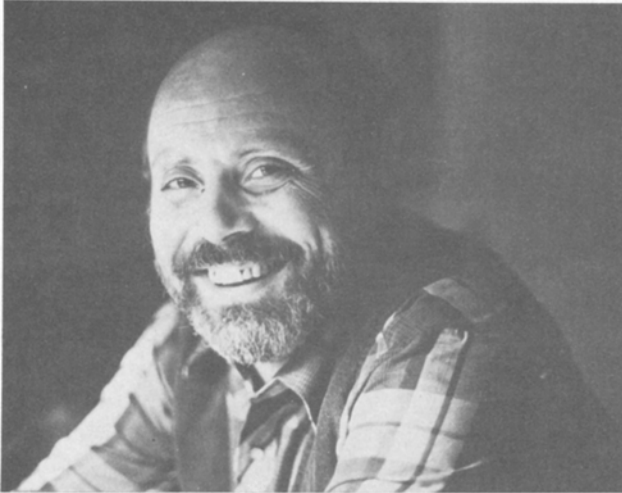


*In Memoriam*



Richard K. Gershon  
December 24, 1932 – July 11, 1983

Dick Gershon, one of the most creative scientists ever to study in the field of immunology, died on July 11, 1983, after a painful downhill struggle against lung cancer. Until his illness became too severe to allow it, he retained his enthusiasm for and interest in our field. Those of us who were his close colleagues can scarcely believe, even now, that he will not walk into our rooms, or, for those not located close to New Haven, into a meeting, and ask a refreshing, irreverent and humorous question that, no matter how improbable it sounds at the time, turns out later to be *the* question. Dick's was a unique and irreplaceable talent. Our field has lost one of its best friends, and it will suffer from his absence, as will we.

Dick aroused strong feelings in people. Those who knew him well were devoted to him. The number of friends who traveled great distances to spend time with him during his illness was striking. As a person, he was kind, a gracious host, always ready with a nice story, a glass of vintage wine, a flip remark, a twinkle in his eye. He was incapable of saying negative things to people, however much they provoked him. The devotion of his former and present trainees clearly demonstrates his enormous personal charm and the positive feelings he evoked in those who knew him well. During his research career, he, however, also aroused strong negative feelings in many people; but these, I believe, were based on a misapprehension of Dick as a person and of his work. It was Dick's approach to science that annoyed many of his colleagues. He had an enormous gift of pure intellect. He could see connections between apparently unrelated pieces of information. Many of his arguments were by seemingly overstretched analogy. Things that seemed painfully obvious to him were painfully difficult for many of us to grasp at all. And it was, I

believe, the pain of having to stretch our ideas, our minds, that led many to reject Dick and his ideas. It is right to equate Dick with his ideas, since his life was a life of ideas, of mind; his own identity was deeply invested in his scientific opus. I also believe many of us rejected Dick's ideas out of a mistaken notion that they were not well documented by his own experiments. This, surely, is a matter of degree. Immunologists are used to enormous effects; antibody titers or counts per minute in the hundreds of thousands are our working milieu. Most of us feel satisfied only with big numbers. But Dick was looking at the down-side of this phenomenology; for him, a 50% reduction was important, 75% better than could reasonably be expected. Indeed, if one looks at the current literature on suppressor T cells, such effects are now often acclaimed as "profound suppression"; but this was not the case when Dick first confronted his colleagues with his idea about immunoregulation, or infectious tolerance, as he initially called the phenomenon of dominant, T-cell-mediated down regulation of the immune response.

Dick, indeed, was not like the rest of us. For him, ideas came first, and the facts had to be amassed to support them. But having worked with him over several years, having spent many hours poring over data with him, I never saw him in a hurry to have a particular result. He loved looking over the results of an experiment; almost any experiment would do, be it his or anyone else's. In each experiment, he would be looking for clues, for the minor annoying quirks that most of us dismiss, but which would fit into his concept like pieces of a jigsaw puzzle. Dick was a man of vision, a man for whom ideas seemed to lead experiment; but this was the case only in the positive sense of luck favoring the prepared mind. For him the actual data were sacred, warts and all. I believe that this was so because he, unlike the rest of us, knew what the warts meant, and would get around to them when it became important to do so.

Dick grew up in New York and attended Harvard College, graduating in 1954 with a class that 25 years later boasted three United States Senators, and was said to be the most illustrious ever to graduate from Harvard. In the fall of 1954, he came to New Haven to attend Yale Medical School, and he remained there essentially for the rest of his life. He felt that New Haven offered intellectual stimulation without the problems of big city life, and he was close enough to his true home in New York, his parents and brother, to allow him to visit whenever he wished. I think it is a tribute to Yale Medical School that it recognized Dick for the talent he was, and supported him even at times when conventional scientists were deriding him. He repaid that support with intense loyalty, and never seriously considered moving elsewhere, even after he became famous and attracted all sorts of grand offers.

