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The Prevalence and Consequences of Mis-reinnervation in Facial Neuritis[1, 2]

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The phenomenon of mis-reinnervation was reported in leprosy for the first time in an earlier report ([9]). This misdirection of regenerating axons was noted, chiefly in the facial nerve, by a number of investigators following Bell's palsy ([12, 13]) in inflammation due to a nearby focus of infection ([3]) and following trauma ([3, 10]). While there is no reason to think that mis-reinnervation should not occur in leprosy, nevertheless, since this had never been reported, the evidence for it was unexpected. The evidence noted was voluntary co-contraction of physiologically unrelated muscles seen 21 times in 16 of 22 patients, and 7 co-contractions associated with the reflex act of blinking (blink bursts) in muscles which are not normally activated by the blink reflex. The abundance of this evidence made us wonder how such an apparently common phenomenon could have escaped recognition for so long (Fig. 1).

It was postulated in our article that possibly this is not so common and the prevalence was unusually high because the patients in this series were special cases; all with an established paralysis of more than two years' duration and all with severe enough paralysis to require temporalis transfer. Consequently, a new study was undertaken to determine the prevalence of mis-reinnervation in all patients admitted for whatever reason to the department of reconstructive surgery at this hospital.

MATERIALS AND METHODS

During the 13 month period, 7 December 1971 to 8 January 1973, 770 patients were admitted either for trophic ulcer treatment or for reconstructive surgery. Each patient was subjected to a thorough medical assessment for the purpose of determining the presence and nature of deformities. Seventeen patients with facial paralysis and/or paresis were detected, 5 unilateral and 12 bilateral, providing a total of 29 face halves to be studied. One patient was female. Their ages ranged from 25 to 65 with an average age of 43 years. The duration of paralysis ranged from 4 days to 18 years with an average of 6.25 years. The classification of the 17 patients was 4 lepromatous, 12 borderline and 1 tuberculoid. None of them had a recent history of reaction involving the facial nerve.

In all cases, the m. frontalis a centimeter above the center of the eyebrow, the m. orbicularis oculi of both lids near the center of each lid margin, and the m. levator labii superioris just above the naso-labial fold were studied using a Medlec MS3R 2-channel electromyograph machine and concentric needle electrodes. As in our earlier study, a single insertion technic of muscle sampling was employed, and the needle was moved about deep to the skin to make sure that it was in the desired muscle. This was particularly important in cases showing no activity.

The pars orbitalis was not deliberately studied but when co-contractions were detected on needling the m. frontalis it was necessary to determine whether they were being picked up from frontalis or from the pars orbitalis of upper lid orbicularis oculi, and abnormal findings in the latter also were recorded. These were distinguished from m. frontalis activity either by simultaneous clinically evident downward movement of the eyebrow or by the radically different nature of the sound and wave form from those of voluntary m. frontalis activity. In the lower lid the pars orbitalis was also explored in those cases with clinically apparent blink bursts (or voluntary co-contractions), but not routinely.

