Aspectos clínicos da reação reversa / *Clinical aspects of the reversal reaction*

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Introduction

Nerve damage leading to permanent disabilities and impairments is the major problem in the course of a leprosy infection (Fig. 1). Were it not for this, leprosy would be a rather innocuous skin disease, whereas even today, it is one of the most feared diseases often associated with serious social repercussions.

The nerve damage may occur before antimycobacterial treatment, during the treatment and even in patients who are labelled cured (1, 2). Especially when it occurs during or after treatment it is frustrating to the patient and embarrassing to the physician (Table 1).

Table I - Reversal Reaction in leprosy on MDT attending the leprosy clinic at the Erasmus University in Rotterdan (n = 115; PB 72; MB 43)

	during treatment	after treatment
Paucibacillary	7%	3%
Multibacillary	9%	9%

In borderline leprosy (BT, BB and BL) such damage usually develops during a "Reversal Reaction" (RR). Peripheral nerve trunks at specific sites become swollen and tender and may show deterioration in function. Mostly, this deterioration is rather gradual, taking weeks or even months to become irreversible. Occasionally, severe nerve damage may occur overnight (1).

In lepromatous leprosy (BL, LL_S and LL_P) the damage develops gradually, taking years to develop, or increases suddenly during a reactional episode, usually a phenomenon called Erythema Nodosum Leprosum (ENL) (1), in a few cases admixed with a reversal reaction.

Reactions must be diagnosed early and treated adequately without undue delay if permanent disability is to be avoided (2, 3). In order to achieve this it is of utmost importance to understand the mechanisms behind the reactional states and to detect and diagnose the reactions correctly and in time. Untreated reactions with an increase of impairments are a shame to the leprosy programme and a disgrace to its management (2).

This paper will be helpful in the recognition of a reversal reaction

Many names have been attached to this type of reaction which has led to fierce arguments among leprologists who did not understand each others' definitions and terminology and hardly listened to each others' arguments. As result, for quite some time there was an Anglosaxon-French leprology and a Spanish-Portuguese-South American leprology. Some of the "terms" used: reversal reaction, borderline leprosy reaction, tuberculoid reaction, tuberculoid in reaction, active tuberculoid leprosy, downgrading borderline leprosy, upgrading versus downgrading reaction and Jopling type I reaction. Some of these terms cover each other partly, others completely but are conceptually different. However, recently leprologists reluctantly start to speak the same language.

Diagnosis of reaction (1)

Skin involvement frequently accompanies nerve involvement, but may as well precede or follow the nerve damage. Clinically, a reaction may be suspected when there is increased inflammation of pre-existing skin lesions.

Hypopigmented or only slightly erythematous macules become red and swollen (Fig. 2), form plaques and occasionally undergo ulceration (Fig. 3). Crops of new lesions may suddenly appear in previously clinically uninvolved skin (Fig. 4). Sometimes, extensive oedema of the extremities or face may be present, in particular in BL-patients (Fig. 5).

Patients may complain of a burning, stinging sensation in the skin lesions and complain of aches and pains in the extremities or in the face and of loss of strength and/or sensory perception. They may suddenly start to drop things from their hands or stumble when walking. They also may develop blisters without knowing the cause (Fig. 6). However, contrary to patients with ENL they are not ill. Some have remarkedly few complaints; therefore, detection may be delayed or even missed, thus objective parameters are necessary. These consist of mapping (drawing) the lesions, which is tedious but certainly worthwhile, and of careful assessment of nerve functions. It is important to note whether hands and feet are sweating or have new dry areas. The appearance of dry areas or an increase in size is often a first sign of an incipient reaction. Nerves may become swollen and feel thickened, and are tender on palpation. The Tinell sign may become positive, e.g. pressure exerted on the nerve gives distally a tingling pain.

It is very important to let a patient close his eyes lightly, and to notice any flicker movement of an eyelid or a slight gap in the closure which may herald further damage (Fig. 7). It must be noted that when a patient is asked to close his eyes firmly such a minimal damage will pass unnoticed.

