Structural nerve changes at wrist level in workers exposed to vibration

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Abstract

***Objectives*—To analyse the character of morphological changes occurring in a well defined peripheral nerve in humans exposed to vibration from hand held tools.**

***Methods*—Biopsies of the dorsal interosseus nerve just proximal to the wrist were taken from 10 men exposed to vibration and from 12 male age matched necropsy controls. The nerve was resected for pain relief either as the sole procedure or in conjunction with carpal tunnel release. All specimens were sectioned and examined by light microscopy in standard sections, thin epon sections, and teasing preparations.**

***Results*—The combined results of the analyses showed pathological changes in all 10 patients dominated by breakdown of myelin and by interstitial and perineurial fibrosis. All but one of the 12 controls were normal.**

***Conclusion*—These findings often show severe nerve injury previously not described at this level. They indicate that demyelination may be the primary lesion in neuropathy induced by vibration followed by fibrosis associated with incomplete regeneration or with organisation of oedema. Vibration can induce structural changes in peripheral nerves just proximal to the wrist and such changes may constitute a structural component in carpal tunnel syndrome among people exposed to vibration. This may help to explain the poor results achieved by carpal tunnel release in these patients.**

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Long term use of hand held vibrating tools can induce not only changes in peripheral circulation—such as white fingers—but also sensory disturbances and muscle weakness.[1–6] It has been reported that the impaired sensibility of the hand may be associated with characteristic changes in nerve conduction in the median as well as in the digital nerves.[7–9] The structural basis for these symptoms and signs is not known, but the lesion may be located in the skin receptors, in the nerve fibres along the length of the nerve, or in the nerve cell bodies. There have been reports indicating the possibility of injury at any one of these levels.[7–13] In various animal models structural changes have been reported in both myelinated and non-myelinated nerve fibres after exposure to vibration.[13–16] In finger biopsies from patients with vibration induced white fingers changes in the nerve fibres as well as in the connective tissue components of peripheral nerves have been found.[17–19] No such studies, however, have been done on more proximally located nerves. The aim of our study was to search for structural changes in biopsies of the dorsal interosseus nerve just proximal to the wrist in patients exposed to vibrating hand held tools.

Table 1 Age, exposure time, profession, and tools of patients exposed to vibration

Case	Age (y)	Exposure time (y)	Tools	Profession
1	55	28	Grinder, chipping hammer	Welder
2	54	> 20	Chipping hammer, nut driver, grinder	Plater and welder
3	48	25	Chain saw	Farmer
4	44	19	Nut driver, grinder	Mechanic
5	37	18	Chisel	Plater and welder
6	58	30	Chisel	Shipyard worker
7	53	27	Chisel, chipping hammer	Welder
8	63	30	Chisel, grinder	Welder
9	62	26	Vibrator, chisel, drill	Construction worker
10	41	20	Chain saw	Farmer

Materials and methods

SUBJECTS

Biopsies were taken from the dorsal interosseus nerve 5 cm proximal to the wrist from 10 consecutive male patients with wrist pain who were exposed to vibration (median (range) age 53·5 (37–63) years). All biopsies were taken in connection with partial or total wrist denervations performed as pain relieving procedures either as the sole procedure in Kienböck's disease (one case) or in conjunction with carpal tunnel release (nine cases).[20] Simultaneously other surgical procedures were performed: one distal and one proximal ulnar neurolysis and two tenosynovectomies for de Quervain's disease. The patients had been exposed to various vibrating hand held tools (table 1) for 17–30 (median 25·5) years for one to eight hours daily (median two hours). Eight patients were right handed. Six of the biopsies were taken from the dominant side. None of the patients had diabetes or polyneuropathy nor had they sustained any injuries to the biopsied limb. One patient had cervical radiculopathy.

Twelve consecutive control biopsies from the dorsal interosseous nerve at the same level were taken from male cadavers with no history of neuropathy or trauma (median (range) age 49 (30–72) years). The control biopsies were taken one to six days (median three days) post-mortem.

BIOPSY

The operations were done under regional block or general anaesthesia. The extremity was exsanguinated and a tourniquet was applied to the upper arm. Through a longitudinal dorsal incision immediately proximal to the extensor retinaculum a 2 cm section of the dorsal interosseus nerve was carefully dissected and resected. The specimens were fixed hanging slightly extended by a 1 g weight in 2% glutaraldehyde in 0·1 M cacodylate buffer, pH 7·2, with 0·1 M sucrose for four to six hours at 4°C.

The fixed samples were divided for four different analyses: embeded in paraffin for routine microscopy; as frozen sections; thin transverse sections after being embedded in epon; and as teasing preparations.

