The paper describes the results of a comprehensive assessment of immune responses in a large group of young children with protein-energy malnutrition. It provided the pioneering concept, now well recognized, that nutrition is an important determinant of immunocompetence and that undernutrition is the commonest cause of immunodeficiency worldwide. [The SCI® indicates that this paper has been cited in over 280 publications.]

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My interest in nutrition-immunity interactions was kindled by two cases: first, the story, with an unhappy ending, of a child; second, the bleak scenario of the Third World.

Eighteen-month-old Kamala was thin, her skin as pale as wax, and her lungs screaming for air. She wore a spectral white death-mask in a frame of black hair. Her shrivelled body and swollen legs were typical of marasmic kwashiorkor, and she had an obvious fulminating infection. Lung aspirate revealed the opportunistic organism Pneumocystis carinii. Despite our best efforts, we lost the child. I speculated that malnutrition had robbed Kamala of her defenses against infection and led to a premature demise. The tears shed on her death were not my own; rather, they were the tears of parents throughout the world, who are losing their children daily in the Third World.

Against this background, in 1966, I applied the available techniques to study immunocompetence of undernourished children. To convey a sense of time, the discipline of immunology was not then even exalted by the general use of terms such as "cell-mediated immunity," "T-lymphocyte subsets," "immunoregulation," and so on. In malnourished patients, we found impaired delayed cutaneous hypersensitivity, lymphocyte proliferation response to mitogens, complement activity, and secondary antibody response to certain antigens. These findings were soon confirmed by several investigators. Our subsequent work5 has demonstrated that protein-energy malnutrition results in a reduced number of rosetting T-lymphocytes, increased deoxyribonucleotidyl transferase activity, decreased serum thymic factor, fewer helper T-cells, impaired production of γ-interferon and interleukin-2, reduced antibody affinity, impaired secretory IgA antibody response, and phagocyte dysfunction. Malnutrition, however, is not a single entity but rather a broad syndrome. We now know that deficiencies of trace elements and vitamins impair immunity. Both in humans and laboratory animals, intrauterine malnutrition causes prolonged, even permanent, depression of immunity in the offspring. Furthermore, nutrition is an important determinant of waning immunity in old age.

I believe this paper has been cited frequently because it was the first comprehensive description of immunocompetence in malnutrition. It led to the acceptance of nutritional immunology as a legitimate scientific endeavor. The paper provided a window to the extraordinary possibilities nutrition offers for gaining insight into and modulating immunoregulatory mechanisms. Our original observations resulted in several practical applications including the use of immunocompetence in the functional assessment of nutritional status and in evaluating postoperative prognosis and the use of nutritional support to prevent opportunistic infection among cancer patients and to improve response to immunization, particularly among the elderly.

Honors received for our work include the Shakuntala-Amichand and Patwardhan Prizes of the Indian Council of Medical Research, the Borden and Newbome-La Roche Awards of the Canadian Nutrition Society, an honorary doctorate from Pontificia Universidad Catolica de Chile, the Samuel Levine Memorial Lectureship, the Wu Lectureship of Columbia University, the Gopalan Gold Medal of the Nutrition Society of India, the Grace Goldsmith Award of the American College of Nutrition, and the Medal in Medicine from the Royal College of Physicians and Surgeons of Canada.