

## Relapse or Late Reversal Reaction?

TO THE EDITOR:

Indeed, relapse or reaction is an important subject for a dialogue. Pannikar, *et al.* (4) may, therefore, be complimented for focusing readers. However, it is hard to share their view, that clinically it is often difficult to differentiate between the two. Should the

cardinal clinical expressions of the disease be conceived well, the diagnosis can be made reasonably.

It is not only a question of differentiating relapse from "late reversal reaction," but also type 1 (lepra) reaction as a whole. At this state, therefore, it is imperative to con-

TABLE 1. *Histopathological and immunological features of upgrading (reversal) and downgrading type 1 (lepra) reactions*<sup>(8,10,11)</sup>.

Upgrading reaction		Downgrading reaction
	<u>Histopathology</u>	
1) Well-formed compact granuloma	Granuloma	1) Loosening granuloma
2) Granuloma approximates the epidermis		2) Granuloma extends downward into the dermis (free subepidermal zone may be present)
3) Exocytosis		3) Relatively clear eosinophilic zone approximates the epidermis
1) Plenty of lymphocytes of epithelioid cells	Cells	1) Increasing macrophage representation in the granuloma, moderate epithelioid cells, and lymphocytes
2) Occasional, or a few, giant cells		2) Giant cells conspicuously absent
1) Increasing destruction of nerves	Nerves	1) Intensely infiltrated, prominent nerves in the granuloma
1) Reduction in BI from 4-5 to 0-2	Acid-fast bacilli	1) BI may increase
	<u>Immunology</u>	
1) A significant increase in T lymphocyte count		1) Decrease in T lymphocytes
2) Decrease in B lymphocytes and IgG level		2) Increase in B lymphocytes and IgG level
3) Significantly augmented NK-cell activity		3) Decreased NK-cell activity
4) Increase in interleukin 2 (IL-2) and IL-2 receptor (IL-2R)		4) No change in interleukin activity

TABLE 2. *Criteria for downgrading reaction and downgrading per se.*

Downgrading reaction	Downgrading per se
	<u>Morphology</u>
1) Lesions in downgrading reaction show	1) Change in morphology as follows:
a) Erythema	a) From well-defined to ill-defined
b) Edema	b) Irregular or serrated margins
c) "Inverted saucer" appearance	c) New satellite lesions
d) Expansion of lesions	2) Conspicuous absence of edema and tenderness
e) Appearance of new lesions	
	<u>Number</u>
1) Increase in number of lesions with preceding features	1) Increase in number of lesions beyond 3 to uncountable
	<u>Nerves</u>
1) Excruciatingly tender enlarged nerves	1) Increase in number of nerves involved, which may or may not be tender
	<u>Bacterial index</u>
1) BI may or may not show significant change	1) BI increases from 0-2 to 4-5
	<u>Lepromin</u>
1) May or may not change significantly	1) Lepromin changes from +++ to ±
	<u>Histopathology</u>
1) Granuloma shows	1) Granuloma shows similar changes as in downgrading reaction; however, edema is conspicuously absent
a) Loosening of granuloma	
b) Increase in histiocytes	
c) Absence of giant cells	
d) Decrease in lymphocytes	
e) Granuloma pushed down to mid- or lower dermis	
f) Edema of collagen fibers manifested as progressive lightening of eosinophilic staining of dermis	

ceive that type 1 (lepra) reaction may manifest either as an "upgrading" (reversal) reaction or a "downgrading" reaction. They are characterized by erythema, edema and tenderness of the macules and/or plaques (<sup>1, 2</sup>). Classically, it expresses itself as an "inverted saucer," in contrast to the "saucer,

the right way up." Of course, the nerves supplying or feeding the patch(es) may be excruciatingly tender or enlarged. Should these changes be confined to one or a couple of lesions, the reaction may be upgrading (reversal) reaction. Occasionally, the immune response may be so severe as to result

TABLE 3. *Criteria differentiating relapse from type 1 (lepra) reaction.*

Relapse	Type 1 (lepra) reaction
1) Adequately treated as per WHO recommendation	1) May or may not have received adequate treatment
2) Complete subsidence of disease with no residual clinical or histopathological evidence of activity	2) Disease may not have subsided completely.
3) Reappearance of lesions from a few previously involved areas or a part of the area involved by previous lesion	3) Appearance of lesion at fresh, previously clinically normal site
4) Classification remains constant: BT, BB, BL	4) Upgrading: BT, BB, BL. Downgrading: BT, BB, BL
5) Reappearance of nerve involvement in previously involved nerves, which had become quiescent following adequate treatment	5) Fresh nerve involvement in addition to aggravation of previously involved nerves
6) Reappearance of activity is insidious and may occur long after treatment is stopped	6) Onset is usually acute and severe
7) Histopathology and lepromin reaction conforms to classification of previous episode	7) There is change in histopathological and lepromin findings during reactional episode
8) Responds to multidrug therapy (MDT) alone	8) Treatment of reaction required in addition to MDT
9) No apparent systemic signs or symptoms	9) May be accompanied by constitutional signs and symptoms

in ulcerative plaques<sup>(9)</sup>; whereas in downgrading reaction, the afore-mentioned features may affect almost all of the existing lesions. In addition, the expansion of the existing plaques and the appearance of fresh lesions<sup>(9, 11)</sup> is contributory. These changes may be attended by pyrexia. Type 1 (lepra) reaction may be recorded in borderline tuberculoid (BT), borderline borderline (BB), and borderline lepromatous (BL) leprosy. Furthermore, intercurrent infections, pregnancy and drugs may precipitate these episodes<sup>(9, 11)</sup>. Type 1 (lepra) reaction, therefore, should be considered as a mirror image of the ameliorating or deteriorating cell-mediated immunity<sup>(8, 10, 11, 13)</sup>. Histopathology and immunology may be complementary to clinical impression and are depicted in Table 1<sup>(7, 11)</sup>.

At this juncture, it is relevant to highlight the clinical as well as histopathological features of downgrading reaction, and downgrading per se<sup>(9)</sup>. The latter phenomenon is a part of the natural evolution of the disease, and is envisaged in the continuous spectrum of leprosy (Table 2).

The term "relapse in leprosy" should preferably be replaced by "reactivation leprosy," a self-explanatory term, in order to avoid confusion. Nevertheless, the relapse/reactivation leprosy should be recognized by the criteria laid down afresh in an abridged form (Table 3). This was considered imperative for few of the parameters appeared superfluous<sup>(4)</sup>.

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