RESULTS

The general pattern of electromyographic

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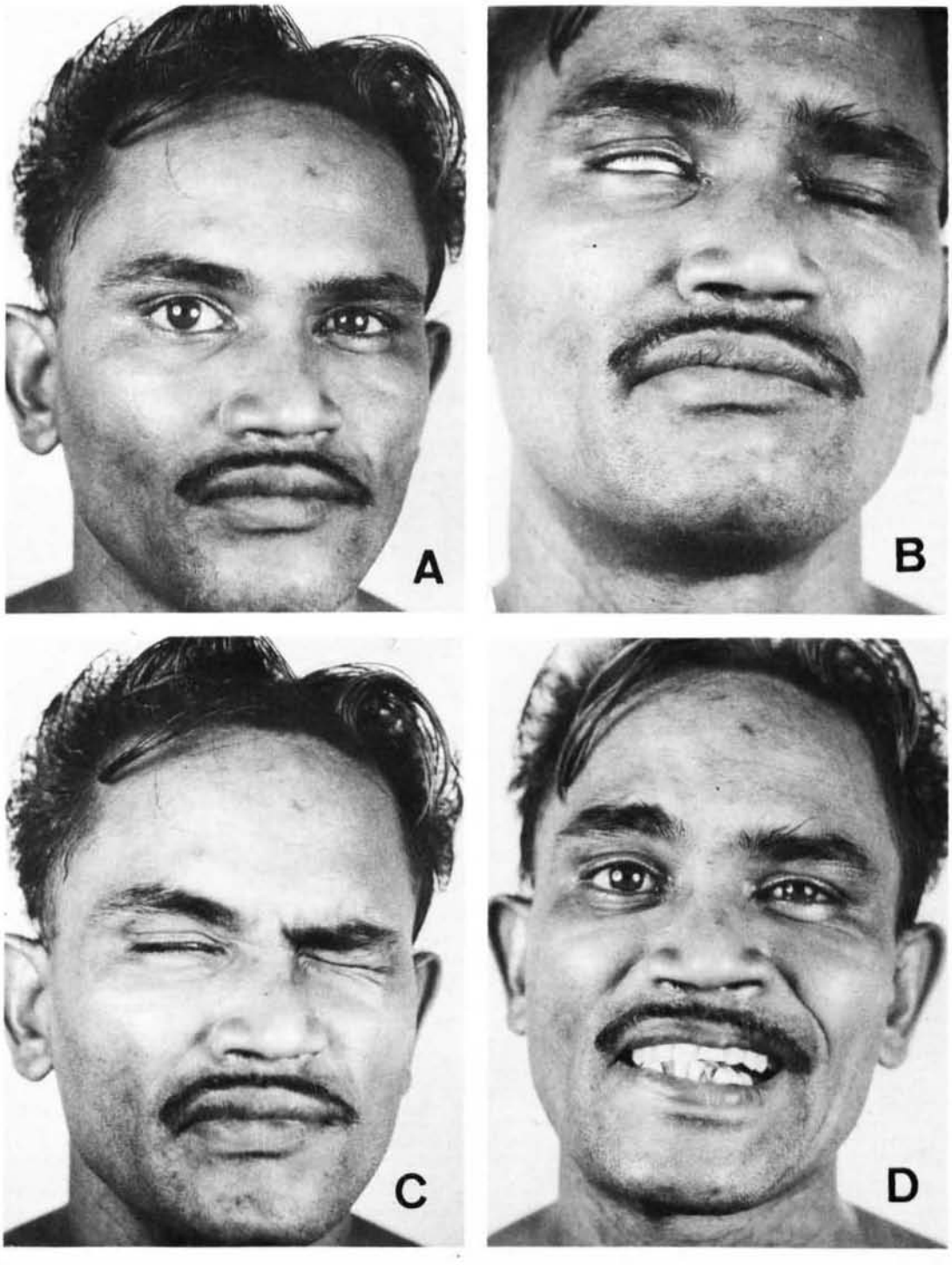

FIG. 1. An unusual but highly instructive case of mis-reinnervation over a long distance (not in the series).

A. Eyes open.
B. Eyes gently closed. Right eye is unable to; instead there is ipsilateral mentalis contraction.
C. Tight closure increases mentalis activity.
D. Lower facial paresis is apparent on the right.

TABLE 1. *Type of electromyographic activity seen in the four muscles studied.*

	Electromyographic wave form			Pathologic activity		
	Full pattern	Incomplete pattern	No activity	Voluntary co-contraction	Blink bursts	Twitch
Frontalis	9	19	1	0	0	0
Upper lid	2	14	13	4[a]	3[a]	0
Lower lid	2	21	6	6	2[a]	0
Levator labii superioris	11	16	2	4	6	1
Total	24	70	22	14	11	1

[a]Occurred in pars orbitalis.

TABLE 2. *Source of misdirected axons responsible for abnormal voluntary contraction and site of reflex activity in the upper and lower halves of the orbicularis oculi and levator labii superioris.* [*See text*]

Patient number & side		Voluntary co-contractions			Blink bursts		
		Upper lid	Lower lid	L.L.S.[a]	Upper lid	Lower lid	L.L.S.
330	R	L.L.S.[b]	Frontalis L.L.S.		+[b]		
566	R			O. oris		+[b]	
566	L		L.L.S.	O. oris		+[b]	+
6181	L		L.L.S.				+
11059	R			O. oculi			+
11194	R	L.L.S.[b]					+
11246	R	L.L.S.[b]	L.L.S. O. oris	O. oculi	+[b]		+
11246	L	L.L.S.[b]			+[b]		+