The routine material was divided into two pieces, one for cross sectioning and the other one for longitudinal sectioning. Paraffin sections were stained with haematoxylin and eosin, van Gieson, cresyl violet, Sevier-Munger, and Naoumenko for axons, and luxol fast blue for myelin with occasional supplementary stainings—such as periodic acid Schiff (PAS).

The frozen sections were stained for neutral fat using the oil red O (ORO) staining method and for metachromatic material with acid cresyl violet. The thin epon transverse sections, 0·5 μm thick, were stained with toluidine blue.

The specimens for teasing were washed in 0·25 M sucrose in 0·01 M buffer, pH 7·2, for 24 hours in a refrigerator. After five minutes of additional washing in 0·1 M cacodylate buffer the specimens were placed in 1% osmium for 24 hours at room temperature and in darkness. After washing in distilled water the specimens went through graded glycerine solutions starting with 33%, then 66%, and lastly by 100% glycerine, 24 hours in each concentration. Under a dissecting microscope the nerve was teased into bundles of 25–30 axons down to a single axon and mounted in pertex on microscope slides.

Table 2 Pathological changes in the dorsal interosseous nerve just proximal to the wrist in patients exposed to vibration and in necropsy controls

Case	*Light microscopy*	*Thin sections*	*Teasing*
Exposed patients:			
1	+ +	−	+ +
2	+ +	+ +	+ + +
3	+ +	+ +	+
4	+ +	+ +	+
5	+	+	0
6	+ +	+ + +	+ + +
7	+ +	+ +	+
8	0	0	+
9	+	+ + +	+
10	+ +	+ +	+ +
Controls:			
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
6	0	0	0
7	0	0	0
8	+ +	+ +	+ +
9	0	0	0
10	0	0	0
11	0	0	0
12	0	0	0

Normal = 0 = no changes; slight = + = vague changes, a suspicion of pathology; moderate = + + = clear cut changes, but sparse; severe = + + + = clear cut changes, plentiful.

MICROSCOPIC ANALYSIS

All sections were coded and one person (AB) carried out a blind qualitative analysis. The changes looked for were fibrosis, breakdown of myelin, the presence of lipids endoneurally and epineurally or in macrophages, and axonal changes. The thin epon sections were evaluated with a light microscope for pathological changes—such as loss of fibres, abnormal distribution pattern of fibres, interstitial fibrosis, and perineurial thickening. Changes looked for in the teasing preparations were digestion chambers and an increase in pale or thin myelin sheaths. The changes found were classified on a four degree scale as none, slight, moderate, or severe. Ultrastructural analysis was not done as the control material was taken at necropsy thus excluding a reliable comparison due to autolytic changes.

Results

There was no difference in age between the patients exposed to vibration and the controls ($P = 0·64$, Mann-Whitney U test). The specimens from all the patients exposed to vibration showed some degree of pathology.

ROUTINE LIGHT MICROSCOPY

Patients exposed to vibration

In nine of the patients exposed to vibration there were pathological changes on light microscopy (table 2). In two cases, the changes were slight and in seven cases they were moderately severe. A general finding was endoneurial fibrosis of varying degree appearing in these nine cases. Lipid deposition and loss of myelin with a reduced number of myelin sheaths as signs of myelin breakdown were seen in six cases, one of which had discernible digestion chambers. There were no signs of an inflammatory reaction and few macrophages. A loss of axons could be shown in some cases although the extent of this loss was somewhat uncertain due to the inherent inconsistency of the silver methods. Vessels appeared unremarkable.