During his student days, Dick took advantage of the freedom of the Yale system of medical education to audit courses in history and the humanities, and to explore the possibilities of scientific research. He also made a number of lifelong friends. While still a student, he spent a year in Paris doing research, and published his first scientific papers, in French. This stay also gave him a start in fine wines; he once told me, with a sneer, that up until the time he lived in France, he had been a Beaujolais drinker (not to belittle Beaujolais, which he would drink on occasion, but when one is used to Premier Cru Burgundies, as Dick was, Beaujolais is a lesser drink). After medical school and training in pathology, also at Yale, he went to Japan as a civilian employee of the Army, and worked with Fred Prince on hepatitis. This col-

laboration contributed to the first understanding of anicteric hepatitis, and led to important work and Dick's lifelong interest in chronic active hepatitis. Perhaps most important, during his stay in Japan Dick first met Kazunari Kondo, who performed all of Dick's early studies on suppressor T cells, and whose hands freed Dick's mind from the hard work of laboratory experiments.

On his return to Yale, two lucky incidents occurred which loomed large to Dick in later years. The first was the retirement due to illness of a chairman who would surely have let Dick leave Yale; the second was that a colleague had to leave to serve in the military, and asked Dick to carry on with studies of an experimental tumor system he had developed. In studying this tumor system Dick became interested in immunology, and the rest of the story is more or less well known to readers of *Immunogenetics*. To learn more of immunology, Dick took a course offered to the medical students by Byron Waksman, recently arrived from Harvard. At that time, Waksman was interested in the role of the thymus in tolerance induction; he and a colleague had observed that injection of antigen into the thymus led to tolerance in the periphery in a very rapid and profound manner. Given the thinking of the time, this was interpreted to mean that immunocompetent cells were generated in the thymus, and were short lived; exposure to antigen in the thymus would lead to loss of cells of that specificity. Dick had a different idea; he thought that thymus-derived cells might be specifically activated to mediate suppression. However, he needed an experimental system in which to test the idea. The hamster tumor model on which he was working showed growth of the tumor in the face of immune effector cells, a finding he also attributed to local suppression, but this system was too complex to analyze in the detail he wanted to test his ideas. He therefore took a year's leave of absence to work with Tony Davies in London. It should be noted that Dick's leaves were always spent in interesting locations, and this was not by accident. One reason we all enjoyed him so much was that he knew so much about life in the wide world, and loved to tell us about his time in these places, which he enjoyed to the full. For instance, while in London, he became a proficient darts player, and, like many of us who have worked in England, greatly enjoyed his time at the local pubs; I believe he even drank the beer. At any rate, starting at this time when the separation of the lymphocytes into T and B cells was new, almost all of Dick's work focused on the response of mice to the antigen sheep red blood cells. While he retained an interest in liver disease and in tumor immunity, his ruling passion was to understand, at the most fundamental level, how the immune response was regulated. It may seem trivial now, but up until that time, it was assumed that responses were controlled by one of two means. In the case of self antigens, there were no responsive lymphocytes; in the case of foreign antigens, the removal of the stimulus through an effective immune response led to cessation of the response. However true these statements may be, both the experimental and the clinical literature now clearly demonstrate that both self tolerance and responses to foreign antigens are tightly regulated by the immune system itself. We owe a good deal of the theoretical as well as the practical understanding of this to Dick Gershon.

It took a number of years for these ideas to catch on, and Dick meanwhile sought ways to extend his ideas into many experimental systems. Thus, he was the first to provide evidence that some major histocompatibility complex-linked failures to respond to antigen were due to dominant suppression rather than to a lack of

responding clones. But Dick was not content to discover and learn everything there was to know about suppressor cells. He was convinced that there would be an elaborate apparatus for the control of the immune response, and he wanted to discover all of its elements. As early as 1974, long before he had any evidence for it, he was writing about contrasuppression, his most recent major discovery and interest in immune regulation. As Dick's ideas were shown to be valid in any serious laboratory studying regulation of the immune response, he gained respect as a scientist, and people who had once severely criticized him became his good friends. Through these friendships, a number of valuable collaborations arose, which have recently allowed a more extensive understanding of the relationships between suppressor and contrasuppressor pathways described in different experimental systems in different laboratories. The most recent paradigm describes three regulatory circuits: first, the feedback suppression circuit, extensively analyzed by Gershon's group, serves to inactivate helper T cells as well as the cells that induce suppressor cells; the second circuit leads to the generation of contrasuppressor cells, which allow immune response to proceed in the face of suppressor cells by protecting helper cells from suppressive signals; the third circuit, originally defined by Tomio Tada and his colleagues, serves to regulate the activation of the contrasuppressor cells, and is thus read out as suppressive. This new paradigm will probably serve us longer in Dick's absence than it would have if he were still contributing to our understanding; however vehemently he defended his idea of the moment, to Dick all paradigms were mainly there to be overturned, and we will miss his irreverence for ideas as much as we will miss his humor and generosity.

Dick has changed the way we think about the immune system and the way we think about human disease. This is no small achievement. He has also left us, his friends, with a lonely feeling. No one will fill the void. The charm, the intense intellectual excitement of a conversation with Dick, the warmth, the plain good fellowship are irretrievably lost, and we are all poorer for it. He has left us several wonderful legacies: former trainees to carry on the work, a large number of brilliant papers, and the endearing cartoons of which he was so fond. But most of all, if we can learn to approach ideas as Dick did, with the same mixture of childish wonder and adult, man-of-the-world skepticism, we will all be better for it.

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