A numerical system has been developed to assess muscle strength, the Voluntary Muscle Testing (VMT) (4). When this test is regularly and carefully done it will assist in the early detection of a reaction. The facial, ulnar, median and peroneal nerve should be assessed. A deterioration in VMT may precede more obvious clinical signs. However, the test is a little crude, so minimal damage may go unnoticed. A more sensitive method, in particular for minimal and mild nerve damage is the graded sensory bristle test (Fig. 8) which uses standardized nylon monofilaments (5).

The graded bristle test can be done by mapping areas for sensory loss and by grading this loss. However, due to its sensitivity and tediousness it is prone to inaccuracy and can therefore only be used effectively by experienced investigators. It is more simple to assess a small defined area like the thenar area for the median nerve, the hypothenar area for the ulnar nerve and the plantar forefoot and heel for the posterior tibial and common peroneal nerve. Care must be taken not to assess within a skin patch when present. Table 2 shows its use in the follow-up of a patient to detect a reaction early.

An other sensory test which may be of use, especially for the foot is the 2-point discrimination test which is done by means of a paperclip bent to a calliper (Fig. 9a,b,c). Its use is shown in Table 3. It is less sensitive than the graded bristle test when this test is used for the mapping of the foot, but nearly as sensitive as the graded bristles when used on defined areas like forefoot or heel (6).

In the field, extensive sensory testing and VMT's are out of reach. However, in our experience limited testing is certainly possible like the VMT of the orbicularis oculi for the facial nerve, of the opponens pollicis brevis for the median, the abductor digiti minimi for the ulnar and the dorsal flexion of the foot for the peroneal nerve. Since the use of only 3 grades as often is done, is too crude the 5 point scale should be used even under field conditions, provided proper supervision and training is continuously provided. The same applies for sensory testing. Ballpoint and pinprick testing are too crude while graded bristle testing is not. In the field, the testing of thenar, hypothenar and foot has shown to be possible by a well trained field staff (Fig. 10).

It should be noted that more sophisticated physiological methods such as EMG, sensory and motor nerve conduction velocity testing (5), evoked response testing and measuring of autonomic reflexes (7) add little to the early detection of a reversal reaction. The same applies to laboratory tests such as the follow-up of cytokines, TNF- , IL-1 or IL-2 (8, 9, 10) or activation products like neopterin (11) and more

Table 2 - Follow-up of a patient developing a RR using different parameters. The ST showed to be very sensitive (arbitrary nummerical system).

Data	24/4	20/6	15/8	9/9	16/9	30/9
Clinical Condition	Well	Well	No complaints	Severe rheumatic pain; obvious reversal reaction	Better	Well
Antireaction treatement	Predni-solone	Stop predni-solone	-	Restart prednisolone	Predni-solone	Predni-solone
VMT	2	2	6	4	4	4
MCV	4	4	4	7	5	5
ST	39	25	56	69	52	37

Table 3 - Two-point discrimination test used on the feet for the follow-up of a patient in the course of a reaction.

				restart treatment	
TD	RFC			obvious relapse	
♂	January 1976 16 mm	July 1977 18 mm	August 1977 25 mm	October 1977 > 30 mm	July 1978 17 mm

elaborate testing of the cell mediated immunity like lymphocyte transformation tests and migration inhibition tests. Even pathology and immunopathology are only of some help (12). It is still the clinician who by careful observation and simple tests has to detect the reaction.

Sometimes, especially in BL and LL_s patients it is difficult to discern a RR from an ENL. They may even occur together. Some signs and investigations may be of help in the differential diagnosis. ENL is a generalized disease, in which beside skin and nerve other organs like joints and lymphglands may be involved. The patient may be ill, during a RR he usually is not, he may have a rised temperature and ESR, and even protein in his urine. The skin lesions in ENL are mostly tender, those in a RR are not. The lesions in a RR may have sensory loss in comparison to the surrounding skin, in ENL this is usually not the case. Palpating the lesions, an ENL plaque consists of confluent papules and nodules and in a RR the lesions feel more homogeneous. Both ENL and RR lesions may ulcerate, but a smear from an ENL lesion shows predominantly polymorphes, that of a RR lesion lymphocytes. Two old tests may be of help. The Ryrie-test: stroking the sole of the foot with the back of a reflex hammer elicits a burning pain which also may be noticed when watching the patient walk, who walks as if he is walking on hot coals. Another test is the Ellis-test: squeezing the wrist during ENL elicits a painful reaction; this does not occur during a RR unless the radiocutaneous nerve is tender (13).

