and all but one of these patients had a leprosy reaction. Among the 17 aCL-negative patients, 6 had one or more reaction episodes during the study period. Of interest, leprosy reactions developed in significantly greater proportion in aCL-positive patients ($p = 0.0343$).

ACL antibodies can occur in several conditions and even in the normal population. Although aCL antibodies are relatively common, they have been more frequently associated with autoimmune disorders ([5]) and should be regarded as a sign of an abnormal autoimmune response.

Polyclonal activation of antibody response is well known in leprosy. Leprosy sera show a range of autoantibodies including rheumatoid factor, anti-DNA, antinuclear, anti-organ and aCL antibodies ([3]). Whether aCL antibodies arise in response to crossreaction to mycobacterial antigens or to tissue damage is not known.

In our study the presence of high levels of aCL antibodies was associated with an increased risk for leprosy reaction. A possible explanation is that aCL-positive patients have a higher susceptibility to hypersensitivity reactions. This immunological condition could predispose leprosy patients to develop reactions whenever trigger factors switch on the hypersensitivity response.

The present series is too small to derive final conclusions on this matter. However, if prospective clinical trials confirm these preliminary findings, aCL-positive leprosy patients could be regarded as subjects at risk for leprosy reactions and monitored for clinical signs of these conditions. This may lead to early detection and treatment of reactional episodes with a resulting reduction in nerve damage and disability.

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The Primary Lesion in Leprosy

To The Editor:

This is with reference to the stimulating article by Job, *et al.*: Histopathologic evidence to show that indeterminate leprosy may be a primary lesion of the disease. Int. J. Lepr. 65 (1997) 443–449. It has raised certain unsettled issues on the pathogenesis of leprosy, and we present our response on the analogies of events as observed in tuberculosis and lepromin reaction. Some points may appear less relevant to indeterminate than tuberculoid leprosy and are presented mainly to support the contention that the latter type is nearer to primary leprosy.

1. The study material included 10 biopsies of which 5 cases had evidence of inde-

terminate leprosy. Three of them showed granuloma consisting of epithelioid cells and giant cells. Since the presence of a granuloma is the dividing point between indeterminate and determinate, these three cases cannot strictly be regarded as indeterminate.

2. A primary lesion in leprosy is both ambiguous and interesting. We presume that in this article the authors refer to the primary lesion equivalent to the primary focus in tuberculosis. The understanding of leprosy has been considerably influenced by the facts available in tuberculosis and some are referred to in this discussion. Primary focus or Ghon's focus in tuberculosis ([7]) heals after development of delayed-type hypersensitivity (DTH) and formation of an organized epithelioid cell granuloma. This is also the case with tubercular chancre of the skin. In contrast, indeterminate leprosy is a nonsensitized pregranulomatous stage in the course of evolution, and thus seems to fall short of the histology and immune response of primary focus/lesion of leprosy.

In leprosy a lesion equivalent to the primary focus of tuberculosis is not well defined. If any type of leprosy at all is nearer to that, it ought to be polar tuberculoid leprosy (TTp). These are localized, self-healing lesions in the majority of cases ([6, 8, 9]) and have an organized epithelioid cell granuloma. Most of the cases are stated to have developed usually at the site of inoculation ([2, 6, 11]). Some workers opine that the ill-defined macules and tuberculoid cases, which appear and disappear with an evolutionary cycle of 6–12 months in the children of endemic areas, are primary leprosy ([1]). We feel, for reasons stated above, that clubbing indeterminate cases with tuberculoid leprosy for this purpose is not in order. Lara and Nolasco ([6]) state that at the uppermost tuberculoid side of the disease spectrum, a group of vaccination lesions including the self healing childhood leprosy is recognised. . . . It is probable that most of them are benign, but there is always the possibility that they may serve as the source of at least some apparently new infection occurring in older children and adults. This statement sounds very much like primary and reactivation leprosy.

Certain special attributes of the epidermis and subepidermal zone (SEZ) also appear to contribute to the evolution of TTp. Most lesions, including the "vaccination" ones of Lara and Nolasco ([6]) which are thought to have developed after cutaneous infection, are tuberculoid leprosy. Denis ([3]) painstakingly compiles the points of view about first skin lesion or primary lesion developing after tattooing and other instrumentation. The compilation shows that all the cases which indicated the type of leprosy were tuberculoid. These observations emphasize that the dermal route of infection favors sensitization. The antigen-presenting role of the epidermal Langerhans' cells is well known in many DTH-mediated diseases of the skin, including leprosy ([16]). These mononuclear phagocytes are known to process and transport *Mycobacterium leprae* antigens through the subepidermal lymphatics to the regional lymph nodes and lymphocytes to effect an immune response ([14]). Such findings are also consistent with Shepard, *et al.*'s thesis that dermal inoculation sensitizes and other routes tolerize ([13]). The final inference drawn from these findings is that the epidermis-SEZ is better suited to favor the evolution of TT leprosy which is proposed to be the primary lesion of leprosy.

Wide variation in the size, intensity of infiltration, and disease activity of tuberculoid leprosy is well known ([10]). At one extreme there are small "button" and "pebbled" lesions with a strong tendency of self-healing, while at the other end one encounters large plaques covering a part or a whole limb and persisting for years. These two extremes are also comparable to primary focus and progressive primary tuberculosis, respectively.

3. The evolutionary course of the lesion in a metastatic site is a complex matter. Lepromin reaction in a tuberculoid patient is comparable to a lesion developing at a metastatic site in a sensitized person. Findings of successive biopsies from lepromin reaction sites taken at different points of time ([4]) show that the epithelioid cell differentiation, which also indicates DTH, starts at the second week after injection. Then it passes through various intensities of reaction, sometimes even with ulceration, and

matures to an organized tubercle by the fourth week. Quite like early dermal lesions of leprosy, the exudate cells crowd around neurovascular bundles and nerve twigs, a reminiscence of indeterminate leprosy, prior to the onset of the granulomatous response. The impression is that both in primary and metastatic (secondary) lesions the morphology of the tissue response is similar. The difference seems to be in the rapidity and intensity of the response. This is also in conformity with what happens in Koch's phenomenon ([7]).

The evolutionary process of the lesion at a metastatic site does not fit that of a classical lepromin reaction. This is probably due to the influence of several variables. The wide variation in the dose of infection and the native immunity of the host are important modifying factors. An autonomy of immune reactions which causes divergent manifestations of leprosy is known to exist ([5]) and this is much more evident in the events taking place in the skin and nerves of the same patient ([15]). Added to all these are some of the already listed local factors which may be active at the point of entry or deposition of the causative agent. It is natural, therefore, that the permutations and combination of factors produce lesions so dissimilar and bizarre.

In conclusion it is stated that: A primary lesion in leprosy may be one that indicates a state of sensitization and indeterminate leprosy seems to fall short of that. Judged by the morphology, immune response, site of development and disease behavior TT leprosy, more accurately the TTp ([12]), seems to be a closer candidate. The primary and metastatic lesions are likely to follow a similar course of evolution. They differ considerably in the intensity and rapidity of response but not in the morphology of lesions produced.

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