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EDITORIALS

Editorials are written by members of the Editorial Board, and occasionally by guest editorial writers at the invitation of the Editor, and opinions expressed are those of the writers.

Effect of Malnutrition on Leprosy

In this issue (p 418) we include an abstract of an interesting editorial[1] which appeared in LEPROSY REVIEW directed at a consideration of common features which appear to be operative in leprosy control.

The abstract of the editorial contains a statement which, though technically correct, is, we feel, too readily dismissive of a very important factor in the host's defense against *M. leprae*. The statement is that "no direct link between malnutrition and leprosy has been convincingly demonstrated." This interpretation is heard not infrequently and is worth examining. Two manuscripts (pp 340 & 346) in this issue of the JOURNAL also are related to this problem.

The subject has been touched on previously in these columns.[2] In our autopsy experience in Hong Kong in the early 1950's, we encountered several instances of severe malnutrition of which one component, as evidenced by low serum protein levels and the presence of generalized serous atrophy of fat, was protein deprivation. In each of these instances the size and distribution of leprous lesions in visceral organs was far more extensive than is otherwise seen. These observations were briefly reported to the Seventh International Congress of Leprology in Tokyo, 1958.[3] In such malnourished patients the ulcerations on the extremities, associated with secondary bacterial invaders, was distressingly extensive and severe.

In the 1940's it was convincingly established from a series of necropsy[4,5] and experimental studies that in protein deprivation there is marked reduction in the production of serum proteins (including humoral antibodies),[6] and of inflammatory cells such as granulocytes,[7] and there is significant impairment of wound healing.[8]

[1] Davey, T. F. Common features in rapidly declining leprosy epidemics. Lepr. Rev. **46** (1975) 5-8.

[2] Skinsnes, O. K. Is leprosy treatment ineffective? Int. J. Lepr. **39** (1971) 890-891.

[3] Skinsnes, O. K. The defense mechanism in leprosy as related to the visceral lesion and malnutrition. Trans. VIIth Int. Congr. Leprology, Tokyo (1958) 222-229.

[4] Cannon, P. R. War, famine and pestilence. Scientific Monthly **56** (1943) 5-14.

[5] Cannon, P. R. Protein metabolism and resistance to infection. J. Mich. State Med. Soc. **43** (1944) 323-326.

[6] Wissler, R. W. The effect of protein-depletion and subsequent immunization upon the response of animals to pneumococcal infection. J. Infect. Dis. **8** (1947) 250-297.

[7] Asirvadham, M. The bone marrow and its leukocytic response to protein deficiency. J. Infect. Dis. **83** (1948) 87-100.

[8] Kobrak, M. W., Benditt, E. P., Wissler, R. W. and Steffee, C. H. The relation of protein deficiency to experimental wound healing. Surg. Gynecol. Obstet. **85** (1947) 751-756.

The problem of the effect of protein deprivation on cell-mediated immunity is a little more difficult to get at, but recently a series of studies have been reported from India which show experimentally that, as would be expected, there is a distinct deleterious effect. Thus, *in vivo* (homograft survival) and *in vitro* (macrophage migration inhibition) tests employing mice revealed depressed cell-mediated immunity (CMI) in protein deficiency.[9] In another study[10] utilizing rabbits, there was a marked retardation of macrophage mobilization and granuloma formation in response to BCG challenge after having been immunized to BCG during the period of protein deprivation.

The debilitating effects of malnutrition are, of course, not directed only against acquired immunity, but affect the very basic functions underlying these as connoted by the terms "inherent" or "innate" immunity.

In our studies[11] of protein-deprived mice challenged with *M. lepraemurium*, we noted not only deficient response in numbers of macrophages but found a significant diminution in response of macrophage marker lysosomal enzymes in both immunized and nonimmunized, protein deprived animals.

There is, it is true, no evidence that any specific or group of dietary substances is promotive of leprous inflammation as was postulated by Bernhard de Gordon, a teacher at Montpellier (1285-1307) and reiterated by Jonathan Hutchinson who held that leprosy was "Fisheaters gout." Oberdoeffer's promulgation in 1938 that *Colocassia antiquorum* is etiogenic of leprosy also rapidly fell by the wayside.

Thus for leprosy, as for infectious disease generally, there is both direct and indirect evidence that malnutrition has a deleterious effect on the host's biological defense mechanisms against the invading pathogen. It is quite some time since it has been advocated that one tries to treat an infectious disease by starving the pathogen through starvation of the host.

Recently we determined that *M. leprae* and *M. lepraemurium* have the enzyme β-glucuronidase needed for the metabolism of hyaluronic acid.[12] We noted that vitamin C, as a noncompetitive inhibitor of β-glucuronidase, could inhibit the development of infection by *M. leprae* in the human and *M. lepraemurium* in mice.[13] This has recently been confirmed[14] in a very nice dose response study employing *M. leprae* in the mouse foot pad. Thus, a dietary agent given in quantities higher than that found in the usual human diet has an effect on the usual course of leprosy. There is perhaps some validity to the speculation that one of the factors in the decline of the leprosy endemic in Europe was related to the development of organized gardening together with, as noted by Tisseuil,[15] a rising standard of living. It is not improbable that improved dietary factors, such as increased vitamin C consumption and reduced malnutrition, were major influences in the disappearance of leprosy even as they presently probably play a role in the diminishing endemics.[16]

—Olaf K. Skinsnes

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[9] Gautam, S. C., Aikat, B. K. and Sehgal, S. Immunological studies in protein malnutrition. 1. Humoral and cell-mediated immune response in protein deficient mice. Indian J. Med. Res. **61** (1973) 78-85.

[10] Purkayastha, S., Kapoor, B. M. L. and Deo, M. G. Influence of protein deficiency on homograft rejection and histocompatible antigens in rabbits. Indian J. Med. Res. **63** (1975) 1150-1154.

[11] Yang, H. Y. and Skinsnes, O. K. Intracellular modulation in cellular immunity. 1. Morphologic studies of macrophages in murine leprosy under conditions of immunity enhancement and suppression. Int. J. Lepr. **37** (1969) 111-129; 2. Macrophage enzymes in immunized protein-depleted and control mice during *M. lepraemurium* infection. Int. J. Lepr. **37** (1969) 253-262.

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[14] Hastings, Robert C. Personal communication of studies now in manuscript.

[15] Tisseuil, J. La regression de la lèpre ne fut-elle pas aussi fonction de l'evolution economique aux XIV^{e} siècle? [Was not lepra regression also a function of the economic development in the 14th century?] Bull. Soc. Pathol. Exot. **68** (1975) 352-355.

[16] Skinsnes, O. K. Immuno-epidemiology of leprosy. Int. J. Lepr. **43** (1975) 145-148.