In conclusion, when during and/or after treatment there is an increase in nerve damage due to a RR the leprosy control programme can be blamed, since an adequate follow-up of a patient and proper treatment of a RR are no distant possibilities.

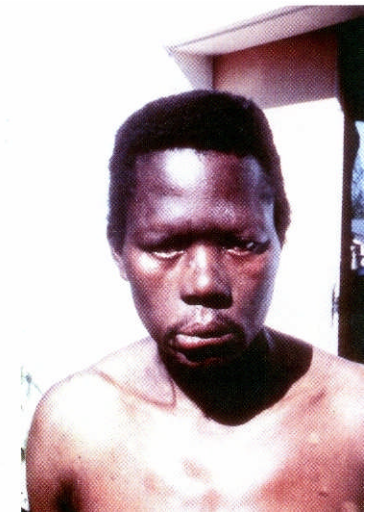

Fig. 1: No facial expression, difficulties in non-verbal communication (BL patient).

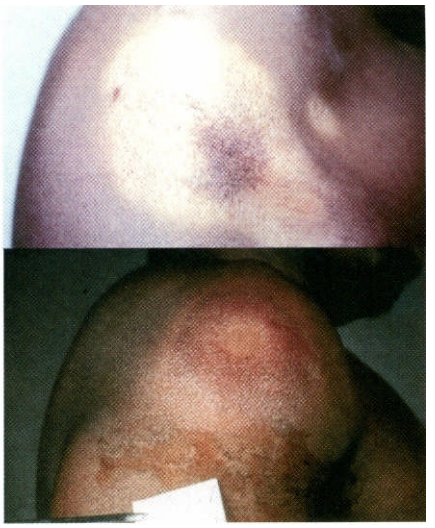

Fig. 2ab: Before and after the start of a **RR:** new inflamed leasion(BL patient).

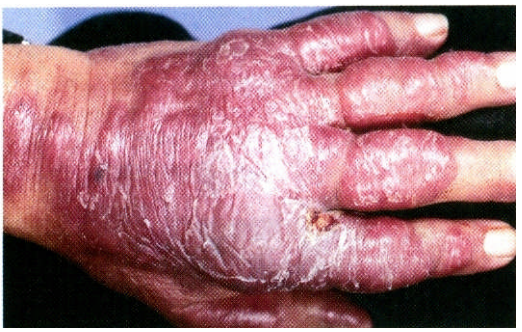

Fig. 3: Ulceration during an active RR in a BB patient).

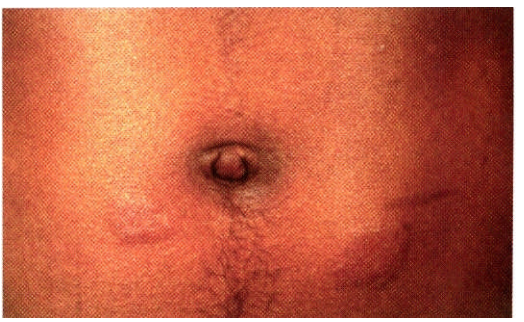

Fig. 4: New lesion accompanyng a RR in a BT-BB patient.

