

## Hanseniasis: The Polar Concept as It Stands Today

A reappraisal of the polar concept in Hanseniasis is offered based on a lifetime's experience and emphasizing the Latin-American contributions in the field. In accordance with the recommendations of International Leprosy Congresses in Havana in 1948, Madrid in 1953, Rio de Janeiro in 1963, Bergen in 1973, and taking into account the recent findings in clinical, histopathological, and immunological fields, we have recently proposed an actualization of the polar concept initially proposed by Rabello in 1938<sup>1</sup> and by Latapi in 1948<sup>2</sup>.

In our view, a spectrum of immuno-clinical forms of Hanseniasis can be acknowledged only with the qualification that this spectrum is a rather limited one. According to the immune-response, this limited spectrum embodies two definitely opposed *groups*, namely immune-negative or L (V), i.e., lepromatous or Virchowian, and immune-positive or T, i.e., tuberculoid, leaving a group, I, "indeterminate" or imma-

ture with respect to the immunological response. These three *groups* are by definition unstable and changeable, constituting the dynamic aspect of the approach, the zone of instability of Orbaneja and Puchol<sup>3</sup>. In marked contrast with these groups, forms can be found characterized by their rigid stability and mutual incompatibility, namely the polar *types* L (V) and T (the so-called full polar LL and TT).

We disagree with the proposal advanced in Madrid in 1953 and suggest that the so-called "group" B, borderline, or D, dimorphous, should be eliminated. Most of these forms are, in fact, included in the immune-negative, L (V) *group*, representing a series of histotypes labeled B, BB, and BL, according to Ridley and Jopling<sup>4</sup>. These forms make up fewer than 10% of all the forms of the disease when the immune-positive and lipid negative tuberculoid reactional forms (TR) are correctly removed from this "group."

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<sup>1</sup> Rabello, F. E. Faits nouveaux de l'immunologie de la lèpre, conséquences qui en découlent pour notre conception de la maladie. Bull. Soc. Fr. Dermatol. Syphiligr. **45** (1938) 823-827.

<sup>2</sup> Latapi, F. Clasificación de la lepra (tipo, grupo, forma y caso). Abst. V Int. Lepr. Congress. Int. J. Lepr. **16** (1948) 256.

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<sup>3</sup> Orbaneja, J. G. and Puchol, J. R. Un caso atípico de lepra de forma bipolar incompleta y alternada. Int. J. Lepr. **19** (1951) 29-36.

<sup>4</sup> Ridley, D. S. and Jopling, W. H. Classification of leprosy according to immunity. A five-group system. Int. J. Lepr. **34** (1966) 255-273.

Marked advances are to be found in the field of certain forms that within the L (V) group constitute the L (V) type (the so-called full polar LL forms). These immunoclinical forms have the lowest level of resistance or the maximum value of the S factor of Blumberg<sup>5</sup>. Among these we find the well known "diffuse" forms and the variant, perhaps due to geographic or ethnic factors, described by Latapi's group<sup>6</sup>. Here also are to be found the "rheumatoid arthritis-like" forms described by Karat<sup>7</sup> and studied by Pereira, Jr.<sup>8</sup> under the leadership of the present writer. Of great interest are also the forms observed since the introduction of the sulfones, which are described as "pseudo-exacerbation"<sup>9</sup> or as "acute infiltration"<sup>10</sup>. These forms represent temporary expressions of an attempted healing process occurring in patients with malignant forms of Hanseniasis. These have been defined as "up-grading" phenomena by Ridley<sup>11</sup> and are thought to be manifestations of a gradual increase of cellular immunity or, in other words, an attempt at changing from predominantly humoral to predominantly cellular immunity.

From the biological and epidemiological points of view, great importance should be attached to the forms within group T that constitute the T type (the so-called full polar TT). We would like to call attention to the nodular infantile T forms of Souza Campos<sup>12</sup> and the colliquative T neuritis

("nerve abscess")<sup>13,14</sup>. These forms are an expression of the highest resistance ("the citadel of resistance")<sup>15</sup> or the maximum value of the N factor<sup>16</sup>. These forms of high resistance should not be included in the zone of instability because they are not susceptible to immunological modulations.