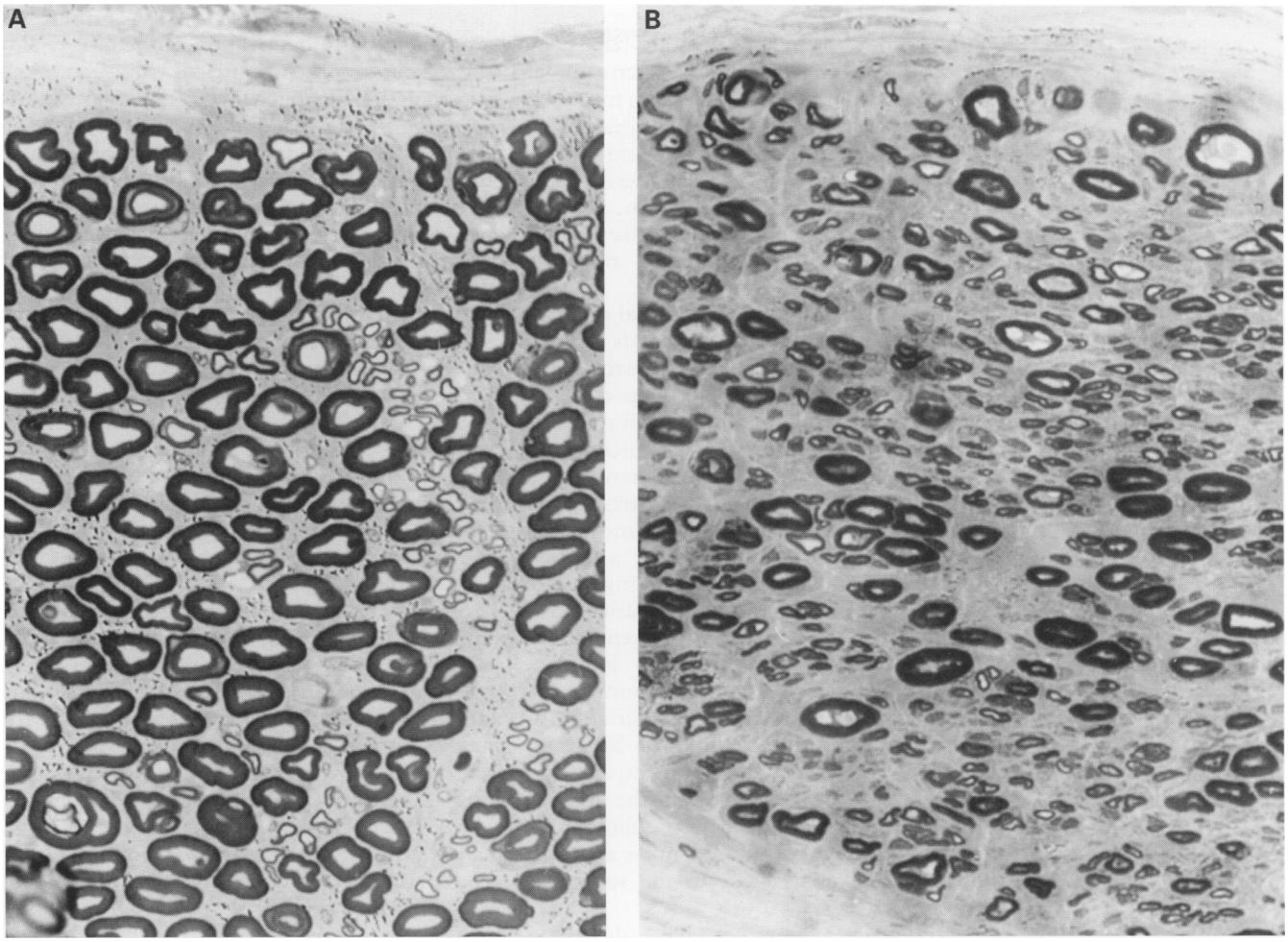
Control patients

In the control material there were no changes except for one case showing obvious pathology with a slight increase in the number of fibrocytes, a moderate degree of endoneurial fibrosis, and a slight to moderate loss of myelin sheaths. Some of the remaining sheaths had a granular structure. Neither inflammatory changes nor abnormal lipid were found. The man had been a farmer. Further examination of his medical history showed that he had had Raynaud's phenomenon of the hands requiring medication with topical vasodilators and with calcium blockers.

THIN EPON SECTIONS

Patients exposed to vibration

The changes were slight in one patient, moderate in five, and severe in two. One patient had a normal finding. In one case the analysis could not be performed due to insufficient material. The myelin sheaths were diminished in thick-



Dorsal interosseous nerve: transverse section 0·5 μm thick in epon, stained with toluidine blue, showing myelin sheaths as dark structures encircling the axons. In a normal nerve (A), the sheaths are regularly sized and distributed. In a nerve from a man exposed to vibration (B), only a few of the myelin sheaths are of normal size and many are small and irregularly distributed in a dense matrix of reactive connective tissue (case 2). Originally × 70.

ness and diameter and reduced in number and showed an abnormal uneven distribution pattern. The matrix was fibrous and abundant and the endoneurium and the perineurium showed an increase in collagen (figure). The results were in good agreement with those of the other analyses. The patient with no changes also had normal routine light microscopic findings, but pathology on teasing, whereas the patient with slight changes had a normal finding on the teased preparation.

Control patients

The controls were normal again, with the exception of the case which had appeared as an instance of unexpected pathology.

TEASING

Patients exposed to vibration

The changes seen on teasing were slight in five patients, moderate in two, and severe in two. One patient had no changes (table 2). In most cases there were nerve fibres of varying thickness and staining intensity and fibrosis. Occasional pale or empty sheaths were seen. In three cases (2, 6, and 10) the pathology was more severe with digestion chambers, uneven osmium staining, variation in myelin sheath thickness, and pale sheaths. Combinations of demyelination in various stages of development and fibrosis were seen in four cases.

Thus there were cases of ongoing demyelination, late or end stage demyelination, and combinations of both indicating a pathological process covering an extended period.

