NEUROPATHOLOGIST, ELECTRONMICROSCOPIST,  
CLOSE COLLABORATOR  
Robert Terry, M.D.

Saul Korey

Having been in academic medicine for more than 40 years, I can unequivocally say that Saul was the best chairman I've ever worked with. Robert Katzman, one of Saul's trainees, would be next. Saul was deeply involved with the clinical service and its problems. Unlike those chairmen who are trying to make it as "investigators," Saul's mind was on clinical problems and how they could more ideally be dealt with. He was concerned with his faculty and how he could best help them advance and work contentedly. He loved to teach, and a listener could almost hear his mind shifting gears as novel ideas flowed through it. He'd often stop, as if suddenly something new had struck him. Clearly, research was his greatest interest. But it was primarily clinical problems – neurologic diseases – that he wanted to solve. Finally, Saul was an excellent judge of people. He had, after all, chosen Herb Vaughn, Labe Scheinberg, Bob Katzman, Bill Norton, Isabelle Rapin, Bob Ledeen, and me for his faculty.

Saul recruited me to the Pathology Department at Einstein in 1959. I guess that he might well have felt that he needed an electron microscopist to flesh out an almost entirely chemically oriented research group. Within weeks of my arrival from Montefiore, Saul and I began to think of disease to research as a team effort. I'm not sure that there were such teams in academic neurology at that time. We sought our possible targets not in the research literature, but rather in the index of Houston Merritt's neurology text book! We were looking for one or two disorders that offered combined opportunities (i.e., questions) in chemistry and morphology. We came to Alzheimer’s disease and Tay-Sachs disease (TSD) in the alphabetic search. In neither area was there evidence of significant planned work elsewhere. There seemed to be no real competition.
I believe that I had brought with me from Montefiore a small NILI grant which mentioned Alzheimer’s disease as a sort of minor fishing expedition using electron microscopy. It turned out that it was the first grant application on Alzheimer’s disease that the NIH had ever received! Saul and I set about enlarging the program, planning brain biopsies (of less than one gram) to be used for chemistry, electron microscopy and pathology. He, of course, had been well trained in neurochemistry as it was known at that time. He did amino acid and lipid analyses, as well as Warburg respirometry; I did the EM and the neuropathology. We started with Tay-Sachs patients because there seemed to be so many of them in the New York area, and many of the parents were eager to support any research on their personal catastrophe. Saul persuaded Leo Davidoff to do the biopsies. Davidoff was, without question, one of the world's great neurosurgeons. He'd been trained by Harvey Cushing and had a huge clinical practice, but was extraordinarily patient with a young neuropathologist. In the operating room I stood behind Dr. Davidoff with a small, chilled plastic tray holding a drop of the fixative: buffered osmic acid or glutaraldehyde. The surgeon cut a large bone flap in the cranium over the right frontal lobe. He then chose a gyrus relatively free of large vessels and stabbed through the leptomeninges a square a bit smaller than a centimeter. This he lifted with a flattened scoop through the superficial white matter, turned and dropped the tissue on my tray. I moved to a table in the OR set for the purpose and began to divide the tissue into three parts: the first slice into formalin for pathology, the next into the `glut' or osmium for EM, and the residue into dry ice for chemistry. Note that the second or central piece was the least traumatized by the operative procedure. I then went on to cut the EM piece into minute bits, each less than a cubic millimeter, so that fixation was very prompt and thorough. It should also be pointed out that Dr. Davidoff's patients who went through this biopsy procedure never had any post-op complications. This whole program had been planned in great detail with Saul.
The pathology always displayed the typical ballooned neurons of TSD. The chemistry showed large amounts of gangliosides in molecular proportions to triglycerides and cholesterol. The electron micrographs were spectacular, and I showed them to Saul with great pleasure and no little pride. One was, some years later, chosen to be exhibited in a show titled "Once Invisible," in the Museum of Modern Art, in NYC. We discussed their meaning and the molecular proportions of the isolated membranous cytoplasmic bodies or MCB as we came to call them. Finally I wrote a paper, showed it to Saul who rejected it -- "fill it out" he shouted. Well, we went on to write five papers -- Methods, EM, Biochemistry, MCB, and the Membrane of the MCB. They filled one issue of the Journal of Neuropathology and Experimental Neurology in January, 1963, and established many of us.

The Alzheimer’s project started concurrently with the TSD, but proved much more difficult. We began with familial cases, following the text books, all of which described Alzheimer’s disease as rare, involving only pre-senile patients, and caused by a dominant gene. The chemical work was not very helpful in that they were not able to extract the amyloid, and the respirometry was unremarkable as were the lipids. The electron micrographs of tangles were easy, but I mistakenly and stubbornly called them "twisted tubules" rather than paired helical filaments. By the time that I began to understand the ultrastructure of the plaque, Saul was already ill. I remember very clearly being with him in Atlantic City at the neuropathology and neurology meetings. We were standing in the shade of a hotel wall as he complained of back pain. I tried to brush it off, but he insisted that he had cancer. Again Saul was right.

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