Marked advances are also to be found in the field of the immune-positive forms of the T group, among which the following have been described: tuberculoid reactional (TR)<sup>17</sup>, maculo-anaesthetic tuberculoid (MAT)<sup>18,19</sup>, and low resistant tuberculoid (LRT)<sup>20</sup>. In regard to the reactional tuberculoid forms, it must be emphasized that they should be separated from borderline or dimorphous forms. As a matter of fact, these forms are for the most part immune-positive, and they are negative for lipid stains in nearly 100% of cases as shown by Garrido Neves on 8972 sections<sup>21</sup>.

At the International Leprosy Congress in Mexico City, it was once more apparent that there are differences between our points of view and those of some English-speaking authorities. In our view, the concept advanced by Jopling<sup>22</sup>, limiting the whole picture of reactive episodes of the disease to only two types, the classical erythema nodosum leprosum (ENL) and the so-called "reversal reaction" in the course of the malignant B (D) and perhaps L (V) forms, is an oversimplification. In our view,

<sup>5</sup> Blumberg, B. S. and Melartin, L. Conjectures on inherited susceptibility to lepromatous leprosy. *Int. J. Lepr.* 34 (1966) 60-64.

<sup>6</sup> Rodriguez, O., Ortiz, Y., Giner, M., Novales, J., Estrada-Parra, S., Rojas-Espinosa, O., Quesada-Pascual, F., Castro, M. E., Padierna, J., Jiménez, L. and Saúl, A. Avances recientes en la lepra de Lucio. *Dermatol. Rev. Mex.* 22 (1978) 117-182.

<sup>7</sup> Karat, A. B. A. Acute exudative arthritis in leprosy. Rheumatoid arthritis-like syndrome in association with erythema nodosum leprosum. *Brit. Med. J.* 3 (1967) 770-772.

<sup>8</sup> Pereira, Jr., A. C. Novas dimensões da Hanseníase virchowiana. Thesis. Rio de Janeiro. 1970.

<sup>9</sup> Souza Lima, L. The pseudo-exacerbation reactional state of leprosy. *Int. J. Lepr.* 23 (1955) 429-435.

<sup>10</sup> Tajari, J. On acute infiltration reaction of the lepromatous type of leprosy. *Int. J. Lepr.* 23 (1955) 370-384.

<sup>11</sup> Ridley, D. S. Immunological aspects of reactions in leprosy. *Int. J. Lepr.* 36 (1968) 628.

<sup>12</sup> Souza Campos, N. Aspects cliniques de la lèpre tuberculoïde chez l'enfant. *Rev. Bras. Leprol.* 5 (1937) 99-113.

<sup>13</sup> Lowe, J. A further note on nerve abscess in leprosy. *Int. J. Lepr.* 2 (1934) 301-304.

<sup>14</sup> Souza Campos, N. Tuméfaction caséuse des nerfs au cours de la lèpre. *Int. J. Lepr.* 4 (1936) 1-23.

<sup>15</sup> Rabello, F. E. A doutrina de hanseníase na concepção dos hansenólogos de formação latina (1938-1974). *Medicina Cutânea* 3 (1976) 217-226.

<sup>16</sup> Rotberg, A. Some aspects of immunity in leprosy and their importance in epidemiology, pathogenesis and classification of forms of the disease based on 1529 lepromin-tested cases. *Rev. Bras. Leprol.* 5 (1937) 45-97.

<sup>17</sup> Souza Campos, N. Lepra tuberculoïde reacional. *Rev. Bras. Leprol.* 8 (1940) 251-263.

<sup>18</sup> Dharmendra. The maculo-anaesthetic form of leprosy. *Int. J. Lepr.* 31 (1963) 161-177.

<sup>19</sup> Noussitou, F. M. Lepra infantil. Monograph. World Health Organization. 1976.

<sup>20</sup> Leiker, D. L. Low-resistant tuberculoid leprosy. *Int. J. Lepr.* 32 (1964) 359-367.

<sup>21</sup> Garrido Neves, R. A Coloração de Lípidios pelo Sudão. III. Importância na Classificação Histopatológica da Hanseníase. Thesis. Rio de Janeiro. 1976.

