Volume 73, Number 1
Printed in the U.S.A.
(ISSN 0148-916X)

CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of the Journal is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the Journal and thus interfere with its prime purpose.

Some Considerations on the Origin of Type 1 Reactions in Leprosy[1]

To the Editor:

The World Health Organization (WHO) suggests the use of corticosteroids to differentiate a relapse from a reaction in cases in which new lesions appear after the completion of treatment with multi-drug therapy (MDT) ([8]). If lesions improve, it is a case of type 1 reaction that must be treated only with such drugs. This immunological phenomenon would not have significance other than the fact of being a response to remaining *Mycobacterium leprae* antigens that would be exposed to the host defenses. If a patient keeps having reactional episodes after anti-leprosy treatment, the anti-inflammatory therapy should be continued.

Nevertheless, I believe that reactional episodes may result from multiplication of bacilli that were not destroyed by treatment. If this hypothesis could be demonstrated, these reactions would be considered relapses, and that would be a reason for the WHO's statistics on relapses to be changed.

In general, type 1 reactions occur in pre-existing lesions that may appear as hypochromic macules with sensory changes, sensation or well constituted borderline or tuberculoid lesions with chronic evolution. These reactions are often times exuberant and occur before, during, or even after release from treatment ([3]).

All these reactions are presented with the same clinical characteristics. The bacilloscopy may be negative or positive, and if positive, bacilli may show degeneration in reactional episodes occurring before treatment, as well as during treatment.

In the pre-sulphone era, the authors carefully observed the natural history of some reactional cases and reported tuberculoid patients with certain reactions in which bacilli and lesions disappeared spontaneously. After some time or even years of quiescence, reactions reappeared with lesions and bacilli ([1, 5, 6]). These observations suggest that the *M. leprae* may remain for long periods in a state of metabolic inactivity, inaccessible to organic defenses (possibly as persisters). At a certain moment, maybe because of intercurrent diseases or other immunological changes, bacilli start to multiply again, initiating a new reactional episode.

If that happened in the past, it may also happen today, i.e., the bacilli can remain as persisters and not be destroyed by the immune defenses or treatment. The cell mediated type 1 reaction may somehow be related to multiplication of bacilli. The degenerated aspect of the bacilli may result from the multiplication of bacilli and their exposure to the effects of drugs that are being used, or to the immune defenses. The microorganisms are destroyed and release antigens that give rise to a hypersensitivity reaction (type 1 reaction). In reactions occurring after treatment, if the number of bacilli is low, the patients become cured because the body defenses destroy the bacilli. If there are many bacilli and the organic defenses are unable to control the infection, there will be new reactions and

risk of nerve involvement and development of disabilities.

Recently, Shetty, *et al*. ([4]) studied 25 cases of borderline-tuberculoid leprosy that presented with new lesions from 1 to 13 years after being released from treatment. Viable bacilli were found in the footpad of inoculated mice in 48% of the biopsies of those patients. Remarkably, the incidence of viable bacilli was higher (58%) in those patients whose histopathology showed evidences of reversal reaction.

Waters ([7]) commentary on Shetty's work, referred to his own patient with a tuberculoid lesion on the face that appeared 40 years after the patient had been apparently cured, and admitted that the authors presented evidence that viable bacilli can cause relapse in borderline-tuberculoid leprosy, and that these relapses may be associated with reversal reactions.

I also studied a patient similar to Waters ([2]). She was a patient who presented with extensive erythemato-hypochromic flat lesions on the trunk and extremities, with a negative bacilloscopic index (BI), which disappeared after 2 years of treatment with chaulmoogra oil. More than 40 years later she presented a reactional episode with large erythematous plaques on the entire skin, with a positive BI (++++) of the lesions, during an unbalanced diabetes mellitus.

These observations reinforce my interpretation of type 1 reactions, i.e., they are the result of multiplication of persisters.

There are no proofs of this hypothesis being true, but on the other hand, there is nothing showing it to be wrong.

I think the WHO should look at type 1 reactions more carefully during the evaluation of MDT results.

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Dr. Opromolla passed away while this issue was in production. The JOURNAL extends its condolences to the family of this longtime professional in the leprosy field. Dr. Opromolla's obituary will appear in the June issue of the JOURNAL.