[a]L.L.S. = levator labii superioris.
[b]Occurred in pars orbitalis.

activity in the 29 face halves studied is shown in Table 1. The highest number of incomplete patterns occurred in the lower lid and the lowest number in the upper lid. Of all muscles studied, the upper lid had the highest prevalence of complete paralysis (13 of 29), but only six lower lids were completely paralyzed. In the upper lid voluntary co-contractions were limited to the less effective pars orbitalis whereas in the lower lid six of the voluntary co-contractions seen were in the lid portion (pars palpebralis).

Of the 17 patients studied, six (35%) showed electromyographic evidence of misreinnervation. This was clinically apparent in only four. Eight of the 29 nerves (28%) supplied muscles in which 14 voluntary co-contractions in the form of one or two tri- or biphasic motor unit potentials and 11 blink bursts took place. Neither of these phenomena occurred in the frontalis muscle. By definition, blink activity in the m. orbicularis oculi can only be considered abnormal (i.e., a blink burst) if it occurs in the pars orbitalis, which under normal circumstances is under voluntary control only. Hence, blink burst activity can only be ascribed, in the case of this muscle, to the pars orbitalis.

Only one "twitch" occurred electromyographically. Three were seen clinically but, on electrical study, two revealed themselves to be blink bursts. The third was a continuous low pitched 40 microvolt potential in the lower lid not related to blink activity or any

apparent activity of other muscles. This increased in amplitude to 60 microvolts on activating the m. levator labii superioris, but, as no tonic activity could be demonstrated in the latter muscle between episodes of voluntary activity, this motor unit potential has not been listed as a voluntary co-contraction. Fibrillation potentials and giant motor units were not seen in this series.

Table 2 shows the source of misdirected axons responsible for abnormal muscle contractions. The upper lid was mis-reinnervated in four instances by nerves which normally supply the levator labii superioris. The same was true of the lower lid, but two of the lower lids mis-reinnervated as above, also received nerve fibers from other sources, namely nerves to the m. frontalis in one instance and orbicularis oris in the other. The levator labii superioris was mis-reinnervated in two instances from above by nerves to the m. orbicularis oculi and in another two from below by those of the m. orbicularis oris (Fig. 2).

The reflex contractions (blink bursts) listed in Table 2 had as their source nerves to the pars palpebralis of m. orbicularis oculi. Therefore, blink bursts noted in the lids were in each instance clinically visible contractions in the pars orbitalis confirmed electromyographically to coincide with pars palpebralis contractions in the same lid.

DISCUSSION

As in our previous study ([9]), the upper lid was more completely paralyzed than the lower. This statement refers to the neurological status and is of interest with respect to the pathogenesis of the nerve lesion. Clinically a gravity-assisted upper lid closes much more effectively than a lower lid with one or two motor units working against gravity. This distinction needs to be made quite clearly in view of the statements in the literature that the lower lid is more often affected ([1, 2]). Even after electromyographic studies, some workers have stated that the upper lid is more severely paralyzed ([2, 7]). In this series with only two upper and two lower lids showing a normal EMG pattern the upper and lower lids were equally affected.

The lower lid was less often completely paralyzed, but the degree of muscle activity remaining was not enough to give the lower

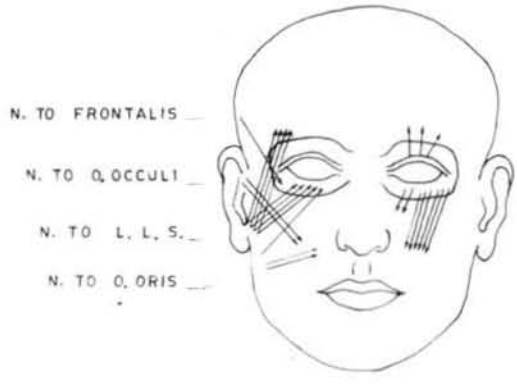

FIG. 2. Diagrammatic summation of all evidence of mis-reinnervation in eight facial nerves.

lid a clear functional advantage over the upper. It is difficult to assess the functional value of the extra motor units available due to mis-reinnervation. While in this series the functional effect of lower lid activity was not under investigation, it is commonly noted by those treating lagophthalmos that paralysis or paresis of the lower lid is functionally more important and clinically more apparent. However, our interest here is in the pathologic process taking place in the facial nerve and it is chiefly in this regard that there is a significant difference between those fibers supplying the upper lid and those supplying the lower. Of the 27 affected upper lids, 13 had no activity in the site explored compared with 6 with no activity in the same number of affected lower lids.