<sup>22</sup> Jopling, W. H. Reactional leprosy. (correspondence) *Lepr. Rev.* 30 (1959) 194-196.

these proposed reactive "types 1 and 2" must include a wider roster:

- 1) the classical "lepra reaction" and its ENL
- 2) acute lepromatization<sup>23</sup>
- 3) tuberculoid reactional<sup>17</sup>
- 4) tuberculoid reactivation<sup>24</sup>
- 5) and finally tuberculoid pseudo-exacerbation or RR<sup>9</sup>

In our view, there is no substantial advantage in simply multiplying the number of forms and their proposed marker points, BL, B, BB, BT, to cover the field between the polar groups, L (V) and T, as suggested by Ridley and Jopling<sup>4</sup>. Analysis of the so-called BT histotype shows that we are dealing with an abstract entity in deep contrast with the physical reality of the three well characterized clinical syndromes: tuberculoid reactional or TR<sup>17</sup>, maculo-anaesthetic tuberculoid or MAT<sup>18, 19</sup> and low resistant tuberculoid or LRT<sup>20</sup>.

A most important phase of the pathogenic processes in Hanseniasis is to be found in *group I* (here renamed incipient or *immature*), which makes up up to 50–70% of all forms of the disease. This is the "endemic matrix"<sup>15</sup>, a precious tool in field-work. Hansenologists of the Latin-American endemic countries attach utmost importance to the I group. An adequate designation that can encompass all cases of this I group of patients is of particular interest in terms of the epidemiologic approach.

Based on recent technical advances, the concept of these I cases rests on even more solid grounds. In our view, terms like "uncharacteristic" or "indeterminate" are no longer acceptable. The latter word brings up false subjective connotations and, surprisingly for us, is being used as a synonym for "borderline." This is a misunderstanding certainly to be avoided! It leads to confusion between the pregranuloma forms that are truly I and the advanced forms of the granulomatous area, which show the

TABLE. *Hanseniasis: a key for its types, groups, and clinical varieties.*<sup>a, b, c</sup>

HI—Hanseniasis: the <i>immature</i> group (better than indeterminate), making up up to 50–70% of all cases of the disease (the endemic matrix)
HV—Hanseniasis: the full Virchowian ("lepromatous") polar type and its variants: <ul style="list-style-type: none"> <li>—Virchowian erythema nodosum</li> <li>—Virchowian primary diffuse Lucio-Latapi's syndrome</li> </ul>
Hv—Hanseniasis: the Virchowian ("lepromatous") group and its variants: <ul style="list-style-type: none"> <li>—Virchowian histoid</li> <li>—Virchowian borderline syndrome (B)</li> <li>—BL<sup>21</sup>, borderline lesions close to the Virchowian syndrome</li> </ul>
HT—Hanseniasis: the full tuberculoid polar type and its variants (the "citadel of resistance"): <ul style="list-style-type: none"> <li>—nodular infantile tuberculoid<sup>12</sup></li> <li>—colliquative tuberculoid neuritis ("nerve abscess")<sup>13, 14</sup></li> <li>—micropapuloid tuberculoid Hansenids ("leprids")</li> </ul>
Ht—Hanseniasis: the tuberculoid group including: <ul style="list-style-type: none"> <li>—tuberculoid reactional<sup>17</sup></li> <li>—maculo-anaesthetic tuberculoid<sup>18, 19</sup></li> <li>—low resistant tuberculoid<sup>20</sup></li> <li>—BT<sup>21</sup>, borderline lesions close to the tuberculoid syndrome</li> </ul>

<sup>a</sup> The capital letters V and T are used for the *types*, and the lower case letters v and t are used for the *groups*, with the sole exception of the HI *group*.

<sup>b</sup> Definition of types and groups by Latapi<sup>2</sup> as offered at the Madrid Congress (1953):

*Type*—connotes clinically and biologically stereotyped features, characterized by marked stability and mutual incompatibility.

*Group*—connotes less distinctive or positive characteristics, less stability, and less certainty with respect to evolution.

<sup>c</sup> Criteria of genuine polarity:

1. genotypic basis
2. characteristic phenotype markers
3. rigid immutability of types
4. no intermediate links between the polar *types*
5. characteristic immunopathological patterns

utmost instability<sup>3</sup>. In our view, these I cases are a well defined feature of the disease clinically, histologically, and immunologically. It is, in fact, a *Group* in the sense proposed by Latapi<sup>2</sup>, i.e., an aggregate of unstable forms with a relative degree of homogeneity. The present epidemiological point of view, as seen in the impressive material of 4391 I cases by Bel-

<sup>23</sup> Souza Lima, L. Reação leprotica. Monograph. Serviço Nacional de Lepra. Rio de Janeiro. 1949.

