survive the Russian Revolution, make his way to Boston at age 23, and begin again." Both men exemplify an old Russian proverb: *Without effort you cannot even pull a fish out of the pond*.

And Stan has pulled out some big fish. For decades he has been calling attention to the increased neuroinflammation in ALS and documenting how it contributes to motor neuron injury and cell death. And now, at this point in his long career, that research has translated into a clinical trial that offers the hope of slowing down the progress of sporadic ALS. His laboratory recently discovered that regulatory T cell (Treg) numbers are down, and their inflammation-suppressing function impaired, in ALS. Following their expansion, however, that function is restored. These findings paved the way for the first-in-man trial of autologous transplantation of expanded "normalised" Tregs. An initial study showed the procedure is safe and slowed ALS progression—for a while. "We've redesigned the protocol and are optimistic that our follow-on study will give more prolonged benefit", Stan says. As another Russian saying puts it: *We will live—we will see*.

His accomplishments might not seem odd for a lad who graduated from Boston Latin School, well known for its

academic demands. "Four to six hours of studying every night", Stan recalls, "plus the urging of parents who came to the USA, so that their children would have advantages they never had. The mantra was: if you don't like the heat, stay out of the kitchen (or as a Russian might say: *If you are afraid of wolves, don't go to the forest*). And many left. However, the payoff was good and I got a scholarship to Harvard." They do seem odd, however, for a man who went there to study economics, and who admits "my Harvard experience was more of a social and emotional experience than a focus on intellectual-academic development." After graduating he returned for a Master's degree in Business Administration, but knew it wasn't right. A year later he quit, taking a job as a management consultant that didn't suit him either. But any Russian will tell you: *The first pancake is always lumpy*. "I soon realised, I missed not having the challenge of developing expertise that could evolve into a career. And understanding the human brain was an exciting challenge." And somewhere a Russian whisper was spoken: *Become a master, or be gone*.

He was soon on track, taking courses he would need to get into medical school at Tufts University (Medford), finishing his medical degree at Columbia University (New York). "That's when I met Murray Bornstein, a neurologist working in research on neurological diseases. He introduced me to the rigors of the scientific method. Added to the experience of a neurology clerkship I realised that neurology and the neurosciences were to become the basis of my future medical career"—a career that has taken him to Massachusetts General Hospital (Boston), Mount Sinai Hospital (New York), the National Institutes of Health (Bethesda), the University of Pennsylvania (Philadelphia), Duke University (Durham), Baylor College of Medicine (Houston), and now Houston Methodist Hospital.

Rather than his scientific discoveries, he regards his greatest contributions to neurology as "having enhanced the quality of life for many patients afflicted with ALS, and along the way having trained over 250 neurologists, many of whom now hold academic chairs of their own." It won't shock you that as a mentor he has a reputation for pushing people to do all they can do, be all they can be, make every effort. A demanding teacher? Sure. But, an eavesdropper might add: *Good counsel does no harm*.

I ask him whether, when he hangs his hat, he feels he will have complied with another Russian proverb and can do as it directs: *Did the job—go walk boldly*. He can, of course: *Every barber knows that*. But he replies "Who said anything about hanging my hat?"

Adrian Burton