It is in this context that the origin of voluntary co-contractions, chiefly from nerves supplying muscles more inferiorly situated is important (Fig. 2). Eleven of the co-contractions were associated with activity of more inferiorly situated muscles, suggesting that the nerves supplying these muscles were healthy enough to send axons into other denervated, or possibly partially denervated muscles. The ability to do so is probably related to the usually less frequent involvement of lower branches, commonly noted in leprous neuritis. But, for this phenomenon to occur at all, some pathological process must be at work in the nerves which are themselves the source of supply—some interruption in their course. Weiss ([14]) has shown that in nerve tissue culture, guidance factors have, or at least can have, an effect in directing regenerating axons. This is ap-

parent *in vivo* in nerves sutured following trauma. The same mechanism may be operative here as a result of inflammation and resultant interstitial fibrosis.

Of course, this does not mean that humoral factors are not also at work, such as nerve growth factor. Such a substance may be similar to the nerve growth factor described by Levi-Montalcini and her co-workers ([4, 6]). The importance of humoral factors in nerve regeneration is now well recognized ([5]). Sperry, following studies of optic nerve regeneration in the adult goldfish, suggests that such a factor "could be utilized for guiding the respective fiber types into their separate proper channels at each of the numerous forks or decision points which they encounter as they make their way back through what essentially amounts to a multiple Y maze of possible pathways" ([11]). Perhaps the guidance of scar tissue is sufficient explanation, but if humoral factors are present, possibly originating in denervated muscle and possibly with "infiltration over a considerable range, perhaps in a gradient fashion" as suggested by Hamburger ([4]), the high prevalence of mis-reinnervation can be more readily understood.

The fact that m. frontalis did not exhibit voluntary co-contraction may be due to a greater degree of destruction of nerve pathways in the upper branches of the facial nerve, although such activity was reported to a limited degree in our earlier series. Anatomical factors and the relative remoteness of the m. frontalis from a relatively healthier source of nerve supply may be important, but as Figure 1 demonstrates mis-reinnervation can occasionally occur over long distances.

Of the lids, the lower lid, with mis-reinnervation even from the m. frontalis and the m. orbicularis oris, seemed to get a better opportunity for partial recovery by the process of mis-reinnervation (Fig. 2). The functional value of this may not be great but it must help a little, particularly as it occurred in all six cases in the lid portion of the m. orbicularis oculi rather than entirely in the pars orbitalis as was the case with the upper lid. And if the pars orbitalis of the lower lid had been explored in all cases, as it was in the upper lid, it is likely that a few more potentials would have been detected.

Teasdall and Salman ([13]) noted in Bell's palsy that misdirection of axons occurs more often from above down than in the reverse direction. In our series, although there was abundant exchange of axons in both directions, the levator labii superioris received the largest number of misdirected axons of the four muscles studied. Most of these were from above and often resulted in blink burst activity. This misdirection of regenerating nerves of the m. orbicularis oculi to the levator labii superioris represents a loss of axons to the important eye closure mechanism.

This downward loss, six blink bursts and two voluntary co-contractions, is numerically balanced (for what that is worth) by upward contributions responsible for eight voluntary co-contractions to the m. orbicularis oculi from the levator labii superioris, four in each lid. But, the exchange is largely that of uncoordinated and inappropriate voluntary activity to replace reflexly coordinated movement appropriate for eye closure. Thus, in the lids the advantage gained by increased activity due to mis-reinnervation in one direction may be lost by the same phenomenon occurring in the opposite direction. In one patient (e.g., patient 330) the benefits of mis-reinnervation may predominate (Table 2). In another, mis-reinnervation may be harmful (e.g., patient 11059). In others the advantages and disadvantages may balance each other off, with axons being simultaneously directed upward and downward.