REFERENCES

1. LIMA, LAURO DE SOUZA, and MAURANO, FLAVIO. *Reação leprótica.* Rio de Janeiro: Ministério da Saúde, 1949.
2. OPROMOLLA, DILTOR, and ARAÚJO, VLADIMIR. Recidiva ou reação reversa? Hansen Int. Bauru **19(1)** 1994.
3. PFALTZGRAFF, ROY E., and RAMU, GOPAL. Clinical leprosy. In: *Leprosy,* 2nd edn. Edinbugh: Churchill Livingstone, 1994.
4. SHETTY, V. P., WAKADE, A., and ANTIA, N. H. A. A high incidence of viable *Mycobacterium leprae* in post-MDT recurrent lesions in tuberculoid leprosy patients. Lepr. Rev. **72(3)** (2001) 337–344.
5. WADE, H. W. Tuberculoid changes in leprosy. II. Lepra reaction in tuberculoid leprosy. Int. J. Lepr. Other Mycobact. Dis. **2(2)** (1934) 279–292.
6. WADE, H. W., RODRIGUEZ, J. N., and TOLENTINO, J. G. The course of open cases of tuberculoid leprosy at the Cebu Leprosarium. Int. J. Lepr. Other Mycobact. Dis. **7(4)** (1939) 473–494.
7. WATERS, M. F. R. Distinguishing between relapse and late reversal reaction in multidrug (MDT) treated BT leprosy (Editorial). Lepr. Rev. **2(3)** (2001) 250–253.
8. WHO EXPERT COMMITTEE ON LEPROSY. Sixth Report. Geneva: World Health Organization, 1988. Tech. Rep. Ser. 768.

TO THE EDITOR:

It was interesting to read the article "Neuropathic pain in leprosy patients" by Stump, *et al.* ([3]). They have noted that a fair number of patients continue to suffer from neuropathic pain in leprosy. This probably is due to the treatment cut off point of 6 months or 12 months, depending upon the type of leprosy. Some patients do continue to complain of paresthesia even long after the activity is subsided. The series of Stump, *et al*. includes cases that were still on treatment.

The clinical activity takes fairly longer than the bacteriological cure. The World Health Organization regimens are meant to "kill" the maximum number of germs in shortest possible time. The body has to take care of the scavenging and it might suffer in the process. The process of nerve regeneration further complicates the issue, and if irritants are present, paresthesia develops. Moreover, the compressing elements con-

tinue to persist and are "assisted" by intraneural and perineural fibrosis. As a consequence, a "neuroma in continuity" develops and the pain continues.

Mishra, *et al*. ([1, 2]), while reporting their observations on development of leprosy lesions, noted that at least some of the lesions start as a vague dysthesia, meaning that positive phenomena occurs before a negative phenomena (sensory loss). "Painless" nerve damage has been glorified as silent neuropathy. It is very likely that those nerves have whispered before destruction, which patients were not able to hear due to the faintness of the sound or their preoccupation with other things. Logically, pain (including paresthesia and dysthesia is a part of neural affection its intensity may vary depending upon the type of affection and the speed of damage.

Probably, both neuropathic pain and inflammatory pain exist together in leprosy. Even in acute neuritis, the pain is more than what is expected in pain of a purely nociceptive nature. That is probably the reason that many times acute neuritis is referred to as acute painful neuritis. The contribution from inflammation and neuropathy may vary from patient to patient and from time to time. The paresthesia complained of is usually of an annoying type, and with the advancing age of patients many other discomforts are added to it. It will be interesting to relate the paresthesia with disease activity in "cured" patients but, on the other hand, it also scares me. Any suggestion or discussion about pain might exacerbate the problems because patients are relatively unstable emotionally and tend to develop dependence because of peculiar psychosocial effects of the disease.

Mild paresthesia can be managed with suggestions and counseling, whereas disabling paresthesia needs drugs in addition. But before all that can be formulated and put into practice, treatment of leprosy has to be modified from community approach to individualized approach.

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REFERENCES

1. Mishra, B., Mukherjee, A., Girdhar, A., Husain, S., Malaviya, G. N., **a**nd Girdhar, B. K. Evolution of early lesions in leprosy. Lepr. Rev. **64** (1993) 259–266.
2. Mishra, B., Mukherjee, A., Girdhar, A., Husain, S., Malaviya, G. N., and Girdhar, B. K. Neuritic leprosy: further progression and significance. Acta Leprologica **9** (1995) 187–194.
3. Stump, P. R. N. A. G., Baccarelli, R., Marciano, L. H. S. C., Lauris, J. R. P., Teixeira, M. J., Ura, S., and Virmond, M. C. L. Neuropathic pain in leprosy patients. Int J Lepr. Other Mycobact. Dis. **72** (2004) 134–138.