

This Week's Citation Classic®

Chandra R K. Immunocompetence in undernutrition. *J. Pediatrics* 81:1194-200, 1972.
[Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India]

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 *SCF*® 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 fulminant 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 first and would not be my last. There would be another Kamala, and another, and another.

The second case was of the poor nations of the world, with high infant mortality, poor sanitation, contaminated food and water, a low literacy rate, and short life expectancy. Widespread malnutrition and infection were obvious shackles to development. Research into their interactions became a necessity for me.

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.^{1,2}

Our subsequent work³ has demonstrated that protein-energy malnutrition results in a reduced number of rosetting T-lymphocytes, increased deoxy-nucleotidyl 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.⁴ Furthermore, nutrition is an important determinant of waning immunity in old age.⁵

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 endeavour. 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^{2,6} 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.

Honours received for our work include the Shakuntala-Amirchand and Patwardhan Prizes of the Indian Council of Medical Research, the Borden and Hoffmann-La Roche Awards of the Canadian Nutrition Society, an honorary doctorate from Pontificia Universidad Católica de Chile, the Samuel Levine and Golan Memorial Professorships of Cornell University Medical College, the Kullianvanijaya Lectureship of Leeds University, 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.

1. Neumann C G, Lawlor G J, Stiehm E R, Swenseid M E, Newton C, Herbert J, Ammann A J & Jacob M. Immunologic responses in malnourished children. *Amer. J. Clin. Nutr.* 28:89-101, 1975. (Cited 185 times.)
2. Chandra R K & Newberne P M. *Nutrition, immunity and infection: mechanisms of interactions.* New York: Plenum, 1977. 262 p.
3. Chandra R K. Nutrition, immunity and infection: present knowledge and future directions. *Lancet* 1:688-91, 1983.
4. ———. Antibody formation in the first and second generation offspring of nutritionally deprived rats. *Science* 190:289-90, 1975. (Cited 70 times.)
5. Chandra R K, Joshi P, Au B, Woodford G & Chandra S. Nutrition and immunocompetence of the elderly. Effect of short-term nutritional supplementation on cell-mediated immunity and lymphocyte subsets. *Nutr. Res.* 2:223-32, 1982.
6. Puri S & Chandra R K. Nutritional regulation of host resistance and predictive value of immunologic tests in assessment of outcome. *Pediat. Clin. N. Amer.* 32:499-516, 1985.