All four patients with moderate to severe changes on teasing had associated fibrosis of the endoneurium on light microscopy. Three of them had fibrosis of the perineurium or epineurium as well. The fourth had cellular infiltration probably reactive to extensive demyelination. In the five cases with slight changes on teasing the picture was that of a late or end stage injury. However, the teasing technique contains a bias toward less severe changes. In the more advanced cases of demyelination poor or no staining of the nerve fibres and adhesiveness of the tissues make identification of damaged nerve fibres difficult.

Control patients

There were no changes in the control material except for one case in which teasing showed clear cut pathology with pale segments and a few fibres with digestion chambers. This was again the same case in which pathological findings were shown with the other methods.

Discussion

Few reports have been published on the histological changes caused by vibration to the

hands. Most of these papers report on the vascular pathology. The changes found have been an increase of collagen in the perivascular spaces, hypertrophy or fibrosis of the muscular layer, and some intimal or subintimal fibrosis.[17 19 21-25] In experiments on rats and rabbits on the other hand, the intima has been considerably thickened by cell infiltration and the formation of collagen and elastic fibres, whereas the media has remained relatively unaffected.[26 27]

In humans, reports on histological changes in the peripheral nerves in the hands of men exposed to vibration have been scarce. In a single necropsy case Walton[24] reported on degeneration and perineurial infiltration by small round cells affecting the superficial cutaneous plexus and the branches extending to the dermal papillae. The main trunks of the digital nerves were normal. Hashimoto and Craig[25] described the findings in a punch biopsy taken from a finger tip in a single case. They found perineurial and endoneurial fibrosis, demyelination, and axonal degeneration. In finger biopsies of unspecified location, Takeuchi *et al*,[17 18] found demyelination, loss of axons, thick perineurial and endoneurial fibrosis, and an increased number of Schwann cells. They noted that the loss of myelin was more frequent and severe than the loss of axons, which is consistent with the findings in the present study. The tissue samples analysed originated from areas close to the source of vibration.

Several articles, however, have described changes in animal nerves exposed to vibration. Demyelination and degeneration of axons have been found in rabbits by Karpova[14] and by Ho and Yu[16] and in rats by Chang *et al*.[28] Ho and Yu noted that demyelination occurred earlier and was more severe than was loss of axons, which is consistent with findings in our study and other human studies.[17 18] Transient morphological changes have also been found by Lundborg *et al*[13] in non-myelinated nerve fibres of the rat plantar nerves. Experimental studies indicate that both nerve fibres and non-neuronal cells such as Schwann cells are affected by exposure to vibration leading to functional changes in the peripheral nerves.[29-31] In acutely exposed animals vibration can also induce oedema,[32] which, considered together with the morphological changes described, particularly demyelination, makes it attractive to assume that prolonged vibration may lead to fibrosis of peripheral nerves associated with an incomplete regenerative process, with organisation of oedema, or with both. Such fibrosis of peripheral nerves in humans exposed to vibration has been shown not only in distal biopsies of fingers,[17 18 25] but now also in a more proximally located nerve—that is, the dorsal interosseous nerve—in the present study.

Thus, vibration causes nerve damage, but to what extent and at what anatomical levels still remains to be clarified. The situation under which the worker is exposed to vibration is very different from the experimental set up. All histological studies done on arteries and nerves in humans differ from those done on animals in both the location of the biopsy and the duration of exposure to vibration. Any extrapolation of the results of animal experiments to human conditions must therefore be done with great caution. In humans, apart from Walton's necropsy case, only digital punch biopsies or skin biopsies of unspecified nerves have been taken.[17 18 25] In contrast, the present study deals with changes in a well defined peripheral nerve just proximal to the wrist in men with a history of long term exposure to hand held vibrating tools. The findings of demyelination and fibrosis in our study agree well with other studies, both in humans and animals, suggesting that demyelination may be the primary lesion in vibration induced nerve injury. To our knowledge such findings have previously not been reported in such a nerve nor in a location so far removed from the vibrating source.

Pathophysiologically, carpal tunnel syndrome is characterised by locally impaired intraneural microcirculation and—in more advanced cases—demyelination due to external compression of the median nerve.[33] In our study the findings are those of an often severe nerve injury in a well defined nerve just proximal to the wrist in men exposed to vibration. As pathology in men exposed to vibration has been shown distal as well as proximal to the carpal tunnel, there is reason to think that such pathology may occur in the carpal tunnel as well.[17 18 24 25] In fact, changes to the median nerve in the carpal tunnel are likely to be even more severe: further trauma may be added to the nerve from repetitive motions and strenuous manual work and the nerve lies closer to the vibrating source than does the dorsal interosseous nerve. The findings in our study indicate the possibility of two pathophysiological mechanisms in carpal tunnel syndrome among men exposed to vibration, one being nerve compression, the other being changes introduced by vibration. This may help to explain the poor results achieved by carpal tunnel release in this group of patients.[34 35]

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