The prevalence of mis-reinnervation as judged by the presence of either voluntary or reflexly activated abnormal contractions was found to be high: in 35% of patients with facial neuritis and 28% of all facial nerves with clinically apparent paresis or paralysis. Since the source of these contractions has been seen in some cases to be misdirected regenerating axons that normally supply voluntary muscles, they may cause contractions of a few motor units in otherwise paralyzed or partially paralyzed muscles simultaneously with voluntary activity in the muscle which they previously innervated (voluntary co-contractions). Since, alternatively, the source of reinnervation may be nerves which normally induce reflex contraction of the pars palpebralis of the m. orbicularis oculi, contractions in the reinnervated muscle may occur simultaneously with

TABLE 3. *Prevalence of mis-reinnervation. Comparison of this series with earlier series.*

	Vol. co-contr.	Blink bursts	Nerves studied	Nerves affected	Patients studied	Patients affected
Series 1	21	7	27	18 (67%)	22	16 (73%)
Series 2	14	11	29	8 (28%)	17	6 (35%)

blinking (blink bursts). Another type of simultaneous contraction of two muscles has had to be excluded. This is the synergistic activity that occurs on forceful movement, for example, the levator labii superioris contracting on forceful attempts to close the eye. This could lead to a misdiagnosis of voluntary co-contraction. To exclude this possibility all assessments were made with gentle muscle activity only.

The prevalence of mis-reinnervation in this representative survey of all surgical admissions is not as high as in the previous series, which was biased by the preselection of only those cases severe enough to require temporalis transfer, and in which mis-reinnervation was found in 73% of patients (Table 3). The severity of the paralysis in the earlier series also was greater, with 35 of 108 muscles completely paralyzed, as compared with 22 of 116 in this series. There was more mis-reinnervation in the earlier series of more severely affected nerves.

It is of interest to note that the prevalence of facial neuritis in the present series is 2.2% (17 of 770 surgical admissions) and this figure approximates the prevalence of facial neuritis in leprosy patients generally ([8]). Thus, it is tempting to speculate that the prevalence of mis-reinnervation in this series may be to some degree representative of its prevalence on the general patient population. Such speculation is probably not valid and more investigations are warranted.

It would also be of great interest to study the development of mis-reinnervation by repeated examinations of the same patients from a very early point in the development of paralysis to determine how long this phenomenon takes to occur and whether once developed it persists.

SUMMARY

Electromyographic examination of four selected facial muscles was conducted on all patients admitted to the surgical department of the Schieffelin Leprosy Research Sanatorium over a 13 month period, who had clinically evident facial paresis or paralysis. The high preponderance of incomplete patterns in the lower lid and complete paralysis in the upper lid suggest that the neuronal pathways to the lower lid are more receptive both to normal reinnervation and to innervation by misdirected axons. Such mis-reinnervation is common but not necessarily helpful.

RESUMEN

Se hizo un estudio electromiográfico de cuatro músculos faciales preseleccionados a todos los pacientes que fueron admitidos en el departamento quirúrgico del Schieffelin Leprosy Research Sanatorium durante un período de 13 meses, que presentaban clínicamente evidente paresis o parálisis facial. La alta preponderancia de modelos incompletos en el párpado inferior y parálisis completa en el párpado superior sugiere que la vía neuronal hacia el párpado inferior es más receptiva tanto a la re-inervación normal como a la inervación por axones dirigidos erróneamente. Tal re-inervación errónea es común pero no necesariamente provechosa. Sería de gran interés ampliar este tipo de estudio.

RÉSUMÉ

Chez tous les malades admis au département de chirurgie du Schieffelin Leprosy Research Sanatorium, au cours d'une période de 13 mois, et qui présentaient des signes cliniques évidents de parésie ou de paralysie faciale, on a procédé à un examen électromyographique de quatre muscles déterminés du visage. La dominance élevée de profils de paralysie incomplète au niveau de la lèvre inférieure, et de paralysie complète au niveau de la lèvre supérieure, suggère que le tracé que suivent les neurones pour atteindre la lèvre inférieure est plus réceptif à la fois à la réinnervation normale et à l'innervation par des axones égarés. Une telle "mis-réinnervation" est habituelle mais pas nécessairement bénéfique.

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