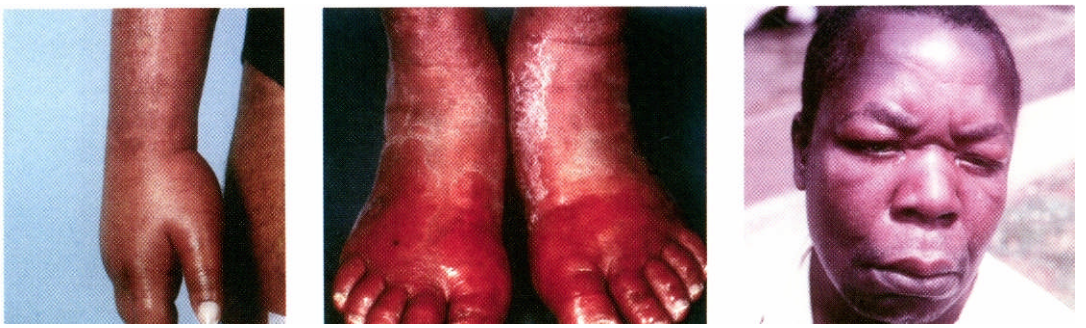

Fig. 5abc: Edema of extremities: a. hand. b. feet. c. face, during a RR in a BB-BL patient.

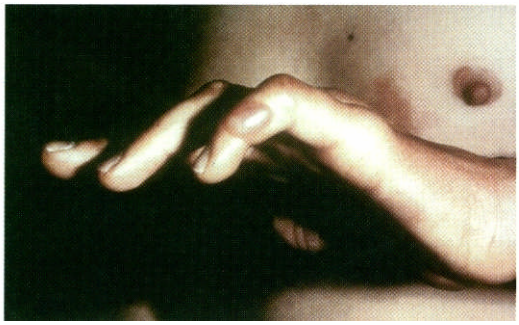

Fig. 6: Blister heralding a RR in a BT patient.

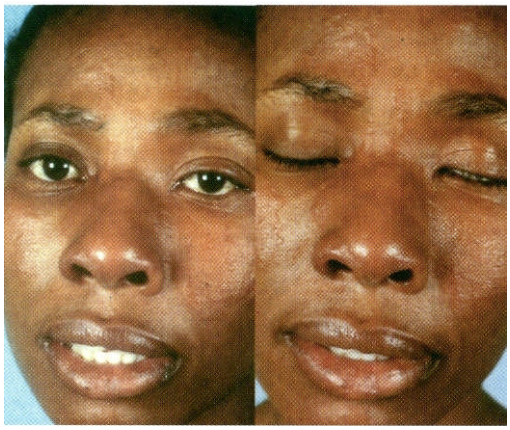

Fig. 7ab: Gap in closure of the eyelid during light closure of the eye in a BL patient.

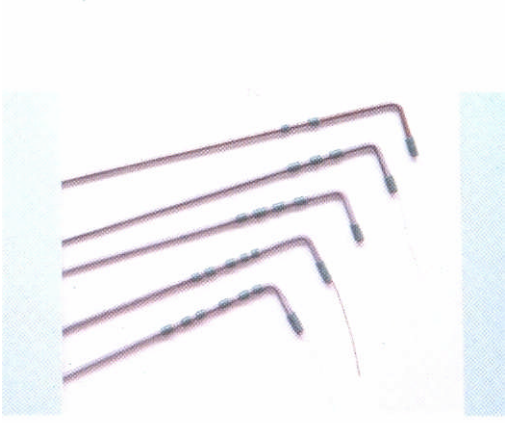

Fig. 8: Graded Bristle Test as used by Weddell, Pearson and myself.

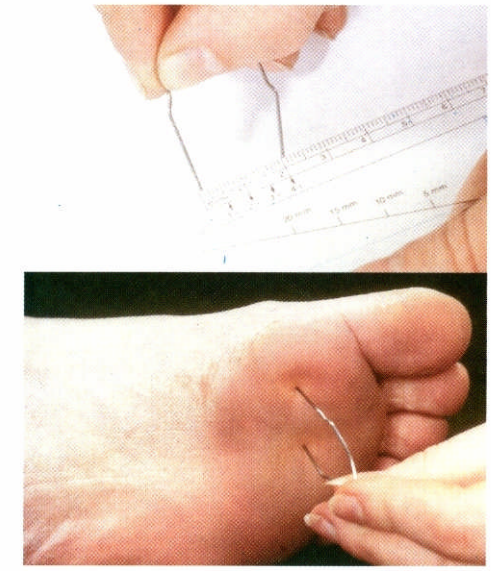

Fig. 9ab: Paperclip used as a calliper for testing the sensation of the foot.

Fig. 10: Sensory Testing by means of Graded Bristle Testing in the field.

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