<sup>24</sup> Souza Campos, N. and Rath de Souza, P. Reactional states in leprosy. Int. J. Lepr. 22 (1954) 259–272.

da<sup>25</sup>, and the immunopathological approach<sup>26</sup>, both show the relative homogeneity of the cases included in the I group. Without the rigidity and the probable genetic stability of *Types*, this I group could well be renamed *Immature* or "undifferentiated," changing in English the capital letter I for U. As a matter of fact, among some French hansenologists the term "Indifférencié" has come into current use.

It must be added that we are already in possession of safe markers for cases that can be labeled as "strictly indeterminate" as represented by clinical findings<sup>19</sup>, histological methods (lipid stains)<sup>21</sup>, and immunological methods<sup>26</sup>. Therefore, at the very root of the concept of Latin-American hansenologists, we have in fact a wide and safe basis for the classification of these early cases of the disease, making the I group the "endemic matrix" of the whole process. The quantitative as well as the qualitative importance of group I is impressive not only in Argentina and Brazil but also in Burma, where a hansenologist saw in "infant leprosy" an undifferentiated hanseniasis in 65.8% of the cases (4605 out of 6990)<sup>27</sup>.

The maintenance of group I provides the systematics of the present classification with "a logical and natural starting point," the elimination of which would mutilate all the system<sup>28</sup>. Along these same lines we must remember the accurate expression of

"sub-polar group" by Serial<sup>29</sup> and the masterly paper presented by Cardama<sup>30</sup> at the Mexico Congress. The possibilities of long permanence as I and even of quite numerous "clinical cures" supported by follow-up periods from five to 35 years<sup>31,32</sup> illustrate the legitimacy and the necessity of this I group.

The author of this paper wishes to make a clear point on the subject of polarity as stated recently by him<sup>33</sup> in terms of a mutual incompatibility, probably genetic, between the polar types of Hanseniasis, a phenomenon unique in human pathology. This is due to the fact that the rigidly stable types L (V) and T, the so-called full polar LL and TT, are not subject to immunological modulations in contrast to the forms which, even presenting a histological picture of B or T (TR), may present these up-and down-grading phenomena. The only known analogy to this phenomenon of polarity in Hanseniasis is found in experimental tuberculosis where Diehl<sup>34</sup> pointed out that certain strains of rabbits develop tuberculosis of soft tissues while other strains show pulmonary tuberculosis. Diehl very properly regarded these forms as occurring in two opposing "poles."

—F. E. Rabello

<sup>25</sup> Belda, W. Contribuição ao estudo da epidemiologia da hanseníase indiferenciada (análise de 4391 casos). *Hansenologia Int.* (in press).

<sup>26</sup> Myrvang, B., Godal, T., Feek, C. M., Ridley, D. S. and Samuel, D. R. Immune response to *Mycobacterium leprae* in indeterminate leprosy patients. *Acta Pathol. Microbiol. Scand. (B)* **81** (1973) 615-620.

<sup>27</sup> Noussitous, F. M. School surveys in Burma. *Abst. VIII Int. Lepr. Cong. Int. J. Lepr.* **31** (1963) 565.

<sup>28</sup> Consigli, C. A. Clasificación de la lepra: ubicación de la forma indeterminada. Importancia capital de este tema. *Hansenologia Int.* **3** (1978) 48-54.

<sup>29</sup> Serial, A. Lepra indeterminada. Fisiopatología y evolución histopatológica. *Leprológia* **19** (1974) 144-147.

<sup>30</sup> Cardama, J. E. Early lesions. *Abst. XI Int. Lepr. Cong. Int. J. Lepr.* **47** (1979) 347.

<sup>31</sup> Alchorne, M. Evolução da Hanseníase em 38 enfermos submetidos à reação de Mitsuda há 23 a 35 anos. Valor prognóstico da reação. Thesis. Recife (Brasil). 1974.

<sup>32</sup> Scott, G. C., Russell, D. A., Boughton, C. R. and Vincin, D. R. Untreated leprosy: probability for shifts in Ridley-Jopling classification. Development of "flares," or disappearance of clinically apparent disease. *Int. J. Lepr.* **44** (1976) 110-122.

<sup>33</sup> Rabello, F. E. Le concept de polarité dans la lèpre. *Ann. Dermatol. Syphiligr. (Paris)* **102** (1975) 251-256.

<sup>34</sup> Diehl, K. Gestaltungsfaktoren bei der Tuberculose. In: *Handbuch der Tuberculose*. Band I. Hein, J., Kleinschmidt, H. and Uehlinger, E., eds. Stuttgart: Georg Thieme Verlag, 1958.